Infusion therapy standards

Rapid evidence review

Acknowledgements

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Executive summary

This report summarises the rapid review of evidence undertaken to support development of updated RCN *Standards for Infusion Therapy*. A rapid evidence assessment (REA) methodological approach selected in order to produce robust results through a systematic search, within the time and resource constraints imposed by the scope of the project. The evidence review was a collaborative project, managed and conducted by the RCN Research and Innovation (Evidence), Library and professional practice teams, as well as an RCN contractor (Bazian).

Two overarching questions guided the review:

1. What is the latest evidence that can be used to update the previous iteration of the infusion therapy standards?
2. What are the facilitators and barriers perceived by patients receiving a range of infusion therapies?

While the RCN *Standards for Infusion Therapy* cover a wide cross-speciality area, the focus of this review was to provide evidence on practice that is relevant to the management of infusion therapy by nurses in a variety of settings, and is linked with clinical effectiveness and patient safety outcomes.

The review sought evidence from the delivery of infusion therapy in in a variety of settings including acute, community and rural settings, as well as self-administration by patients and carers.

The review included 104 studies that addressed the clinical elements of infusion therapy and 22 studies that concerned specifically the patient perspective:

- the area which received the most research attention is infusion-related bloodstream infections
- arterial catheters and subcutaneous infusions produced the lowest volume of literature in the review of clinical evidence
- in the patient perspectives review the evidence was heavily biased towards experiences of dialysis treatment, with a lack of studies conducted in other settings.

In terms of the evidence retrieved, the studies were heterogeneous in nature, making it difficult to combine results to produce robust conclusions. In addition, the volume of research in some areas was very low. However, by synthesising the results of all of the reviews, a picture begins to emerge of where there is strong evidence available and where there is a need for further research or professional consensus.

The findings of the review of clinical literature add to the evidence base in many areas of infusion therapy:

- a large volume of evidence suggests that there is no difference between flushing or locking central venous catheters with heparin or normal saline, however locking with an antimicrobial solution has been linked with decreased infection rates
- in addition, routine replacement of catheters does not appear to result in fewer infections compared with replacement on clinical indication
- chlorhexidine and silver have been demonstrated to be effective antimicrobial agents in a number of contexts including coating of catheters, connector devices and dressings, as well as skin preparation and daily chlorhexidine gluconate bathing of patients
- the evidence also reinforces the effectiveness of evidence-based pre- and post-insertion care bundles for the reduction of catheter-associated bloodstream infections
- there is evidence to suggest that obtaining blood samples from intravenous devices can achieve similar results to those obtained via venepuncture; this is important as the patient perspective review found that patients often find the experience of venepuncture painful and distressing
- sampling from IV ports may not be appropriate however, when testing venous blood gases or anticoagulation parameters.

The patient perspectives study offers useful information about patients' experiences of receiving infusion therapy both in acute and non-acute settings. The studies reviewed provide evidence that in many situations, patients prefer to receive infusion therapy at home or in the community. However, several barriers are identified and it is clear that moving towards increased treatment in the non-acute setting will have considerable implications for resource planning and management, and nursing workload management.

There remain gaps in the literature in many areas, particularly in relation to infusion therapy outside the acute hospital setting. Future research must address these gaps, including the identification of patient and carer needs, as well as ensuring nurses are equipped to manage their increased workload, if infusion therapy is to be successfully delivered in a wider variety of settings.

Section 1: Introduction and methodology

Contents

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Introduction

This report has been produced to support development of an update to the RCN *Standards for Infusion Therapy*, published in 2010. To ensure this update to the standards are evidence informed, an evidence review was commissioned. This report presents the process and findings of this evidence review and comprises: an introductory section containing the background and methodology of the review; three sections detailing the selection, quality assessment and synthesis of the evidence from a clinical and patient perspective; and a concluding section which assesses the findings and implications.

Background

The RCN *Standards for Infusion Therapy* (2010)[1] has proved a popular document and is referenced in numerous publications nationally as an exemplar of best practice. A decision was taken to update the 2010 standards following discussions with stakeholders. Infusion therapy has historically been associated with hospital care but, due to increasing demands, it is now delivered in a variety of settings including community and rural settings, as well as self-administration by patients and carers. In light of this changing health care landscape, there is a need to provide standards for infusion therapy that acknowledge and support the delivery of infusion therapy in different settings, whilst also acknowledging the impact on service provision, nurse workload and patient needs. The updated version explicitly refers to practice settings outside of secondary care and, as such, is relevant across the various settings where infusion therapy is delivered across the UK.

The expert steering board that was set up to manage the RCN standards update under the auspices of the RCN, commissioned the RCN to conduct an evidence review to underpin the development of the revised standards. The project was partly supported by funding from industry sponsors. To accommodate time and resource constraints, the review was underpinned by a robust methodology of rapid evidence assessment (REA). REA is an established research methodology which can be described as a compromise between the requirements of a systematic review and the need to deliver results within a constrained time period[2].

The evidence review was a collaborative project managed and conducted by the RCN Research and Innovation (Evidence) Library and professional practice teams, as well as an RCN contractor (Bazian).

Aims and objectives

The aim of this project was to support the update of the RCN's *Standards for Infusion Therapy* (2010) and placed an explicit focus on all settings where infusion therapy is delivered. The objectives of the project were to identify areas with robust/promising/no evidence, and evidence identifying harmful practice. The project included evidence on the patient perspective of infusion therapy which the authors felt was timely and appropriate in the current health climate. Whilst the purpose of the review was primarily to feed into the infusion standards writing, assessment of the evidence volume, relevance and quality was expected to allow for gaps to be identified in a systematic way and for the identification of areas where professional consensus is required.

Research questions

Two overarching questions guided the review:

1. What is the latest evidence that can be used to update the previous iteration of the standards for infusion therapy?
2. What are the facilitators and barriers perceived by patients receiving a range of infusion therapies?

In addition to the main research question of identifying evidence about infusion therapy that relates to nursing practice and is linked with clinical effectiveness and patient safety outcomes, a number of specific points of research interest were identified as the review process was established and experience with the specific body of evidence progressed. These questions related to various aspects of infusion therapy in line with the 12 areas which comprised the review (Table 2); however, not all of the areas had specific research questions.

Scope

It was important to ensure that the scope of the literature search and review was tightly defined in order to allow for a robust outcome. The following points outline the approach taken:

- the scope of the review was to identify evidence on infusion therapy devices and procedures that are linked to outcomes of safety and effectiveness and are within the realm of nursing practice and responsibility
- there was a particular emphasis on the management of the devices rather than the decision on which to select; management decisions and practices made by health care workers relating to infusion therapy that affect nursing practice were also included
- any practice setting was included – acute and community care, as well as self-management by patient/carer; the standards that the review supported were developed so as to be relevant across all UK care settings
- the new standards will not duplicate existing infusion therapy guidance from other organisations; the new standards will complement, add value and demonstrate relative advantage with respect to existing guidance.

In line with the last point above, a classification scheme of the content of the standards, as agreed by the steering group, was developed in order to structure evidence needs (see Table 1). The current review was focussed on areas one and four in Table

1, whereby evidence was sought in areas of infusion therapy that were nursing specific and where no guidelines existed; and in areas that described the context of the therapy delivery.

Table 1: Content classification scheme used to structure evidence needs
1. Nursing-specific practice/no guidelines and/or primary evidence required
2. Nursing-specific practice/guidelines exist
3. Non-nursing-specific practice/guidelines exist from other professions
4. Contextual factors (education, commissioning, patient perspective)

There were 12 nursing-specific areas of practice that were agreed as requiring primary evidence and thus formed the focus of the clinical aspect of this evidence review (see Table 2).

Table 2: 12 areas of infusion therapy care and management included in the evidence review
Add on devices
Arterial catheters
Blood sampling
Central venous access devices
Flow control devices
Infusion-related bloodstream infection
Infusion therapy phlebitis
Intraosseous access devices
Midline catheters
Parenteral nutrition
Peripheral access devices and flushing
Subcutaneous infusions

Search strategy

The search strategy was designed and executed by the RCN Library. Three key bibliographic databases (British Nursing Index, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and MEDLINE) were selected on the basis of their relevance to nursing research and the fact that they were immediately and freely available. Searches were trialled on these databases during June 2015 to establish appropriate search terms. The general inclusion criteria were agreed with members of the steering board and are detailed below (Table 3).

Table 3: Inclusion criteria	
Publication date	2010 onwards
Geographical scope	UK and OECD countries
Age range	Older adolescents and adults (exclude neonates, infants and children)
Language	English language
Study type	RCTs, systematic reviews, meta-analyses and cohort studies

All three databases were searched during August 2015 using the agreed search strategy. Each of the twelve[i] topics in question were combined with a generic infusion therapy set (where appropriate) and then with each of three additional sets of terms (research designs; standards; complications and adverse events), producing three sets of results per database for each topic. The detailed search strategy and process can be found in Appendix A at the close of this section. The focus of the search was on primary studies of experimental designs and systematic reviews. In addition, searches were conducted on existing published standards or guidelines to ensure coverage of good or accepted practice.

Sifting

Following the searches, all references were initially sifted for relevance. This was followed by a two-phase review of the clinical evidence.

Phase 1 – Randomised controlled trial (RCT) and Systematic review (SR) evidence

Phase 1 involved a sift on the basis of design, including only RCTs and SRs and removal of duplicates. The remaining studies were assessed against the predetermined inclusion and exclusion criteria. Full text versions of studies which met all inclusion criteria – or where a decision could not be made based on title and abstract – were obtained where available, and were further assessed for inclusion based on the inclusion and exclusion criteria. The sponsors also provided a number of references, of which four studies were included, resulting in 56 studies being assessed in Phase 1 of the review. The sifting process is presented in Figure 1 and the full study is detailed in Section 2 of this document.

Phase 2 – Non-RCT and SR evidence

In October 2015, a further sift was undertaken to identify any potentially relevant evidence which was originally rejected on the basis of study design. In this phase, RCTs and SRs were removed from the original list of 315 included papers, and the remaining references assessed against the inclusion and exclusion criteria (with the exception that all quantitative research designs were considered), producing 167 studies to be assessed during the second phase of the REA. A similar sifting process was conducted to that discussed above, providing a further 48 studies to be appraised in this phase of the review. Figure 1 presents the sifting process and Section 3 of this document contains details of the full study.

Additional search: patient experiences

An additional literature review to locate references relating to the patient experience of infusion therapy was carried out during September and October 2015. The databases searched were British Nursing Index, CINAHL and MEDLINE and the inclusion criteria were the same as those identified in the standards infusion review, with the exception of the research design limitation which was not applied.

Searches were trialled in early September in order to establish appropriate terms for the patient experience element of the search, and to reflect differences in database structure and vocabulary. In addition, supplementary terms were identified from the *Warwick Patient Experiences Framework* (WaPEF)[3]; these were included in the search terms and were combined with the infusion set terms

i Searches were initially conducted for 13 topics, splitting 'parenteral nutrition' into two (infusion equipment and total parenteral nutrition) to make the process more manageable; the results of the two searches were later combined and all the analysis was structured around 12 topics.

from the clinical review to produce an overall picture of patient views.

In addition, the following areas were also investigated using the patient experiences sets, which resulted in a total of six lists of references on patient experiences for each database:

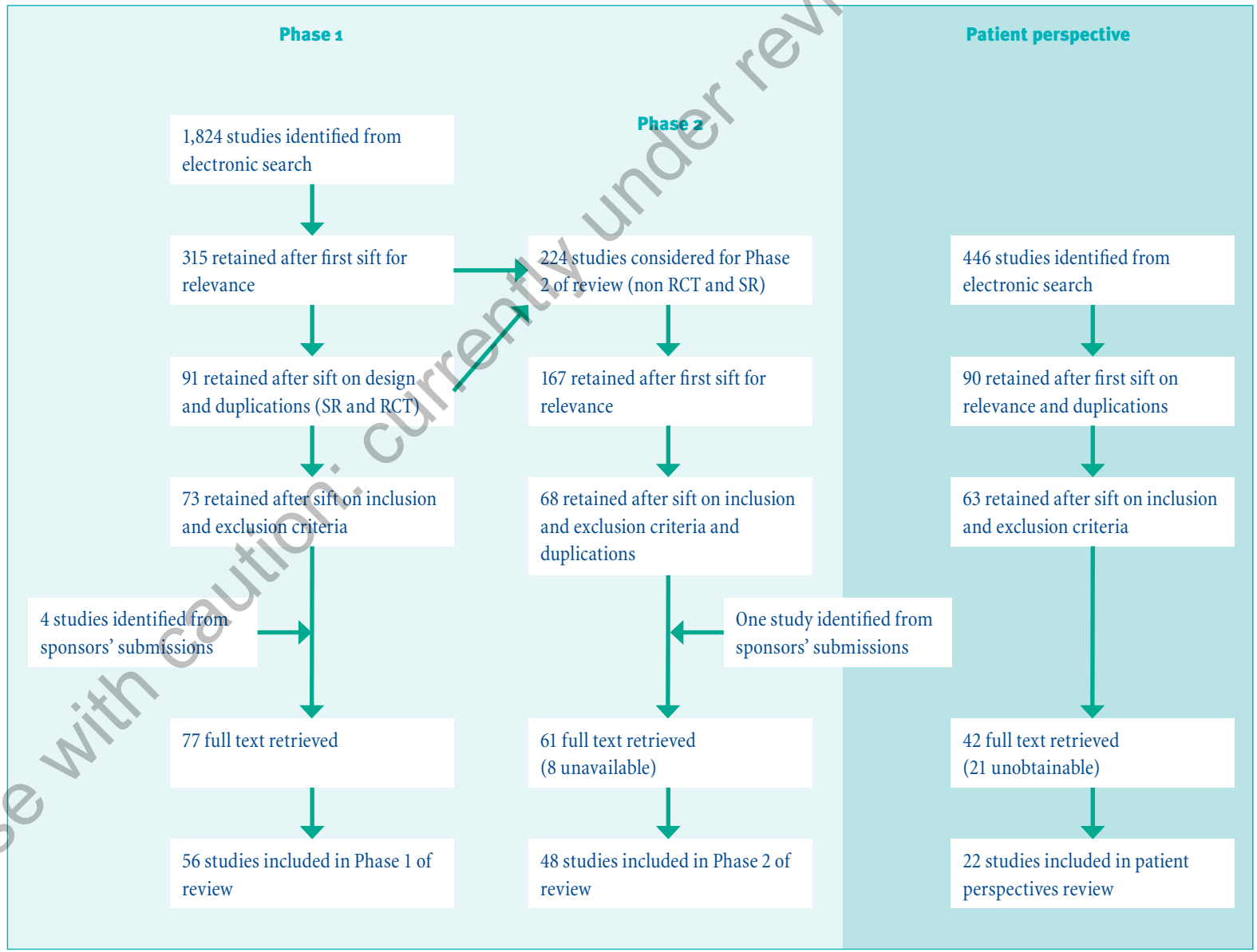
- parenteral nutrition
- chemotherapy infusions (intrathecal and intravenous)
- insulin
- blood transfusions
- renal infusions (dialysis).

The sifting process is presented in Figure 1 and the full study is detailed in Section 4.

Quality appraisal and data extraction

Critical appraisal of clinical evidence is a technical procedure that follows generally agreed principles[4]. Appropriate tools were selected during each review based on the research papers being appraised. Details of quality appraisal and data extraction procedures are provided in each individual report. The evidence identified in Phase 1 of the process was reviewed and the report was produced by an information specialist, operating in an outsourced contract under the auspices of the RCN. The evidence review for Phase 2 and the patient perspective was conducted directly by the RCN.

Figure 1: Study selection procedure for all phases of review



Data mapping and synthesis

During each phase of the review, relevant evidence was mapped to provide an overall picture of the available evidence in each area. Results were then synthesised in order to produce an assessment of the strength and volume of evidence relating to each area.

Three reports have been produced in relation to the three separate searches and analyses carried out in-house and externally (RCT and SR evidence; other quantitative evidence; patient perspective). The final section synthesises all of the evidence and offers an indication of where the volume and strength of the evidence is higher and identifies were gaps exist.

References

1. Royal College of Nursing (2010) *Standards for Infusion Therapy*, London: RCN.

2. Thomas J, Newman M and Oliver S (2013) Rapid evidence assessments of research to inform social policy: taking stock and moving forward, *Evidence and Policy*, 9(1), pp.5-27.

3. Staniszewska S, Boardman F, Gunn L, Roberts J, Clay D, Seers K, Brett J, Avital L, Bullock I and O'Flynn N (2014) The Warwick Patient Experiences Framework: patient-based evidence in clinical guidelines, *International Journal for Quality in Health Care*, 26(2), pp.151-157.

4. Greenhalgh T (1997) How to read a paper: getting your bearings (deciding what the paper is about), *British Medical Journal*, 315(7102), pp.243-246.

Appendix A

Detailed search strategy

The general inclusion criteria are detailed below.

Inclusion criteria:

Publication date:
Work published from 2010 onwards

Geographical scope:
UK and OECD countries (members of the Organisation for Economic Co-operation and Development, an intergovernmental economic organisation with 35 member states)

Age range:
Older adolescents and adults (exclude neonates, infants, and children)

Language:
English language

Study type:
RCTs, systematic reviews, meta-analyses and cohort studies

The British Nursing Index, CINAHL and MEDLINE were searched during August 2015 using the search strategy agreed in advance.

British Nursing Index

The British Nursing Index (BNI) is a leading UK nursing database providing bibliographic references to journal articles from all the major British nursing and midwifery journals, as well as a selection of English-language international journals. It includes selective content from medical, allied health and management titles. The database is updated monthly, and for core UK nursing and midwifery it is the most up-to-date resource available.

Cumulative Index to Nursing and Allied Health Literature (CINAHL Plus)

CINAHL Plus provides bibliographic references to journal articles from hundreds of nursing and allied health journals from the UK, USA and other countries, dating back to 1960. Topics covered include nursing, biomedicine, health sciences librarianship, alternative/complementary medicine, consumer health and 17 allied health disciplines.

MEDLINE

MEDLINE® is the US National Library of Medicine's bibliographic database and indexes the latest articles from more than 3,900 biomedical journals published in more than 70 countries.

The subject scope of MEDLINE is biomedicine and health, broadly defined to encompass those areas of the life sciences, behavioural sciences, chemical sciences, and bioengineering needed by health professionals and others engaged in basic research and clinical care, public health, health policy development, or related educational activities. MEDLINE also covers life sciences vital to biomedical practitioners, researchers, and educators, including aspects of biology, environmental science, marine biology, plant and animal science as well as biophysics and chemistry. Journal articles are covered from 1946 to the present.

Topics searched

The content of the standards was specified by the RCN Infusion Therapy Standards Project Board and the need for evidence was identified in the following 13 areas:

- infusion equipment – add on devices
- infusion equipment – flow control devices
- infusion equipment – parenteral nutrition
- peripheral access devices
- management of midline catheters
- management of central venous access devices
- management of arterial catheters
- intraosseous access
- subcutaneous injection (hypodermocylsis)
- parenteral nutrition – total parenteral nutrition, home parenteral nutrition and infection control
- blood sampling
- phlebitis
- infusion-related blood stream infections.

The topics in question were combined with the infusion therapy set (where appropriate) and then with each of the other sets of terms (research designs; standards; complications and adverse events), producing three sets of results per database for each topic. The precise search strategies used with each of the bibliographic databases are specified below; the search strategy for each database reflects the differences in database structure and vocabulary.

Search strategy: BNI

Research designs were picked up by the following set of terms:

("random* control* trial*" or "quantitative research" or "systematic review*" or "clinical trial*" or "evidence review*" or "cohort stud*" or "case-control*" or "meta-analysis" or research).

Standards, guidelines, protocols, competencies and best/recommended practice were picked up by the following set of terms:

(su(standards and guidelines) or recommendations or "recommended practice" or "best practice" or benchmarking or protocol* or legislation or competenc* or "clinical effectiveness" or su(quality assurance)).

Complications, patient safety, adverse events, clinical errors or substandard practice were picked up by the following set of terms:

("patient* safety" or su(occupational health and safety) or "adverse effect*" or "adverse

event*" or "critical incident*" or "human error*" or complication* or malpractice or "clinical error*" or "bad practice" or "poor practice" or "substandard care").

Methods of infusion and intravenous therapy were picked up by the following set of terms although these sometimes overlapped with the 13 individual search topics (listed below) so were not always required:

"infusion therap*" or su(intravenous therapy) or "infusion pump*" or "peripheral access" or "central access" or central venous" or midline* or picc* or "vascular access" or parenteral or subcutaneous*.

Search strategy: CINAHL

Research designs set:

("random* control* trial*" or "quantitative research" or "systematic review*" or "clinical trial*" or "evidence review*" or MH"Prospective Studies+" or MH"Case Control Studies+" or "meta-analysis" or research).

Standards set:

(MM"Practice Guidelines" or standards or recommendations or "recommended practice" or "best practice" or MM"Benchmarking" or MM"Nursing Protocols" or MM"Protocols" or MH"Legislation+" or competen* or MM"Clinical Effectiveness" or MH"Quality Assurance+").

Complications/adverse events set :

(MH"Patient Safety+" or MM"Occupational Safety" or MH"Adverse Drug Event+" or MH"Adverse Health Care Event+" or "critical incident*" or MM"Human Error" or MH"Catheter-Related Complications+" or MM"Malpractice" or MH"Health Care Errors+").

Infusion therapy set:

("infusion therap*" or MH"Intravenous Therapy+" or "infusion pump*" or MH"Infusion Devices+" or MM"Peripherally Inserted Central Catheters" or MM"Catheterization,Peripheral Central Venous" or MH"Vascular Access Devices+" or MH"Catheterization,Central Venous+" or MH"Central Venous Catheters+" or MM"Catheter Care,Peripherally Inserted Central" or MH"Infusions,Parenteral+" or MH"Infusions,Subcutaneous+").

Search strategy: MEDLINE

Research designs set:

("random* control* trial*" or "quantitative research" or "systematic review*" or "clinical trial*" or "evidence review*" or "cohort studies*" or "case-control stud*" or "meta-analysis" or research).

Standards set:

("guidelines" or recommendation* or "recommended practice*" or MH"Benchmarking" or MH"Clinical Protocols" or MH"Clinical Competence" or "legislation" or "clinical effectiveness" or MH"Quality Assurance, Health Care").

Complications/adverse events set :

(MH"Patient Safety+" or MH"Occupational health" or MH"Drug-Related Side Effects and Adverse Reactions" or "adverse event*" or "critical incident*" or MH"Malpractice" or MH"Medical Errors").

Infusion therapy set:

("infusion therap*" or "intravenous therap*" or MH"infusion pumps" or "peripheral access" or "central access" or midline* or "picc line* or "vascular access" or MH"Infusions,Parenteral").

Example topic

For example the topic Infusion equipment – add on devices had the following search terms applied to all databases:

"traffic light*" or taps or "extension set*" or "stop cock*" or cap or caps or connector* or "needle free" or savy or "bio connector*" or "add on device*" or "add on equipment*",

Which when combined with the various headings produced the following results.

	Research headings	Standards headings	Patient safety headings	Total (duplicates removed)
BNI	3	3	6	9
CINAHL	18	19	28	35
MEDLINE	4	4	6	12

First sift of references retrieved

Once the searches had been carried out on all the databases, using the search strategies above for the 13 topics, the references were sifted to pick out systematic reviews, meta-analyses, RCTs and cohort studies from OECD countries only. The number of references retrieved and subsequently identified by the first sift are indicated in the table on the next page.

Topic	Medline: Results	Medline: 1st sift	CINAHL: Results	CINAHL: 1st sift	BNI: Results	BNI: 1st sift
Add on devices	12	2	35	6	9	4
Flow control devices	41	4	31	4	14	4
Parental nutrition – infusion equipment	12	4	93	32	13	9
Peripheral access devices	7	1	8	4	41	10
Midline catheters	7	3	16	3	13	5
Central venous access devices	107	24	115	16	169	14
Arterial catheters	139	3	73	6	25	3
Intraosseous access	16	6	29	5	6	2
Subcutaneous injections	66	5	43	9	28	2
Parenteral nutrition – total parenteral nutrition, home PN and infection control aspects	128	23	93	19	89	5
Blood sampling	24	2	47	8	13	4
Phlebitis	26	16	25	3	23	6
Blood stream infections	38	7	120	26	30	6
Total (per database)	623	100	728	141	473	74
Total (initial results)	1824					
Total (first sift)	315					

Please note: for the Peripheral access devices search it was necessary to limit the CINAHL and MEDLINE searches to cleaning and flushing aspects only due to the large number of original references, hence – unusually – the BNI located more results for this topic.

Additional search – patient experiences

An additional literature review to locate references relating to the patient experience of infusion therapy was carried out during September and October 2015. The databases searched were BNI, CINAHL and MEDLINE and the inclusion criteria were the same as in the standards infusion review, with the exception of the research design limitation which was not applied.

Searches were trialled in early September in order to establish appropriate terms for the patient experience element of the search, and to reflect differences in database structure and vocabulary. Also the appendix of the Warwick Patient Experiences Framework, as outlined in Staniszewska and colleagues (2014)[3], was checked for any supplementary terms.

The search terms used to capture patient experiences within each of the databases were as follows.

Search strategy BNI:

"patient needs" or "patient experience*" or "patient satisfaction" or su(patients: empowerment) or su(nurse patient relations) or su(consumer satisfaction) or su(patients: attitudes and perceptions) or "patient* preference*" or user* preference*" or "carer* preference*" or "patient* expectation*" or "user* expectation*" or "carer* expectation*".

Search strategy CINAHL:

"patient needs" or "patient experience*" or "patient empowerment" or MM"Patient Attitudes" or MM"Patient Satisfaction" or MM"Consumer Satisfaction" or MM"Nurse-Patient Relations") or "patient* preference*" or user* preference*" or "carer* preference*" or "patient* expectation*" or "user* expectation*" or "carer* expectation*".

Search strategy MEDLINE:

"patient needs" or "patient experience*" or "patient attitudes" or MH"Patient Satisfaction" or MM"Consumer Behavior" or MM"Nurse-Patient Relations" or MH"Patient Participation" or "patient* preference*" or user* preference*" or "carer* preference*" or "patient* expectation*" or "user* expectation*" or "carer* expectation*".

These were combined with the infusion set terms from the infusions standards review to produce an overall picture of patient views.

In addition, the following areas were also investigated using the patient experiences sets:

- parenteral nutrition
- chemotherapy infusions (intrathecal and intravenous)
- insulin
- blood transfusions
- renal infusions (dialysis).

This produced a total of six lists of references on patient experiences for each database.

Section 2: Phase one of the evidence review (clinical practice)

Contents

Section 2 authors – Bazian Ltd

Bazian

Executive summary

This is a rapid review and appraisal of the latest evidence on infusion therapy to enable the Royal College of Nursing (RCN) to update their *Standards for Infusion Therapy* published in 2010. These standards contain advice and guidance to help nursing staff and other professionals involved in the delivery and management of infusion therapy. They cover a wide cross-specialty area, though the focus of this review is on evidence relevant for the management of infusion therapy by nurses. This evidence document is part of multiple strands of work feeding into an update of the standards; the other strands include:

- consideration of the body of evidence from other study designs
- consideration of relevant related guidelines from other professional bodies
- obtaining expert opinion.

The scope for this rapid evidence review is summarised in Table 1. It focuses on systematic reviews (SRs) and randomised controlled trials (RCTs) published since 2010, to identify the highest quality evidence available in the areas covered by the standards. Studies were identified in database searches carried out by the RCN, and these studies were assessed for relevance against the scope of the review. One additional relevant Cochrane systematic review was identified during the preparation of the report and this has also been included.

Overall the report includes 21 SRs, (eight high quality, eight medium quality and five low quality) and 36 RCTs (14 high quality, seven medium quality and 15 low quality). Table 2 provides a brief summary of the main results and gaps in the evidence. In general:

- there were many gaps in the evidence – where a question of interest for the standards was not covered by any of the studies identified
- the body of evidence was quite disparate – with individual RCTs largely addressing different questions, limiting the conclusions which can be drawn.
- though most of the SRs were of moderate to high quality according to their methodology, the actual number, quality and type of studies included in these reviews was very variable, with most including only small low quality observational studies
- most high quality RCTs identified were conducted on intensive care units (ICUs) and so little evidence addressed the basic management of infusions outside of these settings
- few studies covered the basic management of infusion devices by nurses, for example, different flushing frequencies, when to change add-on devices, or different infusion site management techniques
- patient safety was often not covered by the included studies.

As only the SRs and RCTs were considered in this review, additional relevant information is likely to be contained in other study designs, guidelines and expert opinion. The results of this review of evidence published since 2010 need to be considered in the context of the existing infusion standards document.

Table 1: Project scope

Scope	Inclusions	Exclusions
Population	• Adults and adolescents receiving infusion therapy	• Children
Intervention	• Management, decisions and practices made by health care workers relating to infusion therapy, that may affect nursing practice • Aspects of infusion therapy covered by current standards • Education and training • Infection control and safety compliance • Products and documentation • Infusion equipment • Site selection and placement • Site care and maintenance • Specific devices • Infusion therapies • Infusion-related complications	• Interventions that are condition/ disorder specific and not relevant to generic infusion management practice
Comparator	• Any (within scope of current standards)	• None
Outcome	• Safety outcomes • Effectiveness outcomes	• Cost effectiveness
Study designs	• Systematic reviews (SRs • Randomised controlled trials (RCTs)	• Other primary study types • Secondary analyses of RCTs • Non-systematic reviews • Guidelines
Other parameters	• Published between 2010 and 2015 • English language publications	• Published before 2010 • Non-English language • SRs focusing only on countries or settings that were clearly not relevant to the UK setting (for example, developing countries)

Methods

The RCN provided Bazian with the results of a search for relevant systematic reviews (SRs) and randomised controlled trials (RCTs) grouped according to 12 proposed sections of the RCN update of its 2010 *Standards for Infusion Therapy* publication. This comprised 93 studies of which there were two duplicate results. Following a second sift at title and abstract level by Bazian, 73 of these 91 studies appeared to meet the inclusion criteria according to the scope of the project and were obtained in full text for further appraisal. The RCN also provided a list of 20 articles submitted by infusion device manufacturers and six of these met the inclusion criteria, three of which were also identified in the RCN search. Two additional relevant Cochrane SRs were identified during the project on dressings and securement devices for central venous catheters – one published in 2011[1] and the other an updated version published in September 2015[2]. The updated version has been included in the report.

These 76 studies were then assessed at full text and 57 were identified as relevant and included in the review. A list of all excluded studies including abstracts where available can be found in Appendix C. The quality of the SRs was rated according to the AMSTAR 11 item checklist, a measurement tool that assesses the methodological quality of SRs. Items assessed include an a priori design, appropriate pooling of results, and likelihood of publication bias. The AMSTAR rating for each study is provided in Table 15, Appendix A. RCTs were quality assessed using the Cochrane risk of bias tool, the results of which are in Table 16 in Appendix B. For both types of assessment, an overall rating of low, medium or high quality was allocated.

The evidence has been grouped according to the 12 proposed sections of the RCN updated infusion standards. Brief data extraction tables provide the most pertinent outcomes in each section, with a particular emphasis on safety and effectiveness. The body of evidence for each topic is then summarised to indicate the volume of research available for each topic and where there are gaps in the evidence. Cost effectiveness is not included in this review.

Summary findings

Table 2: Summary of findings and gaps in the evidence

Section	Evidence	Gaps
1. Add-on devices	Two SRs[3, 4] of low and medium quality did not find conclusive evidence on how to reduce contamination and infection rates when using different needle-less connectors. One SR[5] of high quality identified very low quality evidence that closed connector devices for central venous catheters reduced risk of infections and improved safety.	No evidence was found on the effect on patient safety and outcomes of: • changing add-on devices with each cannula or administration set replacement • changing add-on devices when integrity of either product is compromised.
2. Arterial catheters	One RCT[6] of low quality did not find that use of radial arterial catheters caused finger or hand ischaemia, nor did hourly blood glucose monitoring using the catheter increase the rate of infection. One RCT[7] of high quality compared different dressings; bordered polyurethane (BPU) with standard polyurethane (SPU) dressing was associated with the least arterial catheter failure. One SR[8] of high quality found inconclusive results about the optimum timing of administration set replacement. One low quality SR[5] found that arteriovenous fistula cannulation was comparable to central venous catheters for intensive haemodialysis in terms of access loss, failure or complications.	No evidence was found on the effect on patient safety and outcomes of: • different line flushing frequencies for arterial catheters • flushing arterial catheters with saline vs heparinised solutions • using different arteries for cannulation.
3. Blood sampling	Three RCTs of low quality looked at the impact of different methods for obtaining blood samples: • sampling speed for taking venous blood from pulmonary artery catheters did not change the level of oxygen (five seconds compared to one to two minutes)[9] • repeat blood glucose levels could be effectively measured using samples from the arterial catheter compared to standard fingertip blood glucose monitoring[6] • blood samples taken by nurses from the IV catheter hub immediately after insertion had similarly high rates of haemolysis as samples taken from the IV catheter hub via an extension tube immediately after insertion[10].	No evidence was found for: • venepuncture interventions to reduce fear, pain and anxiety • the effect of site selection for an infusion cannula on patient safety and outcome • the impact of different infusion device flushing before blood sampling • best practice for different devices.
4. Central venous devices	Two SRs[11, 12] of high and medium quality and one RCT[13] of low quality did not find any difference between flushing with heparin, sodium chloride or ethanol, and locking with heparin or citrate. The medium quality SR found that locking with citrate plus gentamicin, taurolidine or methylene blue plus methylparaben plus propylparaben reduced the risk of catheter-related blood stream infection. Two SRs[14, 15] of medium quality examined the effect of site and vein selection, with peripherally inserted central venous catheters (PICCs) having double the risk of deep vein thrombosis over centrally inserted catheters. One SR[2] and one RCT[16], both high quality, found that chlorhexidine dressings and silver dressings reduce major catheter-related infections, catheter-related blood stream infections and catheter colonisation. Three SRs[15, 17, 18] and five RCTs[19-24] of varying quality considered different types of central venous catheter devices for durability, infection risk and complications, further details can be found in the main body of the report. Four RCTs[25-28] compared insertion techniques but no firm conclusions can be drawn as the studies were either of low quality or were conducted on a manikin. Having the bevel facing down and using ultrasound appeared to be beneficial.	No evidence was found on the effect on patient safety and outcomes of different line flushing frequencies.

5. Flow control devices	Two RCTs[23, 29] compared different types of central venous catheters for haemodialysis: • a high quality RCT[23] found that the twin permanent central venous haemodialysis catheters LifeCath and TesioCath enabled the same flow rate but there were more complications with LifeCath • a low quality RCT[29] found that the Palindrome Symmetric Tip tunnelled catheter gave higher blood flow rate and fewer occlusions than HemoStar but both lasted the same length of time. One RCT[30] of high quality found no benefit in using a local infusion of analgesic into the wound following hiatus hernia repair. One SR[31] of medium quality found that intrathecal pain relief was moderately effective for pain that had not responded to other methods of pain relief.	No evidence was found for: • prognostic factors (age, condition, therapy, care setting) affecting selection of different manual flow control devices on patient outcomes • how different frequencies of flow rate monitoring of different manual flow control devices affect patient outcomes • the effect of electronic devices which generate flow through positive pressure or low pressure devices on patient safety and outcomes.
6. Infusion-related blood stream infections	Prevention: • Two SRs[12, 32] of medium quality found that locking with citrate plus gentamicin, taurolidine or methylene blue plus methylparaben plus propylparaben reduced the risk of catheter-related blood stream infection compared to either heparin or citrate alone, and antibiotic-heparin or antibiotic-citrate were more effective than heparin alone. One RCT[13] of low quality found no difference between heparin and ethanol flushes. • One SR[2] and one RCT[16], both of high quality, found that chlorhexidine dressings and silver dressings reduce catheter-related blood stream infections, and one SR[33] of low quality found they reduced infections in general. One SR[5] of high quality found low quality evidence that topical mupirocin reduces catheter-related blood stream infections for buttonhole arteriovenous cannulation. • One multicentre medium quality RCT[34] found that a 5-item blood stream infection bundle and staff engagement protocol reduced catheter-related blood stream infection by 81%. • Three SRs[4, 17, 18] and 4 RCTs[19, 21, 23, 29] of varying quality compared infection rates for different types of central venous catheters, further details can be found in the main body of the report. • One SR[8] of high quality found insufficient evidence on how often the arterial catheter tubing should be changed or flushed. One RCT[6] of low quality found no difference between a non-waste needle-less setup or non-waste syringe setup for radial arterial catheters. One SR[33], of low quality, found that femoral arterial catheters had double the risk of catheter-related blood stream infection compared to radial arterial catheters. • One high quality SR[35] concluded that administration sets that do not contain lipids, blood or blood products may be left in place for up to 96 hours without increasing the risk of infection. • One high quality RCT[36] was inconclusive regarding the optimal removal time for peripheral catheters on risk of catheter-related blood stream infection.	No evidence was found on the management of infusion-related blood stream infections.

7. Infusion therapy parenteral nutrition	One SR[37] of low quality highlighted the importance of hand hygiene and training for home parenteral nutrition as gram positive human skin flora caused the most infections. Two high quality RCTs[38, 39] did not find any improvement in outcomes by starting parenteral nutrition early on during admission of adults to ICUs. One low quality RCT[40] found that total parenteral nutrition (TPN) and enteral nutrition were both effective routes for people with total brain injury. One medium quality SR[41] found that omega-3 fatty acid supplements did not improve mortality, infectious complications or length of ICU stay. Four RCTs [42-45] of low to high quality found no difference in outcomes between parenteral nutrition (PN) supplements if based on soybean, medium-chain triglycerides, olive oil or fish oil.	No evidence was found for: • the effect of different frequencies of change of parenteral nutrition administration sets and add-on devices on patient safety and outcomes • the performance of nutrition screening tools to assess nutritional status • the effect of different ways of monitoring for metabolic related complications and electrolyte imbalances and catheter-related complications on patient safety and outcomes.
8. Infusion therapy phlebitis	One high quality RCT[36] found that the incidence of phlebitis was 7% whether peripheral intravenous catheters were replaced routinely every three days or replaced according to clinical indications. One high quality RCT[21] found that the rate of phlebitis for PVP PICCs was half that for DVS PICCs. One medium quality RCT[46] found that phlebitis was less likely with closed-system peripheral intravenous catheters than open-systems. One low quality SR[47] identified that there are 71 different phlebitis scales. One high quality RCT[48] found that a "catheter care station" in operating rooms reduced the combined rate of phlebitis and health care associated infection.	No evidence was found on the impact of different phlebitis severity/ degrees on patient safety and outcomes.
9. Intraosseous access	One low quality RCT[49] found that intraosseous tibial access was faster, more initially successful and less likely to dislodge than humeral intraosseous access. One SR[50] of high quality found intraosseous access much more likely to succeed than intravenous access for infants, though in both infants and adults, dislodgement was twice as likely. Intravenous routes were also found to be able to deliver more fluids.	No evidence was found on the effect on patient safety and outcomes of: • different durations of intraosseous access device • different durations of intraosseous ports • different intraosseous devices • site management after removal.
10. Midline catheters	One low quality RCT[51] concluded that vancomycin can be safely given through a midline catheter, with similar complication rates to PICC.	No evidence was found on the effects on patient safety and outcomes of: • different flushing frequencies • flushing lines with saline versus heparinised solutions • use of different veins • effect of site selection.

11. Peripheral access devices and flushing	One high quality RCT[52] found flushing with 3ml 100 IU heparin/ml was better than normal saline. One high quality RCT[36] found peripheral venous catheters could be changed according to clinical indication rather than routinely on Day 3. A high quality SR[8] was inconclusive about the optimal duration of time for peripheral arterial catheter administration sets. One medium quality RCT[46] found that open system peripheral venous catheters were more likely to be inserted first time and less likely to rupture a vein than closed system peripheral venous catheters but closed systems stayed in place longer. One small low quality RCT[53] found no difference between four techniques of securing peripheral venous catheters. One low quality SR[54] found ultrasound-guided peripheral venous access for people of any age with difficult venous access had higher success rates compared to traditional techniques.	No evidence was found on the effects on patient safety and outcomes of: • different line flushing frequencies for peripheral access devices • use of different veins • effect of site selection.
12. Subcutaneous infusions	One RCT[55] of medium quality found that smaller needles caused less pain for subcutaneous injections. One low quality RCT[56] found that retractable fixed needles caused less bruising. One high quality SR[57] found low quality evidence that subcutaneous injection of heparin over 30 seconds may be less painful than fast injection over 10 seconds. One low quality RCT[58] found that subcutaneous morphine infusions were less initially effective than intravenous morphine post-operatively.	No evidence was found on the effects on patient safety and outcomes of: • electronic devices for this procedure • site selection • site management • solution tonicity • electrolytes used (e.g. sodium chloride, dextrose saline, dextrose 5%).

Abbreviations

AMSTAR	Assessing the Methodological Quality of Systematic Reviews
ARR	Absolute risk reduction
AST	Accelerated Seldinger technique
BPU	Bordered polyurethane
CI	Confidence interval
COS	Closed-system
CUSP	Comprehensive Unit-based Safety Program
DVS	Distal valve silicone
FDA	Food and Drug Administration
HR	Hazard ratio
ICU	Intensive care unit
IV	Intravenous
MOS	Open-system
MST	Modified Seldinger technique
N	Number
NA	Not applicable
NR	Not reported
OR	Odds ratio
PN	Parenteral nutrition
PICC	Peripherally inserted central venous catheter
PVP	Proximal valve polyurethane
RCT	Randomised controlled trial
RR	Relative risk
SPU	Standard polyurethane
SR	Systematic review
TA	Tissue adhesive
TPN	Total parenteral nutrition

Evidence review

1: Add on devices

The RCN search for add on devices included use and management of the following: traffic lights; three way taps; extension sets; stop cocks; cap connectors; needle free; 'savy' systems; bio connectors. Three SRs were identified, and details can be found in Table 3. None of these included any RCTs[3-5].

These SRs provided evidence for:

- Needle-less devices:
  - One low quality SR by Moureau et al. (2015)[3] of observational and laboratory studies described the incidence of contamination of needle-less connector hubs as ranging from 33% to 45%. Disinfection of needle-less connector hubs for peripheral and central lines prior to use, occurred as low as 10% of the time in some studies. No optimal disinfection technique was identified but scrubbing with 70% alcohol for 5 to 60 seconds was recommended, even though this was not fully effective in some studies.
  - An SR of medium quality by Tabak et al. (2014)[4] found that in before and after studies, there were fewer catheter associated blood stream infections for the "Max-plus" positive-displacement needle-less connector for central venous catheters compared to negative or neutral-displacement needle-less connectors. However the results may have been affected by the addition of other infection prevention measures also implemented.
- Closed connector devices:
  - Very low quality evidence from small observational studies identified in a high quality SR by Mustafa et al. (2013)[5] found that closed connector devices may reduce the risk of central venous catheter associated infections compared to standard luer-lock connectors. These studies evaluated the "Tego" closed connector device. With regards to safety, in another observational study, an open connector device was associated with a fatal case of air embolism. The authors of the SR call on the need for a robust RCT to further assess the safety and effectiveness of closed connector devices compared to open ones.

No evidence was identified which covered the other add on devices in the search strategy or which answered the following specific RCN question:

- What is the effect of changing add-on devices with each cannula or administration set replacement or when integrity of either product is compromised on patient safety and outcomes?

Table 3: Evidence table for add on devices

Study	Participants	Intervention	Comparator	Outcomes	Quality
Moureau et al. 2015[3] SR RCT=0 Non-RCT=140	Laboratory and human observational studies of needle-less connector hubs for peripheral and central lines. Setting: NR	Disinfection of needle-less connector hubs (N=NR).	NA	**Outcomes:** 33% to 45% of needle-less connector hubs were reported to be contaminated. Disinfection of the needle-less connector hub before use was performed as low as 10% of the time. No optimal disinfection technique was identified, but scrubbing with 70% alcohol for 5 to 60 seconds was recommended even though this was not fully effective in some studies. **Safety:** NR	**Low quality SR**
Mustafa et al. 2013[5] SR RCT=0 Non-RCT=5	Adults and adolescents requiring intensive haemodialysis for more than three months of ≥5 times per week and/or ≥5.5 hours per day or conventional haemodialysis. Setting: home or hospital.	Closed connector device for central venous catheter (N=NR).	Standard luer-lock connectors for central venous catheter (N=NR).	**Outcomes:** No RCTs or observational studies were found comparing the two different types of connectors. One observational study of 23 adults found no thrombosis or infection with the Tego closed connector device. A further observational study of children, adolescents and young adults on haemodialysis found that in the 21 participants who did not use the Tego device, the rate of infection was 7.8 per 1,000 patient days. In the 29 people who then used the Tego device, the rate was 3.62 per 1,000 patient days. **Safety:** One case of fatal air embolism occurred in a study where a closed connector device had not been used.	**High quality SR** Very low body of evidence.

Study	Participants	Intervention	Comparator	Outcomes	Quality
Tabak et al. 2014[4] SR and Meta-analysis RCT=0 Non-RCT=7	Pre-test versus post-test design of needle-less intravenous connector devices. Setting: ICU, hospital and home	Max-plus positive-displacement needle-less connector for central venous catheters (N=95,383 catheter days).	Negative or neutral-displacement needleless connector for central venous catheters (N=111,255 catheter days).	**Outcomes:** Central venous catheter associated blood stream infection rate was 67% lower for the Max-plus positive-displacement needle-less connector design at 0.5 events per 1,000 central venous line days compared to 1.5 events for the comparator (relative risk [RR] 0.37, 95% CI 0.16 to 0.90). **Safety:** NR	**Medium quality SR** Meta-analysis reliant on before and after studies. Other preventive measures were also put in place in some of the studies which could have affected the results such as aseptic insertion technique, hand hygiene and use of chlorhexidine and alcohol.

2: Arterial catheters

The RCN search for evidence on the management of arterial catheters identified 2 SRs[5, 8] and two RCTs[6,7], the details of which can be found in Table 4. One of the RCTs was relevant for the RCN focus question:

- What is the effect of site selection on patient safety and outcomes?
    - The low quality RCT by Raurell-Torredà et al.,[6] did not find that radial arterial catheters caused finger or hand ischaemia in 814 adults on the ICU. Increased use of the arterial catheter for hourly blood glucose monitoring for 90 people did not increase the rate of bacterial colonisation and none of the participants had a catheter-related infection.

No evidence covered the following specific RCN research questions:

- What are the effects of different line flushing frequencies for arterial catheters on patient safety and outcomes?
- What are the effects of flushing lines with saline vs heparinised solutions for arterial catheters on patient safety and outcomes?
- What are the effects of different arteries being used in terms of patient safety and outcomes?

Other results from the literature identified were:

- Arterial catheter dressing:
    - One high quality RCT by Edwards et al. (2014)[7] was identified which compared different dressings for arterial catheters. Bordered polyurethane (BPU) with standard polyurethane (SPU) dressing was associated with the least arterial catheter failure and SPU with the most.
- Administration set replacement:
    - One high quality SR by Daud et al. (2013)[8] identified three RCTs and three cohort studies regarding the optimum duration of arterial catheter administration sets. Results were inconclusive due to small sample sizes and methodological inadequacies.
- Arteriovenous fistula or graft catheter:
    - One SR of high quality by Mustafa et al. (2013)[5] compared arteriovenous fistula or graft catheter use with central venous catheters for adults requiring intensive haemodialysis. Access loss, failure or complication rates were low for both types of access.

Table 4: Evidence table for arterial catheters

Study	Participants	Intervention	Comparator	Outcomes	Quality
Daud et al. 2013[8] SR RCT=3 Non-RCT=3	120 critically ill adults with peripheral arterial catheters that have intra-arterial pressure monitoring. Setting: single ICU.	Administration set (the tubing attached to the peripheral arterial catheter) changed every four (N=19) or eight days (N=39).	Administration set changed every two days (N=62).	**Outcomes:** In the Luskin et al. 1986 RCT, 2/39 (5.1%) of patients who had an administration set for between four to eight days had an infusate colonisation compared to none in the group who had it changed every two days, but this was not significant (p>0.05). Infusion-related blood stream infection was 1/58 (1.7%) when administration set was changed every four to eight days and 0/62 for those having it changed every two days (p=NR). **Safety:** NR	**High quality SR** Results based on low quality RCTs. Cohort studies not included in the results here as quality very low.
	30 critically ill adults with peripheral arterial catheters that have intra-arterial pressure monitoring. Setting: single hospital, multiple ICUs.	Group 1: change of flush solution and pressure-monitoring tubing every 24 hours (N=10). Group 2: change of flush solution every 24 hours and tubing every 48 hours (N=10). Group 3: change of flush solution and tubing every 48 hours (N=10).	All groups compared with each other.	**Outcomes:** In the Covey et al. 1988 RCT, there was no catheter-related blood stream infection or infusion-related blood stream infection in any of the three groups. **Safety:** NR	
	76 critically ill adults and children with peripheral arterial catheters that have intra-arterial pressure monitoring. Setting: single hospital.	Administration set changed every 72 hours (N=38).	Administration set changed every 48 hours (N=38).	**Outcomes:** The McLane et al. 1998 RCT, found stopcock colonisation was 3/26 (11.5%) for administration set change every 48 hours and 10/23 (43.5%) when changed every 72 hours (p<0.01). There was no infusate colonisation or catheter-related blood stream infection in either group. **Safety:** NR	

Study	Participants	Intervention	Comparator	Outcomes	Quality
Edwards et al. 2014[7] RCT	224 surgical cardiac patients and general ICU patients requiring an arterial catheter. Setting: Single centre operating theatres and ICU	BPU + SPU dressing (N=59); tissue adhesive (TA) + SPU dressing (N=57); sutureless securement device +SPU dressing (no sutures)(N=52).	SPU dressing (N=56)	**Outcomes:** SPU dressing was significantly associated with more arterial catheter failure than BPU + SPU (21% versus 5%: p=0.03) but not the other adhesive combinations. **Safety:** NR	**High quality RCT**
Mustafa et al. 2013[5] SR RCT= 0 Non-RCT=31	Adults requiring intensive haemodialysis for more than three months of ≥5 times per week and/or ≥5.5 hours per day. Setting: home or hospital.	Arteriovenous fistula or arteriovenous graft catheter access (N=NR).	Central venous catheter (N=NR).	**Outcomes:** Access loss or failure was slightly lower for arteriovenous fistula or graft catheter access at 0.02 to 0.64 per patient-year compared to 0.43 to 1.07 for central venous catheters. **Safety:** Complication rates were slightly lower for arteriovenous fistula or graft catheter access at 0.01 to 1.73 per patient-year compared to 0.46 to 2.66 for central venous catheters. Bleeding rates were low in both groups: arteriovenous fistula or graft arterial catheter rates were 0.00 to 0.11 per patient-year versus 0.01 for central venous catheter.	**High quality SR** Lack of studies performing direct comparison.
		Arteriovenous fistula catheter access using buttonhole technique (N=NR).	Arteriovenous fistula using rope-ladder cannulation (N=NR).	**Outcomes:** NA **Safety:** One study found that the rate ratio for any infection or other problem was 3.0 for buttonhole compared to rope-ladder cannulation (95% confidence interval [CI] 1.04 to 8.66; p=0.04).	

Study	Participants	Intervention	Comparator	Outcomes	Quality
Raurell-Torredà et al. 2014[6] RCT	814 critical patients with a radial arterial catheter requiring hourly blood glucose monitoring for intensive insulin therapy. Setting: single ICU.	Non-waste needle-less setup or non-waste syringe setup for blood glucose monitoring using the arterial catheter (N=90).	Arterial catheter used for blood pressure measurement and daily blood tests. Fingertip blood samples were used for glucose monitoring (N=724).	**Outcomes:** Blood glucose monitoring was equally effective in each group unless haematocrit was less than 25%, when there was a significant difference between arterial blood glucose and fingertip samples. **Safety:** There were no cases of finger or hand ischaemia from the arterial catheters in either group. There were no catheter-related infections in the arterial group and there was no difference between the groups for bacterial colonisation.	Low quality RCT

3: Blood sampling

The RCN searched for evidence on blood sampling for the following topics: venepuncture; blood sampling; blood collection; blood sampling/ collection via vascular access devices; tubes; methods and preparation.

Three RCTs were identified for the following RCN question and details of the studies are provided in Table 5 [6, 9, 10]:

- What is the impact of different methods for obtaining blood samples through the device on patient safety and outcomes? Push pull or missing method, discard method or reinfusion method.
    - One small RCT of low quality by Jaschke et al. (2014)[9] found that the speed of sampling of venous blood from pulmonary artery catheters did not significantly change the level of oxygen – taking blood over five seconds was comparable to taking it over one to two minutes.
    - A low quality RCT by Raurell-Torredà et al. (2014)[6] found that repeat blood glucose levels could be effectively measured using samples from the arterial catheter compared to standard fingertip blood glucose monitoring unless haematocrit was less than 25%, when there was a significant difference between arterial blood glucose and fingertip samples. Arterial blood glucose measurement avoided the pain from fingertip sampling. Returning the clearing volume of blood was estimated to reduce procedure-related blood loss by 50%.
    - A low quality RCT by Stauss et al. (2012)[10] found that blood samples taken by nurses from the intravenous (IV) catheter hub immediately after insertion had similarly high rates of haemolysis as samples taken from the IV catheter hub via an extension tube immediately after insertion. Nurses were significantly more likely to think a sample was haemolysed when it wasn't and not haemolysed when it was.

No evidence covered the following specific research questions identified by the RCN:

- What interventions reduce fear, pain and anxiety in patients undergoing venepuncture?
- What is the effect of site selection for venepuncture on patient safety and outcome in patients with an infusion cannula?
- What is the impact of different infusion device flushing before blood sampling through the device on patient safety and outcomes?
- What is best practice for different devices?

Table 5: Evidence table for blood sampling

Study	Participants	Intervention(s)	Comparator	Outcomes	Quality
Jaschke et al. 2014[9] RCT – crossover	50 people with heart failure with pulmonary artery catheters. Setting: single ICU.	Blood sample obtained in five seconds. Cross-over to have blood sample over one to two minutes (N=26).	Blood sample obtained over one to two minutes. Cross-over to have blood sample over five seconds (N=24).	**Outcomes:** The mean difference in venous oxygen saturation between the two sampling speeds was negligible (0.3%, CI 1.5% to 0.8%; p=0.55). **Safety:** NR	Low quality RCT
Raurell-Torredà et al. 2014[6] RCT	814 critical patients with a radial arterial catheter requiring hourly blood glucose monitoring for intensive insulin therapy. Setting: single ICU.	Non-waste needle-less setup or non-waste syringe setup. (N=90) Non-waste method was used for all samples; reinfusing blood aspirated prior to the sample being taken.	Standard set-up with fingertip blood glucose monitoring (N=724)	**Outcomes:** Blood glucose levels could be effectively measured using samples from the arterial catheter compared to standard fingertip blood glucose monitoring unless haematocrit was less than 25%, when there was a significant difference between arterial blood glucose and fingertip samples. Arterial sampling avoided the pain from fingertip pricks. **Safety:** Returning the clearing volume of blood was estimated to reduce procedure-related blood loss by 50%. There were negligible arterial catheter complications.	Low quality RCT
Stauss et al. 2012[10] RCT	120 adult patients who required a coagulation sample and insertion of a 20-guage IV catheter. Setting: single emergency department.	Blood samples obtained by nurses from the IV catheter hub immediately after insertion (N=60).	Blood samples obtained by nurses from the IV catheter hub via an extension tube immediately after insertion (N=60).	**Outcomes:** Both techniques had high rates of haemolysed samples, hub 31.67% and hub plus tubing 30% (p=0.84). Nurses were significantly more likely to think a sample was haemolysed when it wasn't and not haemolysed when it was (p<0.001). **Safety:** NR	Low quality

4: Central venous catheter devices

The RCN search was focussed on the management of central lines rather than insertion, but covered: central venous devices; tunnelled catheters; non-tunnelled catheters; catheter selection; catheter management and care of catheters. The search identified four SRs[11, 12, 14, 15] and one RCT[13] which addressed the RCN questions regarding flushing lines with heparin and the effect of site selection. A further RCT16 looked at the effect of different dressings on outcomes, three SRs[15, 17, 18] and five RCTs[19-23] considered the effectiveness of different types of central venous catheter devices and four RCTs[25-28] compared insertion techniques. Details of the studies can be found in Table 6.

The following evidence was identified which was relevant for two of the RCN specific questions:

- What are the effects of flushing lines with saline versus heparinised solutions for central venous catheter devices on patient safety and outcomes?
  - A high quality SR by Lopez-Briz et al. (2014)[11] found no clear evidence of a difference between flushing the central venous catheter with heparin at any dose (10 to 5000 IU/ml) compared with 0.9% sodium chloride in terms of occlusion or duration of patency of the catheter. There was also no difference in safety for incidence of catheter-related sepsis, mortality or haemorrhage at any site.
  - An SR of medium quality by Zhao et al. (2014)[12] found that there was no difference between use of a heparin lock or citrate lock either alone or in combination for risk of exit site infection, catheter removal for poor flow, need for thrombolytic treatment, duration of use, catheter-related readmission, catheter-related blood stream survival or all-cause death. Citrate alone did not reduce the risk of catheter-related blood stream infection compared to heparin, but did reduce the risk by 55% to 75% when it was in combination with either gentamicin, taurolidine or methylene blue plus methylparaben plus propylparaben.
  - A small low quality RCT by Worth et al. (2014)[13] found no difference between heparin flush and ethanol flush in terms of catheter-related blood stream infection, thrombosis, exit-site infection or tunnel/pocket infection. The first regime tested was daily flushing of the central venous catheter with 10ml normal saline followed by 2ml of heparinized saline (50 units in 5ml) which was left for two hours, before 5-10ml aliquot was aspirated and then the line locked under positive pressure. The second regime was similar but used 2ml of 70% ethanol instead of heparin. Three patients reported chest discomfort with the ethanol flush and one reported nausea, though this was not significant compared with heparin.
- What is the effect of site selection and different veins being used on patient safety and outcomes?
  - In a medium quality SR of comparison studies by Chopra et al. (2013)[14], the risk of deep vein thrombosis was over double with PICCs compared to centrally inserted central venous catheters. According to the other observational studies, this risk was higher for people who were critically ill and those with cancer.
  - A medium quality SR of RCTs by Mitchell et al. (2013)[15] also found evidence to suggest that PICCs and femoral insertion may increase the risk of catheter-related thrombosis compared to centrally-inserted central venous catheters. Results were inconclusive when comparing the jugular or subclavian sites.

No evidence covered the following specific research question identified by the RCN:

- What are the effects of different line flushing frequencies for central venous catheter devices on patient safety and outcomes?

Other results from the literature identified were:

- Dressings:
  - A high quality SR by Ullman et al. (2015)[2] found high quality evidence that chlorhexidine gluconate impregnated dressings and silver impregnated dressings reduce the risk of catheter-related blood stream infections compared to all other types of dressings (RR 0.60, 95% CI 0.39 to 0.93). Chlorhexidine gluconate-impregnated dressings reduce the frequency of catheter-related blood stream infections compared to standard polyurethane dressings per 1,000 patient days and catheter tip colonisation. There was unclear evidence of any difference between different dressings for incidence of skin irritation or damage or failed securement.
  - A large high quality RCT by Timsit et al. (2012)[16] found that chlorhexidine dressings had 67% lower rates of major catheter-related infections, 60% lower catheter-related blood stream infections and 59% lower catheter colonisation compared to non-chlorhexidine dressings. They were estimated to prevent one major catheter-related infection for every 71 catheters left for an average of 10 days. It also found that highly adhesive dressings had 65% more catheter colonisations though no difference for catheter-related blood stream infection or major catheter-related infections compared to standard dressings. The highly adhesive dressings lasted longer and fewer were required.
- Central venous catheter type:
  - One RCT by Antonelli et al. (2012)[19] of high quality found no difference in rate of catheter bacterial colonisation or mortality for AgTive silver-nanoparticle-impregnated central venous catheter versus conventional central venous catheters.

- A medium quality SR by Wang et al. (2010)[17] found that catheter colonisation was lower for the following catheter types compared to standard central venous catheters: adjusted silver iontophoretic, chlorhexidine and silver sulfadiazine, chlorhexidine and silver sulfadiazine blue plus, minocycline-rifampicin catheters and miconazole-rifampicin catheters. Compared to standard catheters, catheter-related blood stream infections was lower for adjusted heparin-bonded catheters and minocycline-rifampicin catheters.
- A low quality RCT by Schindler et al. (2010)[24] found a lower rate of bacterial colonisation of the catheter tip for bismuth-coated non-tunnelled central venous catheters compared to standard non-tunnelled central venous catheters.
- A medium quality RCT by Itkin et al. (2014)[20] did not find any difference in rate of thrombosis or safety between non-tapered and reverse tapered PICCs.
- A high quality SR by Lai et al. (2013)[18] found no difference in safety between antimicrobial impregnated central venous catheters and non-impregnated catheters in terms of thrombosis, thrombophlebitis, bleeding, erythema or tenderness at insertion site. Antimicrobial impregnation did significantly reduce catheter-related blood stream infection by 2% and catheter colonisation by 10% but had no effect on sepsis or mortality.
- The medium quality SR by Mitchell et al. (2013)[15] found low quality evidence to suggest that valved ports and silver-coated catheters had no effect on catheter-related thrombosis.
- A high quality RCT by Ong et al. (2010)[21] found that proximal valve polyurethane (PVP) PICCs were superior to distal valve silicone (DVS) PICCs in terms of durability and complication rate.
- A low quality RCT by Pittiruti et al. (2014)[22] found no clinical advantage of power-injectable valved vs power-injectable non-valved PICCs.
- An RCT by Power et al. (2014)[23] of high quality found that the TesioCath twin permanent central venous catheter achieved similarly adequate blood flow rates to the LifeCath twin permanent central venous catheter for long-term haemodialysis, but were less likely to require infusions of urokinase to unblock them. Catheter-related admissions were also slightly more common with LifeCath, but catheter-related bacteraemia, exit site infection and survival rates were similar for both groups.

Insertion technique:

- One low quality RCT by Caparas et al. (2014)[25] found that the accelerated Seldinger technique for central catheter insertion was faster with slightly less blood loss than the modified Seldinger technique though both had the same high initial insertion success rate.
- A medium quality RCT by Lim et al. (2012)[26] found that having the bevel facing down during the Seldinger technique with ultrasound for central catheter insertion caused less haematomas than having the bevel facing up.
- A medium quality small RCT by Fenik et al. (2013)[27] found that central catheter insertion using a pre-packaged kit was faster, with fewer major or minor mistakes for junior doctors assisted by nursing students when practicing on a manikin.
- A low quality RCT by Fragou et al. (2011)[28] found ultrasound-guided central catheter cannulation superior to the Landmark method in terms of success rate, number of attempts required and safety.

Table 6: Evidence table for central venous catheter devices

Study	Participants	Intervention	Comparator	Outcomes	Quality
Antonelli et al. 2012[19] RCT	338 adults requiring central venous catheters. Setting: Five ICUs	AgTive silver-nanoparticle-impregnated central venous catheter. (N=135)	Conventional central venous catheter (N=137).	**Outcomes:** Colonisation rates were similar (32.6% for silver impregnated versus 30% for conventional, p=0.7). Catheter-related blood stream infection rates were the same for each type, 3.36 infections per 1,000 catheter-days. **Safety:** ICU mortality was similar in each group (46% silver catheter versus 43% conventional, p=0.7).	**High quality RCT** Also included in the infusion-related blood stream infection section.
Caparas et al. 2014[25] RCT	30 adults requiring PICCs. Setting: single hospital.	Accelerated Seldinger technique (AST) for inserting a central venous catheter. This technique uses an all-in-one device with all four components. (N=14)	Modified Seldinger technique (MST) for inserting a central venous catheter. This uses a needle, guidewire and combined dilator and sheath. (N=16)	**Outcomes:** Same insertion success rate (MST 81.3% versus AST 85.7%). AST insertion was significantly faster, 1.27 min versus 4.21 min for MST (p= 0.0048). **Safety:** Blood loss was significantly smaller with AST, though both techniques had minimal blood loss (AST 2.4cm blood spot on gauze versus 4.2cm for MST; p=0.0295).	**Low quality RCT** Small unblinded trial, lead author is a paid lecturer on the advantages of AST system which is a potential conflict of interest.
Chopra et al. 2013[14] SR RCT=0 Comparison studies=12 Non-RCT=52	29,503 adults requiring PICCs or central venous catheter. Settings: multiple.	Adults with PICC (N=NR).	Adults with a central venous catheter (N=NR).	**Outcomes:** Meta-analysis of 11 comparison studies found that PICCs were associated with over double the risk of deep vein thrombosis compared to central venous catheters (odds [OR] ratio 2.55, 95% CI 1.54 to 4.23, p<0.001). From the other non-RCTs, the weighted frequency of deep vein thrombosis was highest in people who were critically ill (13.91%) and those with cancer (6.67%). **Safety:** No pulmonary emboli occurred in the 11 comparison studies. PICCs are associated with a higher risk of deep vein thrombosis than are central venous catheters, especially in patients who are critically ill or those with a malignancy. The decision to insert PICCs should be guided by weighing of the risk of thrombosis against the benefit provided by these devices.	**Medium quality SR** No RCTs were identified which reduces the reliability of the results.

Study	Participants	Intervention	Comparator	Outcomes	Quality
Fenik et al. 2013[27] RCT	30 final year medical students and recently qualified doctors performing central line insertion on a manikin, assisted by first year nursing students. Setting: single hospital.	Pre-packaged kit for central line insertion (N=15).	Standard kit of a central vein catheter. The participants then had to decide which other individual components they needed, which were all separately packaged (N=15).	**Outcomes:** The pre-packaged group were better on 4 out of 5 aspects: • faster (26:26±3:50 min versus 31:27±5:57 min, p=0.01) • major technical mistake (3.1±1.4 versus 4.8±2.6, p=0.03) • minor technical mistake (5.2±1.7 versus 8.0±3.2, p=0.01) • correct steps (83±5% versus 75±11%, p=0.02) Not adhering to the aseptic technique occurred at similar rates in each group. **Safety:** NR	Medium quality RCT
Fragou et al. 2011[28] RCT	463 adults on mechanical ventilators requiring central venous catheter by physicians with at least 6 years of experience of insertion. Setting: single ICU.	Ultrasound-guided subclavian vein cannulation (N=200).	Landmark method - Seldinger's technique for infraclavicular approach (N=201).	**Outcomes:** Ultrasound guided cannulation was superior for: • success rate (100% versus 87.5%, p<0.05) • average number of attempts (1.1 versus 1.9, p<0.05). **Safety:** Ultrasound guided cannulation was safer in terms of: • artery puncture (0.5% versus 5.4%) • haematoma (1.5% versus 5.4%) • pneumothorax (0% versus 4.9%) • haemothorax (0% versus 4.4%) • injury of the brachial plexus (0% versus 2.9%) • phrenic nerve injury (0% versus 1.5%).	Low quality RCT
Itkin et al. 2014[20] RCT	332 adults requiring a double-lumen PICC. Setting: single hospital.	Non-tapered PICC (N=164).	Reverse tapered PICC (N=168).	**Outcomes:** Peripheral venous thrombosis rate was high in both groups at around 72%. It was symptomatic in 4% in each group. Thrombosis was more likely in people with cancer. **Safety:** No difference in complication rate, which included: • purulence at entry site • fever • oedema. • pain	Medium quality RCT

Study	Participants	Intervention	Comparator	Outcomes	Quality
Lai et al. 2013[18] SR RCT=56	16,512 catheters (N=not available). Settings: ICUs, haematological and oncology units.	11 types of antimicrobial central venous catheter impregnation (N=NA).	Non-impregnated catheter or catheters with a different antimicrobial impregnation (N=NA).	**Outcomes:** Catheter impregnation significantly reduced: • catheter-related blood stream infection by 2% (Absolute risk reduction [ARR] 2%, 95% CI 3% to 1%) • catheter colonisation by 10% (ARR 10%, 95% CI 13% to 7%). Catheter impregnation made no difference to: • sepsis (RR 1.0, 95% CI 0.88 to 1.13) • all-cause mortality (RR 0.88, 95% CI 0.75 to 1.05). Sub-group analysis found that the benefits were more likely in the ICU setting, and less likely on haematology or oncology units, or for people on long-term TPN. **Safety:** No difference was found between impregnated and non-impregnated catheters in terms of: • thrombosis • thrombophlebitis • bleeding • erythema • tenderness at insertion site. Antimicrobial central venous catheters improve such outcomes as catheter-related blood stream infection and catheter colonization when used in ICUs. Unclear outcomes in other settings.	High quality SR
Lim et al. 2012[26] RCT	338 thoracic surgery patients to assess if the bevel-down approach reduced damage to the wall of the blood vessel. Setting: single hospital.	Bevel-down during central venous catheterisation using Seldinger technique with ultrasound (N=169).	Bevel-up during central venous catheterisation using Seldinger technique with ultrasound (N=169).	**Outcomes:** Bevel-down approach caused significantly less posterior haematoma (6 versus 17, p=0.031). No difference in puncture on withdrawal between the two techniques. **Safety:** One case of arterial puncture in the bevel-up group.	Medium quality RCT

Study	Participants	Intervention	Comparator	Outcomes	Quality
Lopez-Briz et al. 2014[11] SR RCT=6	1,433 adults with central venous catheters.	Flushing central venous catheter with heparin at any dose (10 to 5000 IU/ml) (N=715).	Flushing central venous catheter with 0.9% normal saline (N=734).	**Outcomes:** No clear evidence of a difference between Heparin v 0.9% sodium chloride for flushing central lines for efficacy in terms of occlusion or duration of patency of the catheter. **Safety:** No difference was found for catheter-related sepsis, mortality or haemorrhage at any site.	**High quality SR**
Mitchell et al. 2013[15] SR RCT=10	1,378 adults with a central venous catheter. Setting: multiple.	Any non-drug intervention to reduce catheter-related thrombosis (N=NR).	Any other intervention or none (N=NR).	**Outcomes:** PICCs and femoral insertion may increase the risk of catheter-related thrombosis compared to centrally-inserted central venous catheters. Low quality evidence was inconclusive about jugular versus subclavian sites. Low quality evidence suggested that valved ports and silver-coated catheters had no effect on catheter-related thrombosis. **Safety:** NR	**Medium quality SR** Qualitative synthesis as studies very heterogeneous.

Ong et al. 2010[21]
RCT
	326 adults with PICC by interventional radiologists.
	Setting: single hospital.
		PVP PICC under ultrasound guidance (N=198).	DVS PICC under ultrasound guidance (N=194).	**Outcomes:**
				The PVP PICC lasted on average for longer at a mean of 27.8 days compared to 23.3 days for the DVS PICC and was superior for:
				• catheter-related infection:
				  • 2% PVP PICC versus 6.2% DVS PICC(p=0.043)
				• phlebitis:
				  • 11.6% PVP PICC versus 23.2% DVS PICC(p=0.003).
				Safety:
				Less complications occurred with PVP PICC at 26.8% compared to 47.9% for DVS PICC (p<0.001).
				There was no difference for catheter occlusion, fracture or dislodgement.
					High quality RCT

Study	Participants	Intervention	Comparator	Outcomes	Quality
Pittiruti et al. 2014[22] RCT	180 adults requiring chemotherapy. Catheters inserted under ultrasound guidance. Setting: single oncology unit.	Power-injectable PICC with Solo-2 proximal valve (Bard) (N=61). Power-injectable PICC with pressure activated safety proximal valve (Navilyst) (N=60).	Non-valved power-injectable PICC (Medcomp) (N=59).	**Outcomes:** No clinical advantage of valved vs non-valved PICCs (valved are marketed as being less likely to occlude). **Safety:** The trial was discontinued because of three cases of rupture with the Bard catheter.	**Low quality RCT**
Power et al. 2014[23] RCT	80 people requiring medium to long-term haemodialysis with a central venous catheter. Setting: single hospital.	LifeCath twin permanent haemodialysis central venous catheter (N=41).	TesioCath twin permanent haemodialysis central venous catheter (N=39).	**Outcomes:** LifeCath achieved the targeted blood flow rate of 450ml/min during the first session of haemodialysis (44% LifeCath versus 10% TesioCath, p=0.001). Both types of catheters achieved similarly adequate flow rates after the fourth session. Six people with LifeCath required infusions of urokinase to unblock them versus none in the TesioCath group (p=0.01). Two LifeCath needed to be replaced with the standard TesioCath. **Safety:** Patient survival was similar in both groups. Central venous catheter complications requiring admission were more common in the LifeCath group (0.94 events per 1,000 catheter days versus 0.24 events, p=0.02). Catheter-related bacteraemia and exit site infection rates were similar in each group.	**High quality RCT** Small number of participants.
Schindler et al. 2010[24] RCT	77 adults on short-term extracorporeal therapy. Setting: three high dependency units.	Bismuth-coated non-tunnelled central venous catheter (N=38).	Standard non-tunnelled central venous catheter (N=39).	**Outcomes:** Catheter survival was similar for both groups, 15.1±2 days for the bismuth-coated and 18.5±2 for the standard catheter. Bacterial colonisation of the tip was lower for the bismuth-coated (3.5±1.6 colony forming units versus 63±29, p<0.001). **Safety:** Similar number of catheters malfunctioned in each group (two bismuth versus three standard) and were removed due to suspected infection (four bismuth versus six standard).	**Low quality RCT**

Study	Participants	Intervention	Comparator	Outcomes	Quality
Timsit et al. 2012[16] RCT	1,879 people with central venous catheters expected to be in place for at least 48 hours. Setting: 12 ICUs.	Chlorhexidine dressings (N=938).	Non-chlorhexidine dressings (N=941).	**Outcomes:** Chlorhexidine dressings had 67% lower rates of major catheter-related infections compared to non-chlorhexidine dressings at 0.7 versus 2.11 per 1,000 catheter days (hazard ratio [HR] 0.328, 95% CI 0.174 to 0.619, p=0.0006). Chlorhexidine dressings were estimated to prevent one major catheter-related infection for every 71 catheters left for an average of ten days. Chlorhexidine dressings also had a 60% lower rate of catheter-related blood stream infections at 0.5 compared to 1.3 per 1,000 catheter days for non-chlorhexidine dressings (HR 0.402, 95% CI 0.186 to 0.868, p=0.02). Catheter colonisation was 59% lower with chlorhexidine dressings at 4.3 compared to 10.9 per 1,000 catheter days (HR 0.412, 95% CI 0.306 to 0.556, p<0.0001). **Safety:** NR	High quality RCT
		Highly adhesive non-chlorhexidine dressings (N=465).	Standard dressings (N=476).	**Outcomes:** Highly adhesive dressings had 65% more catheter colonisations at 12.5 versus 9.6 per 1,000 catheter days (HR 1.651, 95% CI 1.208 to 2.256, p=0.0016). There was no difference between the dressings in terms of catheter-related blood stream infection or major catheter-related infections. Highly adhesive dressings were less likely to detach, with a rate of 64.3% versus 71.9% (p<0.0001). Fewer dressings were required with highly adhesive dressings, two (range 1 to 4) versus three (range 1 to 5), p<0.0001. **Safety:** NR	

Study	Participants	Intervention	Comparator	Outcomes	Quality
Ullman et al. 2015[2] SR RCT=22	7,436 participants with a central venous catheter. Setting: ICUs, haematological units, general hospitals and home.	Comparison of nine different types of securement devices and dressings.	NA	**Outcomes:** Chlorhexidine gluconate impregnated dressings and silver impregnated dressings reduce the risk of catheter-related blood stream infections compared to all other types of dressings (RR 0.60, 95% CI 0.39 to 0.93). This was rated as high quality evidence. Chlorhexidine gluconate-impregnated dressings reduce the frequency of catheter-related blood stream infections compared to standard polyurethane dressings per 1,000 patient days (RR 0.51, 95% CI 0.33 to 0.78) and catheter tip colonisation (RR 0.58, 95% CI 0.47 to 0.73). **Safety:** No clear evidence of a difference between gauze and tape, chlorhexidine gluconate, standard polyurethane dressings and sutureless securement devices for incidence of skin irritation or damage or failed securement.	**High quality SR** This SR includes the RCT by Timsit et al. 2012.

Study	Participants	Intervention	Comparator	Outcomes	Quality
Wang et al. 2010[17] SR RCT=48	12,828 central venous catheters in 11,525 people.	Silver alloy-coated. Silver-impregnated. Adjusted silver iontophoretic catheters. Chlorhexidine and silver sulfadiazine catheters. Chlorhexidine and silver sulfadiazine blue plus catheters. Minocycline-rifampicin catheters. Miconazole-rifampicin catheters. Adjusted heparin-bonded catheters. Benzalkonium chloride.	Standard central venous catheters	**Outcomes:** The following had a lower rate of catheter colonisation compared to standard catheters: • adjusted silver iontophoretic catheters (OR 0.58, 95% CI 0.33 to 0.95, p=0.043) • chlorhexidine and silver sulfadiazine catheters (OR 0.49, 95% CI 0.36 to 0.64, p<0.001) • chlorhexidine and silver sulfadiazine blue plus catheters (OR 0.37, 95% CI 0.17 to 0.69, p=0.005) • minocycline-rifampicin catheters (OR 0.28, 95% CI 0.17 to 0.43, p<0.001) • miconazole-rifampicin catheters (OR 0.11, 95% CI 0.02 to 0.33, p=0.005). Compared to standard catheters, prevention of catheter-related blood stream infections was lower for: • adjusted heparin-bonded catheters (OR 0.20, 95% CI 0.06 to 0.44, p=0.002) • minocycline-rifampicin catheters (OR 0.18, 95% CI 0.08 to 0.34, p<0.001). **Safety:** NR	**Medium quality SR**
Worth et al. 2014[13] RCT	85 adults with a haematological malignancy. Setting: Single haematology and bone marrow transplant unit.	Daily flush of central venous catheter with 10ml normal saline followed by 2ml of heparinized saline (50 units in 5ml) and left for 2 hours, before 5-10ml aliquot was aspirated and then the line locked under positive pressure (N=43).	Daily flush of central venous catheter with 10ml normal saline followed by 2ml of 70% ethanol and left for two hours, before 5-10ml aliquot was aspirated and then the line locked under positive pressure (N=42).	**Outcomes:** There was no difference between the types of flush and rate of catheter-related blood stream infection, thrombosis, exit-site infection or tunnel/pocket infection. **Safety:** Three patients reported chest discomfort with the ethanol flush and one reported nausea but this was not enough people to be of statistical significance.	**Low quality RCT** Small study size means it was underpowered.

Study	Participants	Intervention	Comparator	Outcomes	Quality
Zhao et al. 2014[12] SR RCT=13	1,770 adults with a central venous catheter for haemodialysis. Settings: multiple.	Citrate lock for central venous catheter with or without an antimicrobial (gentamicin, taurolidine or methylene blue plus methylparaben plus propylparaben) (N=NR).	Heparin lock for central venous catheter (N=NR).	**Outcomes:** Subgroup analysis found that compared to heparin lock, the risk of catheter-related blood stream infection is: • similar for citrate alone (RR 0.54, 95% CI 0.22 to 1.30, p=0.2) • 75% less likely for citrate plus gentamicin (RR 0.25, 95% CI 0.13 to 0.47, p<0.001) • 55% less likely for citrate plus taurolidine (RR 0.45, 95% CI 0.27 to 0.77, p=0.003) • 71% less likely for citrate plus methylene blue plus methylparaben plus propylparaben (RR 0.29, 95% CI 0.12 to 0.72, p=0.008). **Safety:** Bleeding was 52% lower with citrate locks (RR 0.48, 95% CI 0.30 to 0.76, p=0.002). There was no difference for exit site infection, catheter removal for poor flow, need for thrombolytic treatment, duration of use, catheter-related readmission, catheter-related blood stream survival or all-cause death between the locks.	**Medium quality SR** Some included studies had small sample sizes.

5: Flow control devices

The RCN searched for evidence on: infusion flow control devices; infusion pumps; accurate delivery of intravenous or infusion therapy; incidents and patient safety. One SR[31] and 3 RCTs[23, 29, 30] were relevant for this section, and further details can be found in Table 7.

No evidence covered the following specific research questions identified by the RCN:

- What prognostic factors (for example, age, condition, therapy, care setting) affect the selection of different manual flow control devices on patient outcomes?
- How do different frequencies of flow rate monitoring of different manual flow control devices affect patient outcomes?
- What is the effect of electronic devices which generate flow through positive pressure or low pressure devices on patient safety and outcomes?

Other results from the literature identified were:

- Central venous catheter type:
  - A high quality RCT by Power et al. (2014)[23] found no difference in the long-term blood flow rate during haemodialysis between the twin permanent central venous haemodialysis catheters: LifeCath and TesioCath. However, LifeCath was associated with more complications requiring hospital admission.
  - A low quality RCT by Van der Meersch et al. (2014)[29] found that the Palindrome Symmetric Tip tunnelled cuffed catheter remained effective for the same length of time as the HemoStar catheter but blood flow rate was significantly higher (333.1ml/min Palindrome versus 303.8ml/min HemoStar, $p<0.001$) and fewer people required urokinase to unblock the catheter. Both were similar in terms of safety.
- Wound infusion:
  - A small high quality RCT by Bell et al. (2012)[30] found no significant benefit of 0.5% bupivacaine infusion into the wound following hiatus hernia repair compared to normal saline placebo in terms of pain relief.
- Intrathecal pain relief:
  - An SR by Hayek et al. (2011)[31] of medium quality found that intrathecal delivery of analgesia was moderately effective for people with cancer-related and non-cancer-related pain that had not fully responded to other methods of pain relief. The study designs were mainly observational which limits the reliability of the findings.

Table 7: Evidence table for flow control devices

Study	Participants	Intervention	Comparator	Outcomes	Quality
Bell et al. 2012[30] RCT	39 adults with laparoscopic hiatus hernia repair.	0.5% bupivacaine infusion to the diaphragm wound for five days (N=19).	0.9% sodium chloride infusion to the diaphragm wound for five days (N=20).	**Outcomes:** No difference in amount of postoperative oxycodone required for pain relief. **Safety:** Complications in the treatment group included difficulty swallowing, and hiccoughs.	**High quality RCT** Small number of participants reduced the power of the results.
Hayek et al. 2011[31] SR RCT=2 Non-RCT=19	One RCT and four observational studies of at least 25 people with cancer-related pain for more than six months.	Intrathecal drug delivery system for at least three months (N=NR).	Comprehensive medical management in the RCT. No comparator for observational studies (N=NR).	**Outcomes:** Intrathecal analgesia was moderately effective in controlling refractory pain, based on one high quality RCT. **Safety:** Moderately safe.	**Medium quality SR** Study designs do not make it possible to separate out the patient characteristics that make this a more useful treatment option and results are complicated by other concomitant pain relief.
	15 observational studies of at least 25 people with non-cancer-related pain for more than six months.	Intrathecal drug delivery system for at least 12 months (N=NR).	None.	**Outcomes:** Intrathecal analgesia was moderately effective in controlling refractory pain based on moderate quality of evidence. **Safety:** Moderately safe.	
Power et al. 2014[23] RCT	80 people requiring medium to long-term haemodialysis with a central venous catheter. Setting: single hospital.	LifeCath twin permanent haemodialysis catheter (N=41).	TesioCath twin permanent haemodialysis catheter (N=39).	**Outcomes:** LifeCath achieved the targeted blood flow rate of 450ml/min during the first session of haemodialysis (44% LifeCath versus 10% TesioCath, p=0.001). Both types of catheters achieved similarly adequate flow rates after the fourth session. Six people with LifeCath required infusions of urokinase to unblock them versus none in the TesioCath group (p=0.01). Two needed to be replaced with the standard TesioCath. **Safety:** Patient survival was similar in both groups. Central venous catheter complications requiring admission were more common in the LifeCath group (0.24 events per 1,000 catheter days versus 0.94 events, p=0.02).	**High quality RCT**

Study	Participants	Intervention	Comparator	Outcomes	Quality
Van der Meersch et al. 2014[29] RCT	239 people on haemodialysis requiring a tunnelled cuffed catheter. Setting: single hospital.	Palindrome Symmetric Tip Dialysis Catheter placements (N=151).	HemoStar Long-Term Haemodialysis Catheter placements (N=151).	**Outcomes:** Mean effective blood flow rate was significantly higher for the Palindrome catheter (333.1ml/min versus 303.8ml/min, p<0.001). There was no difference in the length of time the catheters remained effective between the two groups. Fewer people in the Palindrome group required urokinase (17 per 1,000 catheter-days vs. 35 for HemoStar, p<0.001). **Safety:** There was no difference in catheter-related infection rate between the two groups. Incidence of thrombosis was similar across the two groups.	**Low quality RCT** 63 people who had the catheter removed and required another one were eligible to participate again in the study.

6: Infusion-related blood stream infections

The RCN search covered: blood stream infection prevention, management and catheter associated blood stream infection. There were no specific RCN questions for this section.

All studies identified focused on blood stream infection prevention and details are in Table 8. Some of the studies are also reported in other relevant sections.

Flush and lock solutions:

- A medium quality SR by Zhao et al. (2014)[12] found that compared to heparin lock, the risk of catheter-related blood stream infection is similar for citrate locks, but 75% less likely for citrate plus gentamicin locks, 71% less likely for citrate plus methylene blue plus methylparaben plus propylparaben locks and 55% less likely for citrate plus taurolidine locks.
- A medium quality SR by Snaterse et al. (2010)[32] found that antibiotic-heparin and antibiotic-citrate lock solutions were more effective than heparin only in preventing catheter-related blood stream infections in haematology patients, with a number needed to treat of 3 to prevent one infection.
- A low quality RCT by Worth et al. (2014)[13] found no difference in rate of catheter-related blood stream infection between daily flush of central venous catheters with 10ml normal saline followed by 2ml of heparinised saline (50 units in 5ml), left for two hours before 5-10ml aliquot was aspirated and then the line locked under positive pressure, compared to the same regime but using 70% ethanol instead of heparinised saline.

Dressings:

- A high quality SR by Ullman et al. (2015)[2] found high quality evidence that chlorhexidine gluconate impregnated dressings and silver impregnated dressings reduce the risk of catheter-related blood stream infections compared to all other types of dressings (RR 0.60, 95% CI 0.39 to 0.93). Chlorhexidine gluconate impregnated dressings reduce the frequency of catheter-related blood stream infections compared to standard polyurethane dressings per 1,000 patient days and catheter tip colonisation. There was unclear evidence of any difference between different dressings for incidence of skin irritation or damage or failed securement.
- A high quality RCT by Timsit et al. (2012)[16] found that chlorhexidine dressings had a 60% lower rate of catheter-related blood stream infections than non-chlorhexidine dressings for central venous catheters.
- A low quality SR by O'Horo et al. (2014)[33] reported that small comparison studies did not find any difference between the antiseptics povidone-iodine, triclosan, 2% chlorhexidine, povidone-iodine and isopropyl alcohol though chlorhexidine impregnated dressings decreased the risk of infection for arterial catheters (though this was not specifically blood stream infections).
- A high quality SR by Mustafa et al. (2013)[5] identified one small retrospective cross-over study which found that use of the topical antimicrobial mupirocin for buttonhole arteriovenous cannulation reduced the risk of catheter-related blood stream infection by 6.4 compared to no use.

Central venous catheter protocol:

- A multicentre medium quality RCT by Marsteller et al. (2012)[34] found that a multifaceted ICU intervention reduced catheter-related blood stream infections by 81%, to less than one per 1,000 catheter days. The intervention incorporated a 5-item blood stream infection bundle:
  - hand washing before central venous catheter placement
  - full body drape, hat, gloves, mask and gown
  - avoiding femoral site
  - chlorhexidine to cleanse
  - removing unnecessary lines.

  The Comprehensive Unit-based Safety Program (CUSP) intervention was also implemented which centres around staff engagement with a particular focus on nursing staff:
  - educating staff – for example, a dressing change checklist for nurses
  - evaluating and improving systems
  - teamwork and communication.

Central venous catheter type:

- A medium quality SR and meta-analysis of before and after studies by Tabak et al. (2014)[4] found that central venous catheter associated blood stream infection rate was 67% lower for the Max-plus positive-displacement needle-less connector design compared to the negative- or neutral-displacement needle-less connector.
- A large high quality SR by Lai et al. (2013)[18] found that antimicrobial impregnation of central venous catheters reduced blood stream infection by 2% compared to non-impregnated catheters. There was no impact on sepsis or all-cause mortality.
- A medium quality SR by Wang et al. (2010)[17] found that adjusted heparin-bonded catheters and minocycline-rifampicin catheters were more effective at preventing catheter-related blood stream infections than standard catheters.
- A medium quality RCT by Antonelli et al. (2012)[19] found that central venous catheter-related blood stream infection rates were similar at 3.36 infections per 1,000 catheter days for AgTive silver-nanoparticle-impregnated central venous catheter versus conventional catheters. Colonisation rates were also similar at around 30% and there was no significant difference in ICU mortality rate.

- A high quality RCT by Ong et al. (2010)[21] found that proximal valve polyurethane PICCs had a similar incidence of catheter-related blood stream infection.
- A high quality small RCT by Power et al. (2014)[23] found no difference in the incidence of catheter-related blood stream infection between the TesioCath twin permanent haemodialysis central venous catheter and the LifeCath twin permanent haemodialysis central venous catheter.
- A low quality RCT by Van der Meersch et al. (2014)[29] found no difference in catheter-related blood stream infection rate between Palindrome Symmetric Tip tunnelled cuffed catheters and HemoStar Long-Term Haemodialysis tunnelled cuffed catheters.

Arterial catheter management:

- An SR of low quality by O'Horo et al. (2014)[33] found that femoral arterial catheters had double the risk of catheter-related blood stream infection compared to radial arterial catheters.
- A low quality RCT by Raurell-Torredà et al. (2014)[6] found that use of a non-waste needle-less setup or non-waste syringe setup for radial arterial catheters did not increase catheter-related blood stream infections.

Frequency of changing access device:

- A high quality SR by Ullman et al. (2013)[35] found that administration sets that do not contain lipids, blood or blood products may be left in place for up to 96 hours without increasing the risk of infection.
- A high quality SR by Daud et al. (2013)[8] found in one RCT that infusion-related blood stream infection was zero when the arterial catheter tubing was changed every two days compared to 1/58 (1.7%) when it was changed every four to eight days. The significance of the result was not reported but is likely to be non-significant due to the low numbers. Two other RCTs which looked at the timing of changing the administration set or flush solution did not report any cases of infusion-related blood stream infection.
- In a large high quality RCT by Rickard et al. (2012)[36], there was only one catheter-related blood stream infection out of 3,283 adults who were participating in a study comparing clinically indicated replacement of peripheral catheters or routine replacement on day 3. This meant that relative risk could not be calculated.

8: Evidence table for Infusion-related blood stream infections

Study	Participants	Intervention	Comparator	Outcomes	Quality
Antonelli et al. 2012[19] RCT	338 adults requiring central venous catheters Setting: five ICUs.	AgTive silver-nanoparticle-impregnated central venous catheter (N=135)	Conventional central venous catheter (N=137).	**Outcomes:** Colonisation rates were similar (32.6% for silver impregnated versus 30% for conventional, p=0.7). Catheter-related blood stream infection rates were the same for each type, 3.36 infections per 1,000 catheter-days. **Safety:** ICU mortality was similar in each group (46% silver catheter versus 43% conventional, p=0.7).	Medium quality RCT Also included in the central venous catheter section.
Daud et al. 2013[8] SR RCT=3 Non-RCT=3	120 critically ill adults with peripheral arterial catheters that have intra-arterial pressure monitoring. Setting: single ICU.	Administration set (the tubing attached to the peripheral arterial catheter) changed every four (N=19) or eight days (N=39).	Administration set changed every two days (N=62).	**Outcomes:** In the Luskin et al. 1986 RCT, 2/39 (5.1%) of patients who had an administration set for between four to eight days had an infusate colonisation compared to none in the group who had it changed every two days, but this was not significant (p>0.05). Infusion-related blood stream infection was 1/58 (1.7%) for administration set changed every four to eight days and 0/62 for those having it changed every two days (p=NR). **Safety:** NR	High quality SR
	30 critically ill adults with peripheral arterial catheters that have intra-arterial pressure monitoring. Setting: single hospital, multiple ICUs.	Group 1: change of flush solution and pressure-monitoring tubing every 24 hours (N=NR). Group 2: change of flush solution every 24 hours and tubing every 48 hours (N=NR). Group 3: change of flush solution and tubing every 48 hours (N=NR).	All groups compared with each other (N=NR).	**Outcomes:** In the Covey et al. 1988 RCT, there was no catheter-related blood stream infection or infusion-related blood stream infection in any of the three groups. **Safety:** NR	
	76 critically ill adults and children with peripheral arterial catheters that have intra-arterial pressure monitoring. Setting: single hospital.	Administration set changed every 72 hours (N=38).	Administration set changed every 48 hours (N=38).	**Outcomes:** The McLane et al. 1998 RCT, found stopcock colonisation was 3/26 (11.5%) for administration set change every 48 hours and 10/23 (43.5%) when changed every 72 hours (p<0.01). There was no infusate colonisation or catheter-related blood stream infection in either group. **Safety:** NR	

Study	Participants	Intervention	Comparator	Outcomes	Quality
Lai et al. 2013[18] SR RCT=56	16,512 catheters (N=NA). Settings: ICUs, haematological and oncology units.	11 types of antimicrobial central venous catheter impregnation (N=NA).	Non-impregnated catheter (N=NA).	**Outcomes:** Catheter impregnation significantly reduced: • catheter-related blood stream infection by 2% (ARR 2%, 95% CI 3% to 1%) • catheter colonisation by 10% (ARR 10%, 95% CI 13% to 7%). Catheter impregnation made no difference to: • Sepsis (RR 1.0, 95% CI 0.88 to 1.13) • all-cause mortality (RR 0.88, 95% CI 0.75 to 1.05). Sub-group analysis found that the benefits were more likely in the ICU setting, and less likely on haematology or oncology units, or for people on long-term TPN. **Safety:** No difference was found between impregnated and non-impregnated catheters in terms of: • thrombosis • thrombophlebitis • bleeding • erythema • tenderness at insertion site. Antimicrobial central venous catheters improve such outcomes as catheter-related blood stream infection and catheter colonization when used in ICUs. Unclear outcomes in other settings.	High quality SR

Study	Participants	Intervention	Comparator	Outcomes	Quality
Marsteller et al. 2012[34] RCT	45 ICUs performing central venous catheter insertion on adults. Settings: 35 hospitals.	Multifaceted intervention (N=23 ICUs): 5-item blood stream infection bundle: • hand washing before central venous catheter placement • full body drape, hat, gloves, mask and gown • avoiding femoral site • chlorhexidine to cleanse • removing unnecessary lines. CUSP intervention: • engaging staff • educating e.g. dressing change checklist for nurses • evaluate and improve • teamwork and communication.	Usual care (N=22 ICUs) for the first six months of the study. Then the intervention was implemented.	**Outcomes:** Central venous catheter blood stream infection rate per 1,000 catheter days: • after six months, reduced from 4.48 baseline to 1.33 in the intervention group and from 2.71 to 2.16 in the control group (adjusted incidence ratio 0.19, 95% CI 0.06 to 0.57, p=0.003) • by 19 months after the intervention started in the intervention group the level had reduced by 81% to less than one per 1,000 catheter days • by 12 months after it started in the control group, the level was <1 per 1,000 catheter days, a reduction of 69%. **Safety:** NR	**Medium quality RCT**
Mustafa et al. 2013[5] SR	Adults requiring intensive haemodialysis for more than three months of ≥5 times per week and/or ≥5.5 hours per day. Setting: home or hospital.	Arteriovenous fistula using buttonhole technique.	Arteriovenous fistula using rope-ladder cannulation.	Four case series reported that buttonhole rates of blood stream infection were 0.15 to 0.60 per 1,000 patient days and local infection rates were 0.01 to 0.16 per 1,000 patient days. There was no direct comparison available for rope-ladder cannulation rates. One study found that the rate ratio for any infection or other problem was 3.0 for buttonhole compared to rope-ladder cannulation (95% CI 1.04 to 8.66; p=0.04).	**High quality SR** Lack of studies performing direct comparison and low quality of studies included in SR.
		Topical antimicrobial prophylaxis for buttonhole cannulation.	No topical antimicrobial prophylaxis for buttonhole cannulation	A retrospective observational crossover study of 56 people found that the odds ratio for Staphylococcus aureus blood stream infection without topical mupirocin compared to with mupirocin was 6.4 (95% CI 1.3 to 32.3; p=0.02). No infections occurred when mupirocin was used but this was a small retrospective study.	

Study	Participants	Intervention	Comparator	Outcomes	Quality
O'Horo et al. 2014[33] SR RCT=7 Non-RCT=42	35,465 arterial catheters in neonates, children and adults. Setting: 42 studies in ICUs, seven post-surgery.	Incidence of arterial catheter-related infection according to site and management regime (N=NR).	NA	**Outcomes:** Pooled comparison studies found: • femoral arterial catheters had double the risk of catheter-related blood stream infection compared to radial arterial catheters (RR 1.94, 95% CI 1.32 to 2.84, p=0.001). Site cleaning: • no infections reported in one study comparing povidone-iodine with triclosan solution plus regular site cleaning and transparent dressing • One RCT found no difference between 2% chlorhexidine, povidone-iodine and isopropyl alcohol for arterial catheter infections. Maintenance: • the results of two comparison studies found that chlorhexidine impregnated dressings decreased the risk of infection for arterial catheters. **Safety:** NR	**Low quality SR**
Ong et al. 2010[21] RCT	326 adults with PICCs by interventional radiologists. Setting: single hospital.	PVP PICC under ultrasound guidance (N=198).	DVS PICC under ultrasound guidance (N=194).	**Outcomes:** The PVP lasted on average for longer at a mean of 27.8 days compared to 23.3 days for the DVS. There was no significant difference in catheter-related blood stream infection at 1% PVP versus 2.6% DVS for definite infections (p=NR). **Safety:** Less complications occurred with PVP at 26.8% compared to 47.9% for DVS (p<0.001). There was no difference for catheter occlusion, fracture or dislodgement.	**High quality RCT**

Study	Participants	Intervention	Comparator	Outcomes	Quality
Power et al. 2014[23] RCT	80 people requiring medium to long-term haemodialysis with a central venous catheter. Setting: single hospital.	LifeCath twin permanent haemodialysis central venous catheter (N=41).	TesioCath twin permanent haemodialysis central venous catheter (N=39).	**Outcomes:** Catheter-related blood stream infection was similar for TesioCath versus LifeCath (0.40 versus 0.51 per 1,000 catheter days, p=0.7). LifeCath achieved the targeted blood flow rate of 450ml/min during the first session of haemodialysis (44% LifeCath versus 10% TesioCath, p=0.001). Both types of catheters achieved similarly adequate flow rates after the fourth session. Six people with LifeCath required infusions of urokinase to unblock them versus none in the TesioCath group (p=0.01). 2 LifeCath needed to be replaced with the standard TesioCath. **Safety:** Patient survival was similar in both groups. Central venous catheter complications requiring admission were more common in the LifeCath group (0.94 events per 1,000 catheter days versus 0.24 events, p=0.02).	**High quality RCT** Small number of participants.
Raurell-Torredà et al. 2014[6] RCT	814 critical patients with a radial arterial catheter requiring hourly blood glucose monitoring for intensive insulin therapy (IIT). Setting: single ICU.	Non-waste needle-less setup or non-waste syringe setup. (N=90) Non-waste method was used for all samples; reinfusing blood aspirated prior to the sample being taken.	Standard set-up with fingertip blood glucose monitoring (N=724).	**Outcomes:** Catheter-related blood stream infection did not occur in the intervention group. There were two cases in the control group but this was not significant. Blood glucose levels could be effectively measured using samples from the arterial catheter compared to standard fingertip blood glucose monitoring. This avoided the pain from fingertip sampling. **Safety:** Returning the clearing volume of blood was estimated to reduce procedure-related blood loss by 50%. Negligible arterial catheter complications.	**Low quality RCT**

Study	Participants	Intervention	Comparator	Outcomes	Quality
Rickard et al. 2012[36] RCT	3,283 adults expected to have a peripheral venous catheter for longer than four days. Setting: three hospitals.	Clinically indicated replacement of peripheral catheter (N=1,593).	Routine peripheral catheter replacement on day 3 (N=1,690).	**Outcomes:** There was only one catheter-related blood stream infection which occurred in the routine replacement group. Due to the low incidence it was not possible to estimate the relative risk. The average mean length of time that catheters stayed in without the clinical need for removal was 99 hours compared to 70 hours when removed on day 3 regardless of clinical need. Each group required a similar number of hours of intravenous therapy, but the group in which the catheter was changed based on clinical need used a fifth less catheters: clinical need average 1.7 catheters compared to 1.9 catheters, difference = 0.21 catheters (95% CI 0.13 to 0.29; p<0.0001). **Safety:** Phlebitis occurred at 7% in both groups and there were no serious adverse events.	**High quality RCT**

Snaterse et al. 2010[32]
SR
RCT=16
	1,358 catheters in adults, children and neonates with central venous catheters for intermittent use.
	Settings: oncology, haematology, neonatal unit.
		Antibiotic based lock solutions (N=670).	Heparin lock solution (N=688 catheters).	**Outcomes:**
				• Oncology patient trials:
				  • weak evidence on the effectiveness of vancomycin, amikacin or ciprofloxacin compared to heparin for infection rates.
				• Haematology patient trials:
				  • antibiotic-heparin and antibiotic-citrate lock solutions were more effective than heparin only in preventing catheter-related blood stream infection per 1,000 catheter days (incidence density difference 1.96, 95% CI 2.63 to 1.30, p=0.09). NNT to prevent one infection was 3, if mean insertion of catheter was 146 days and average baseline risk of infection was three per 1,000 catheter days. It was not possible to determine which antibiotic was best.
				Safety:
				NR
					Medium quality SR

Study	Participants	Intervention	Comparator	Outcomes	Quality
Tabak et al. 2014[4] SR and Meta-analysis RCT=0 Non-RCT=7	Adults, children and neonates (N=NR). Settings: ICU, home, long-term acute care.	Positive-displacement needle-less connector for central venous catheters (N=95,383 catheter days).	Negative- or neutral-displacement needle-less connector for central venous catheters (N=111,255 catheter days).	**Outcomes:** Central venous catheter associated blood stream infection rate was 67% lower for the Max-plus positive-displacement needle-less connector design at 0.5 events per 1,000 central venous line days compared to 1.5 events for the comparator (RR 0.37, 95% CI 0.16 to 0.90). **Safety:** NR	**Medium quality SR** Meta-analysis reliant on before and after studies.
Timsit et al. 2012[16] RCT	1,879 people with central venous catheters expected to be in place for at least 48 hours. Setting: 12 ICUs.	Chlorhexidine dressings (N=938).	Non-chlorhexidine dressings (N=941).	**Outcomes:** Chlorhexidine dressings had 67% lower rates of major catheter-related infections compared to non-chlorhexidine dressings at 0.7 versus 2.11 per 1,000 catheter days (HR 0.328, 95% CI 0.174 to 0.619, p=0.0006). Chlorhexidine dressings were estimated to prevent one major catheter-related infection for every 71 catheters left for an average of ten days. Chlorhexidine dressings also had a 60% lower rate of catheter-related blood stream infections at 0.5 compared to 1.3 per 1,000 catheter days for non-chlorhexidine dressings (HR 0.402, 95% CI 0.186 to 0.868, p=0.02). Catheter colonisation was 59% lower with chlorhexidine dressings at 4.3 compared to 10.9 per 1,000 catheter days (HR 0.412, 95% CI 0.306 to 0.556, p<0.0001). **Safety:** NR	**High quality RCT**

Study	Participants	Intervention	Comparator	Outcomes	Quality
Ullman et al. 2015[2] SR RCT=22	7,436 participants with a central venous catheter. Setting: ICUs, haematological units, general hospitals and home.	Comparison of nine different types of securement devices and dressings.	NA	**Outcomes:** Chlorhexidine gluconate impregnated dressings and silver impregnated dressings reduce the risk of catheter-related blood stream infections compared to all other types of dressings (RR 0.60, 95% CI 0.39 to 0.93). This was rated as high quality evidence. Chlorhexidine gluconate-impregnated dressings reduce the frequency of catheter-related blood stream infections compared to standard polyurethane dressings per 1,000 patient days (RR 0.51, 95% CI 0.33 to 0.78) and catheter tip colonisation (RR 0.58, 95% CI 0.47 to 0.73). **Safety:** No clear evidence of a difference between gauze and tape, chlorhexidine gluconate, standard polyurethane dressings and sutureless securement devices for incidence of skin irritation or damage or failed securement.	**High quality SR** This SR includes the RCT by Timsit et al. 2012.
Ullman et al. 2013[35] SR RCT=16	5,001 neonates and adults with an intravenous or arterial access device. Setting: Nine on ICUs, multiple other settings.	Several different frequencies of administration set change (N=NR).	Several different frequencies of administration set change (N=NR).	**Outcomes:** Administration sets that do not contain lipids, blood or blood products may be left in place for up to 96 hours without increasing the risk of infection. **Safety:** Low quality evidence indicated that neonatal mortality is increased by infrequent administration set change.	**High quality SR** Most studies were of low quality.
Van der Meersch et al. 2014[29] RCT	239 people on haemodialysis requiring a tunnelled cuffed catheter. Setting: single hospital.	Palindrome Symmetric Tip Dialysis Catheter placements (N=151).	HemoStar Long-Term Haemodialysis Catheter placements (N=151).	**Outcomes:** Mean effective blood flow rate was significantly higher for the Palindrome catheter (333.1ml/min versus 303.8ml/min, p<0.001). There was no difference in the length of time the catheters remained effective between the two groups. Fewer people in the Palindrome group required urokinase (17 per 1000 catheter-days vs. 35 for HemoStar, p<0.001). **Safety:** There was no difference in catheter-related infection rate or catheter-related blood stream infection rate between the two groups. Incidence of thrombosis was similar across the two groups.	**Low quality RCT** 63 people who had the catheter removed and required another one were eligible to participate again in the study.

Study	Participants	Intervention	Comparator	Outcomes	Quality
Wang et al. 2010[17] SR RCT=48	12,828 central venous catheters in 11,525 people.	Any of the following types of venous catheters (N=NR): • silver alloy-coated • silver-impregnated • adjusted silver iontophoretic catheters • chlorhexidine and silver sulfadiazine catheters • chlorhexidine and silver sulfadiazine blue plus catheters • minocycline-rifampicin catheters • miconazole-rifampicin catheters • adjusted heparin-bonded catheters • benzalkonium chloride.	Standard central venous catheters (N=NR)	**Outcomes:** The following had a lower rate of catheter colonisation compared to standard catheters: • adjusted silver iontophoretic catheters (OR 0.58, 95% CI 0.33 to 0.95, p=0.043) • chlorhexidine and silver sulfadiazine catheters (OR 0.49, 95% CI 0.36 to 0.64, p<0.001) • chlorhexidine and silver sulfadiazine blue plus catheters (OR 0.37, 95% CI 0.17 to 0.69, p=0.005) • minocycline-rifampicin catheters (OR 0.28, 95% CI 0.17 to 0.43, p<0.001) • miconazole-rifampicin catheters (OR 0.11, 95% CI 0.02 to 0.33, p=0.005). Compared to standard catheters, prevention of catheter-related blood stream infections was lower for: • Adjusted heparin-bonded catheters (OR 0.20, 95% CI 0.06 to 0.44, p=0.002) • Minocycline-rifampicin catheters (OR 0.18, 95% CI 0.08 to 0.34, p<0.001). **Safety:** NR	Medium quality SR
Worth et al. 2014[13] RCT	85 adults with a haematological malignancy. Setting: single haematology and bone marrow transplant unit.	Daily flush of central venous catheter with 10ml normal saline followed by 2ml of heparinised saline (50 units in 5ml) and left for two hours, before 5-10ml aliquot was aspirated and then the line locked under positive pressure (N=43).	Daily flush of central venous catheter with 10ml normal saline followed by 2ml of 70% ethanol and left for two hours, before 5-10ml aliquot was aspirated and then the line locked under positive pressure (N=42).	**Outcomes:** There was no difference between the types of flush and rate of catheter-related blood stream infection, thrombosis, exit-site infection or tunnel/pocket infection. **Safety:** Three patients reported chest discomfort with the ethanol flush and one reported nausea but this was not enough people to be of statistical significance.	High quality RCT

Study	Participants	Intervention	Comparator	Outcomes	Quality
Zhao et al. 2014[12] SR RCT=13	1,770 adults with a central venous catheter for haemodialysis. Settings: multiple.	Citrate lock for central venous catheter with or without an antimicrobial (gentamicin, taurolidine or methylene blue plus methylparaben plus propylparaben) (N=NR).	Heparin lock for central venous catheter (N=NR).	**Outcomes:** Subgroup analysis found that compared to heparin lock, the risk of catheter-related blood stream infection is: • similar for citrate alone (RR 0.54, 95% CI 0.22 to 1.30, p=0.2) • 75% less likely for citrate plus gentamicin (RR 0.25, 95% CI 0.13 to 0.47, p<0.001) • 55% less likely for citrate plus taurolidine (RR 0.45, 95% CI 0.27 to 0.77, p=0.003) • 71% less likely for citrate plus methylene blue plus methylparaben plus propylparaben (RR 0.29, 95% CI 0.12 to 0.72, p=0.008). **Safety:** Bleeding was 52% lower with citrate locks (RR 0.48, 95% CI 0.30 to 0.76, p=0.002). There was no difference between the locks for exit site infection, catheter removal for poor flow, need for thrombolytic treatment, duration of use, catheter-related readmission, catheter-related blood stream survival or all-cause death.	**Medium quality SR** Some included studies had small sample sizes.

7: Infusion therapy parenteral nutrition

The RCN search covered: parenteral nutrition (PN); TPN; home PN; infection prevention and control; management of PN; sponges and PN and dedicated lines. Two SRs[37, 41] and seven RCTs[38-40, 42-45] were relevant for this section, though no evidence was found for the RCN questions:

- What is the effect of different frequencies of change of PN administration sets and add-on devices on patient safety and outcomes?
- What is the performance of nutrition screening tools to assess nutritional status?
- What is the effect of different ways of monitoring for metabolic-related complications and electrolyte imbalances and catheter-related complications on patient safety and outcomes?

The studies covered the following topics:

- Hand hygiene:
  - One low quality SR by Dreesen et al. 2013[37] highlighted the importance of hand hygiene and training for home PN as gram positive human skin flora caused the most infections across a large number of observational studies.
- Initiation of parenteral nutrition on the ICU:
  - One high quality RCT by Casaer et al. 2011[38] found that starting PN within 48 hours of admission to the ICU in addition to enteral nutrition was associated with staying in the ICU for an extra day and a longer overall hospital admission than people who started PN after eight days on the ICU. People were more likely to be discharged from the ICU within eight days if they did not have PN. Early PN was also associated with an increased risk of infections such as of the lung and airways and wound infections.
  - A high quality RCT by Doig et al. 2013[39] found no difference in 60 day mortality if PN was started on admission to the ICU compared to standard care, where parenteral or enteral nutrition was given around day 2 or not at all. Early PN was associated with half a day less time on mechanical ventilation.
  - A small, low quality RCT by Justo Meirelles et al. 2011[40] did not find any significant difference in mortality between giving parenteral or enteral nutrition to adults admitted to the ICU following traumatic head injury – both were effective routes.
- Parenteral nutrition supplements:
  - A medium quality SR by Palmer et al. 2013[41] found that omega-3 fatty acid supplementation of PN did not improve mortality, infectious complications or length of ICU stay for critically ill adults.
  - A high quality RCT by Klek et al. 2013[42] found no difference between PN based on an emulsion of soybean oil, medium-chain triglycerides, olive oil, fish oil and vitamin E compared to a soybean emulsion in terms of tolerability, outcomes or safety.
  - A small RCT of medium quality by Theilla et al. 2012[43] found that parenteral or enteral nutrition enriched with fish oil slightly slowed the progression of pressure ulcers over the course of 28 days. However, the study did not show that fish oil helped to heal pressure ulcers.
  - A RCT by Umpierrez et al. 2012[44] of high quality found no difference between soybean based and olive oil based PN in terms of mortality or length of hospital stay for 100 critically ill adults on and ICU.
  - A small, low quality RCT by Siqueira et al. 2011[45] found that soybean based PN may increase systolic blood pressure but that olive oil based PN may lower it. This was based on a randomised crossover trial of 12 healthy adults which limits the reliability of the results.

Table 9: Evidence table for infusion therapy parenteral nutrition

Study	Participants	Intervention	Comparator	Outcomes	Quality
Casaer et al. 2011[38] RCT	4,640 adults admitted to ICUs and receiving enteral nutrition. Setting: Seven ICUs.	PN initiated within 48 hours after admission to the ICU (N=2312).	PN not started until after eight days on the ICU (N=2328).	**Outcomes:** Early initiation of PN was associated with a longer stay in ICU of one day (four days versus three days, p=0.02) and longer overall hospital stay (16 days versus 14 days, p=0.004). A higher proportion of people left the ICU alive within eight days who had not started early PN (75.2% versus 71.7%, p=0.007). **Safety:** Early initiation of PN was associated with increased infections such as of the airway or lung (19.3% of cases versus 16.4% of cases, p=0.009) and wound infections (4.2% versus 2.7%, p=0.006).	**High quality RCT**
Doig et al. 2013[39] RCT	1,372 adults admitted to ICUs. Setting: 31 ICUs.	PN started on average 44 minutes after enrolment into the study (N=686).	Standard care (N=686). This was either enteral (N=199) or parenteral (N=186) nutrition and was started on average 2.8 days after admission to the ICU. 278 people did not have either.	**Outcomes:** There was no difference in mortality at 60 days (22.8% standard care versus 21.5% early PN, p=0.60). **Safety:** Early PN was associated with fewer days of invasive ventilation (0.47 days per ten patient X ICU days, 95% CI 0.82 to 0.11, p=0.01).	**High quality**
Dreesen et al. 2013[37] SR RCT=1 Non-RCT=38	Participants from 39 mostly observational studies. Setting: multiple.	Incidence rate of PN catheter-related blood stream infection (N=NR).	NA	**Outcomes:** Catheter-related blood stream infection rate for people on home PN ranged between 0.38 and 4.58 episodes per 1,000 catheter days. Gram positive human skin flora caused most infections for home PN so hand hygiene and training remain essential. Risk factors identified were: • related to the patient • venous access device • education • home parenteral nutrition therapy • follow-up. **Safety:** NR	**Low quality SR** Most included studies were of low quality.

Study	Participants	Intervention	Comparator	Outcomes	Quality
Justo Meirelles et al. 2011[40] RCT	22 adults with moderate total brain injury. Setting: single ICU.	PN started as soon as haemodynamically stable (N=10).	Enteral nutrition started as soon as haemodynamically stable (N=12).	**Outcomes:** Both routes are effective in providing nutritional therapy with no significant difference in outcomes and the same mortality rate (10% for PN versus 8.3% for enteral nutrition, p=1.00). Mean length of stay in the ICU was 14 days for each group. **Safety:** There were more cases of infections in the PN group (40% versus 16.7%, p=NR).	Low quality RCT
Klek et al. 2013[42] RCT	73 adults with stable intestinal failure. Setting: multiple in several different countries.	Soybean/MCT/olive/fish oil emulsion in long-term PN (N=34).	Soybean oil based emulsion in long-term PN (N=39).	**Outcomes:** The emulsion of four oils was tolerated and safe. **Safety:** Similar rates of adverse events occurred in each group and were unrelated to the study treatments.	High quality RCT
Palmer et al. 2013[41] SR RCT=8	391 critically ill adults on ICUs. Setting: ICUs.	Omega-3 fatty acid supplementation of PN (N=217).	PN without omega-3 fatty acid supplementation (N=214).	**Outcomes:** Omega-3 fatty acid supplementation of PN was not shown to improve mortality (RR 0.83, 95% CI 0.57 to 1.20, p=0.32). There was also no difference in length of ICU stay (difference of 0.57 days, 95% CI 5.05 to 3.90, p=0.80), but the results from three trials found that omega-3 supplementation reduced length of hospital stay by 9.49 days (95% CI 16.51 to 2.47, p=0.008). **Safety:** There was no difference between the groups for the rate of new infectious complications (RR 0.78, 95% CI 0.43 to 1.41, p=0.41).	Medium quality SR
Siqueira et al. 2011[45] RCT	12 healthy adults who were given each type of PN over a 24 hour period. Setting: single hospital.	Lipid-free PN (N=12). Soybean based PN (N=12). Olive oil based PN (N=12).	24 hour infusion of normal saline (N=12).	**Outcomes:** Soybean oil-based PN increased systolic blood pressure from baseline by 11.6mm Hg (±16.5, p=0.04) at 12 hours into the infusion. Olive oil based PN reduced systolic blood pressure by 8.3mm Hg (±10.6, p=0.02) at 12 hours. Diastolic blood pressure was not affected. Lipid-free PN and normal saline had no effect on blood pressure. **Safety:** No adverse events reported.	Low quality RCT Small study of healthy adults.

Study	Participants	Intervention	Comparator	Outcomes	Quality
Theilla et al. 2012[43] RCT	40 adults with pressure ulcers of grade 2 or higher on parenteral or enteral feeding for between seven and 28 days. Setting: single ICU.	Parenteral or enteral feeding formula enriched with fish oil (N=20).	Control parenteral or enteral feeding formula (N=20).	**Outcomes:** Parenteral or enteral nutrition enriched with fish oil slightly slowed the progression of pressure ulcers according to the Pressure Ulcer Scale for Healing (PUSH) tool. This ranges from 0 (healed) to 17 (worst score). People receiving fish oil had a baseline score of 9.10 which increased to 9.40 by day 28, compared to the control group which started at 9.25 and increased to 10.75 (p=0.2). **Safety:** NR	Medium quality RCT
Umpierrez et al. 2012[44] RCT	100 critically ill adults. Setting: single ICU.	Soybean oil-based PN for 12.9±8 days (N=49).	Olive oil-based PN for 12.9±8 days (N=51).	**Outcomes:** No difference for length of hospital stay or mortality. **Safety:** Similar rates of complications.	High quality RCT

8: Infusion therapy phlebitis

The RCN search covered: phlebitis; inflammation of the vein; definition of phlebitis; mechanical phlebitis; chemical phlebitis; infective phlebitis; causes of phlebitis; indications for phlebitis monitoring in peripheral access devices; midlines; central access devices; PICCs; incidence and prevalence of phlebitis. One SR[47] and four RCTs[36, 46, 48] examined an aspect of phlebitis.

One RCT was identified which was relevant for the following RCN question:

- What is the effect of monitoring vascular access sites for phlebitis on patient safety and outcomes?
  - One high quality RCT by Rickard et al. (2012)[36] found that the incidence of phlebitis was 7% whether peripheral intravenous catheters were replaced routinely every three days or replaced according to clinical indications.

No evidence covered the following specific research questions identified by the RCN:

- What is the impact of different phlebitis severity/degree on patient safety and outcomes?

Other results from the literature identified were:

- Central intravenous catheter types:
  - A high quality RCT by Ong et al. (2010)[21] found that the rate of phlebitis for PVP PICCs was half that for DVS PICCs.
- Peripheral intravenous catheter types:
  - A medium quality RCT by González López et al. (2014)[46] found that phlebitis was significantly less likely to occur with closed-system peripheral intravenous catheters compared to open-system peripheral intravenous catheters.
- Phlebitis assessment:
  - A low quality SR by Ray-Barruel et al. (2014)[47] found 71 different phlebitis assessment scales, none of which have been thoroughly validated. The researchers concluded that this may impede reporting and comparison rates.
- Catheter care station:
  - A high quality RCT by Loftus et al. (2012)[48] found that use of a designated "catheter care station" in operating rooms reduced the combined rate of phlebitis and health care associated infection by 30 days post-op compared to conventional care. This station included novel equipment caps which were not yet approved by the FDA. There was no change in risk when looking at rates of phlebitis on their own.

Table 10: Evidence for infusion therapy phlebitis

Study	Participants	Intervention	Comparator	Outcomes	Quality
González López et al. 2014[46] RCT	642 adults on general medical and surgical wards. Setting: single hospital.	Closed-system (COS) peripheral intravenous catheter (N=584 catheters).	Open-system (MOS) peripheral intravenous catheter (N=599 catheters).	**Outcomes:** MOS catheters were significantly more likely to be inserted with fewer attempts (76.3% first time for MOS versus 66% for COS; p=0.001). COS catheters stayed in place for longer, median indwell time 137.1 hours versus 96 hours for MOS (p=0.001). **Safety:** MOS was less likely to cause a rupture of the vein during insertion (4.4% of MOS cases versus 12% for COS cases; p<0.001). Phlebitis was significantly less likely with COS (12% of COS cases versus 17% of MOS cases, p=0.004). Bacterial colonisation and catheter-related infection rates were similar in both groups. There were no needlestick injuries in either group.	**Medium quality RCT** Nurses were more familiar with using MOS catheters which may have biased results.
Loftus et al. 2012[48] RCT	Adults undergoing general anaesthesia Settings: 572 operating rooms	Conventional open lumen with novel catheter care bundle (HubScrub and DOCit). The intervention aimed to passively improve compliance with current IV recommendations by having a designated catheter care station. The HubScrub cap cleans needle-less closed and open lumen connectors with isopropyl alcohol and DOCit caps have scrubs on them to decontaminate iv tubing and syringes. (The systems did not have FDA approval at the time of the study). (N=266 operating rooms)	Conventional open lumen three-way stopcock set with standard caps (N=306 operating rooms).	**Outcomes:** Combined incidence of health care associated infection and phlebitis by 30 days post-op was reduced by the catheter care station when adjusted for patient and procedural covariates (adjusted OR 0.589, 95% CI 0.353 to 0.984, p=0.040). Neither rate of phlebitis nor health care associated infection on their own was statistically significantly different across the two groups. **Safety:** The catheter care station reduced stopcock lumen contamination by nearly a third compared to the conventional care (adjusted OR 0.703, 95% CI 0.498 to 0.995, p=0.047).	**High quality RCT** The study was partly funded by the manufacturers of HubScrub and DOCit.

Study	Participants	Intervention	Comparator	Outcomes	Quality

Ong et al. 2010[21]
RCT
	326 adults with PICCs by interventional radiologists.
	Setting: single hospital.
		PVP PICC under ultrasound guidance (N=198).	DVS PICC under ultrasound guidance (N=194).	**Outcomes:**
				The PVP lasted on average for longer at a mean of 27.8 days compared to 23.3 days for the DVS and was superior for:
				• catheter-related infection:
				  • 2% PVP versus 6.2% DVS (p=0.043)
				• phlebitis:
				  • 11.6% PVP versus 23.2% DVS (p=0.003).
				Safety:
				Less complications occurred with PVP at 26.8% compared to 47.9% for DVS (p<0.001).
				There was no difference for catheter occlusion, fracture or dislodgement.
					High quality RCT

Ray-Barruel et al. 2014[47] SR	233 studies of infusion-related phlebitis in adults. Setting: multiple.	Infusion phlebitis assessment.	NA	**Outcomes:** 71 different phlebitis assessment scales were identified, three have had some psychometric analyses but none have been rigorously tested. Infusion phlebitis was the primary outcome measure in 233 identified studies. 180 measured incidence and/or severity of which 101 used a scale and 79 used a definition.	Low quality SR
Rickard et al. 2012[36] RCT	3,283 adults expected to have a peripheral venous catheter for longer than four days. Setting: three hospitals.	Clinically indicated replacement of peripheral catheter (N=1593).	Routine peripheral catheter replacement on day 3 (N=1690).	**Outcomes:** The average mean length of time that catheters stayed in without the clinical need for removal was 99 hours compared to 70 hours when removed on day three regardless of clinical need. Each group required a similar number of hours of intravenous therapy, but the group in which the catheter was changed based on clinical need used a fifth less catheters: clinical need average 1.7 catheters compared to 1.9 catheters, difference = 0.21 catheters (95% CI 0.13 to 0.29; p<0.0001). **Safety:** Phlebitis occurred at 7% in both groups and there were no serious adverse events.	High quality RCT

9: Intraosseous access

The RCN search covered: intraosseous access; intraosseous sampling from intraosseous sites; management of intraosseous infusion; evidence regarding the safety and effectiveness of intraosseous access. This search identified one SR[50] and one low quality RCT[49] which, although included in the SR, is included in this section as pertinent outcomes were not reported in the SR.

One RCT was identified which was relevant for the following RCN question:

- What is the effect of site selection on patient safety and outcomes?
    - A low quality RCT by Reades et al. (2011)[49], found that gaining tibial intraosseous access was more initially successful than humeral intraosseous access (95% versus 71%) when performed by paramedics on adults with out of hospital non-traumatic cardiac arrests. Both were more successfully achieved first time than peripheral venous access (49%).

No evidence covered the following specific research questions identified by the RCN:

- What is the effect of different durations of intraosseous access device on patient safety and outcomes?
- What is the effect of different durations of intraosseous ports on patient safety and outcomes?
- What is the effect of different intraosseous devices on patient safety and outcomes?
- What is the effect of site management after removal of the intraosseous device?

Other results from the literature identified were:

- Intraosseous versus intravenous route:
    - In the RCT by Reades et al. (2011)[49], both tibial and humeral intraosseous access were more successfully achieved first time than peripheral venous access (49%). The time to successful access was significantly quicker for tibial intraosseous access (4.6min) compared to humeral intraosseous access (7.0min), ($p<0.001$), but neither was significantly different to peripheral intravenous access (5.8min). Intravenous dislodgement occurred at a similar rate to tibial intraosseous access at 6%.
    - In the high quality SR by Ker et al. (2015)[50], failure to achieve access was three times more likely in adults for intravenous access compared to intraosseous access and over 20 times more likely in infants. Dislodgement was twice as likely with the intraosseous route, but more fluids can be given intravenously.

Table 11: Evidence table for intraosseous access

Study	Participants	Intervention	Comparator	Outcomes	Quality
Ker et al. 2015[50, 59] SR RCT=2	60 infants aged 30 months to two years with severe dehydration due to diarrhoea and/or vomiting. 182 adults with non-traumatic out-of-hospital cardiac arrest (Reades, 2011). Setting: emergency department and out of hospital.	Intraosseous access (N=115 adults, N=30 infants).	Intravenous access (N=67 adults, N=30 infants).	**Outcomes:** Intraosseous access may be easier and quicker than intravenous, but larger volumes of fluid can be given with the intravenous route. Failure to achieve access was three times more likely in adults for intravenous access compared to intraosseous access (risk ratio [RR] 3.24, 95% CI 2.00 to 5.27; p<0.0001). Failure to achieve access was over 20 times more likely in infants for intravenous access compared to intraosseous access (RR 21.00, 95% CI 1.29 to 342.93, p=0.03). **Safety:** Dislodgement was more likely with the intraosseous route (113 per 1,000 versus 60 per 1,000). One RCT found no statistically significant difference in incidence of bacteraemia between the two groups.	**High quality SR** Based on low to moderate RCTs.
Reades et al. 2011[49] RCT	182 adults with a non-traumatic out-of-hospital cardiac arrest attended by paramedics. Setting: out of hospital.	Tibial intraosseous access (N=64) or humeral intraosseous access (N=51).	Peripheral intravenous access (N=67).	**Outcomes:** First attempt success was significantly more likely with tibial intraosseous access (95%) compared to humeral intraosseous access (71%) or peripheral venous access (49%), (p<0.001). The time to successful access was significantly quicker for tibial intraosseous access (4.6min) compared to humeral intraosseous access (7.0min), (p<0.001), but neither was significantly different to peripheral intravenous access (5.8min). The peripheral intravenous access group had double the amount of fluid administered, 800ml compared to 400ml for intraosseous routes (p<0.001). **Safety:** Humeral intraosseous access was most likely to be displaced, which occurred in 20% compared to 5% of tibial intraosseous access and 6% of peripheral intravenous access.	**Low quality RCT** This RCT was included in the Ker SR above, but with more detailed relevant outcomes. It was not clear whether the increased amount of fluid given via peripheral intravenous access was confounded by different hospital transport times or outcomes such as patients pronounced dead at the scene following resuscitation attempts.

10: Midline catheters

The RCN search identified one RCT by Caparas et al. Jan 2014[51] on the use of midline catheters. This RCT compared the safety of midline catheters with PICCs for vancomycin infusion. This type of infusion has a low pH of 3.9, so was recommended by US nursing guidelines to be given through central lines. The small, low quality RCT concluded that vancomycin could be given safely through midline catheters. There were a similar number of complications in each group though none had phlebitis or thrombosis. Midline catheter complications included dislodgement, infiltration and leaking.

No evidence covered the following specific research questions identified by the RCN:

- What are the effects of different line flushing frequencies for midline catheters on patient safety and outcomes?
- What are the effects of flushing lines with saline versus heparinised solutions for midline catheters on patient safety and outcomes?
- What are the effects of different veins being used in terms of patient safety and outcomes?
- What is the effect of site selection on patient safety and outcomes?

Table 12: Evidence table for midline catheters

Study	Participants	Intervention	Comparator	Outcomes	Quality
Caparas et al. Jan 2014[51] RCT	54 adults due to receive more than 1 dose of vancomycin and less than six days of treatment. Setting: single hospital.	Vancomycin 4mg/ml once or twice daily infusion using a midline catheter device (N=29).	Vancomycin 4mg/ml once or twice daily through a PICC (N=25).	Outcomes: NR Safety: Total complications occurred at a similar level in each group (17.9% PICC versus 19.9% midline) but there were no cases of phlebitis or thrombosis. One person with a PICC had a suspected catheter-associated blood stream infection, and four had dislodgement. Midline catheter complications were infiltration in three people, dislodgement in two and leak in one.	Low quality RCT

11: Peripheral access device and flushing

The RCN search focused on finding the evidence for the most effective and safe frequency and solution for flushing peripheral access devices. From the search, two SRs[8, 54] and four RCTs[36, 46, 52, 53] met the inclusion criteria.

There was limited evidence from two of the RCTs to answer the following specific RCN research question:

- What are the effects of flushing lines with saline vs heparinised solutions for peripheral access devices on patient safety and outcomes?
  - One high quality RCT by Bertolino et al. 2012[52] found that flushing peripheral venous catheters twice per day with 3ml of 100 IU heparin/ml caused significantly fewer cases of phlebitis or occlusion compared to flushing with normal saline. The catheters lasted longer in the heparin group and the patients required on average two rather than three cannulas during their hospital admission. There were no cases of bleeding or heparin-induced low platelets, but people were excluded from the study if they were at risk of bleeding. The participants were adults admitted to hospital for a variety of medical conditions so the results are generalizable.

No evidence covered the following specific research questions identified by the RCN:

- What are the effects of different line flushing frequencies for peripheral access devices on patient safety and outcomes?
- What are the effects of different veins being used in terms of patient safety and outcomes?
- What is the effect of site selection on patient safety and outcomes?

Other results from the literature identified were:

- Duration of peripheral device:
  - A large, high quality RCT by Rickard et al (2012)[36] found that significantly fewer peripheral venous catheters were required if they are changed based on clinical indication rather than routinely on day three. This caused no increase in side effects such as phlebitis.
  - A high quality SR by Daud et al. (2013)[8] identified three small RCTs regarding the optimum duration of arterial catheter administration sets. Results were inconclusive.
- Type of peripheral device:
  - A medium quality large RCT by González López (2014)[46] found that open-system peripheral intravenous catheters were more likely to be inserted first time and less likely to rupture a vein than closed system catheters. However, closed-system catheters stayed in place for longer and caused less cases of phlebitis. Bacterial colonisation and catheter-related infection rates were similar in both groups. Nurses were more familiar with inserting open-system catheters which may have affected the results.
- Device securement method:
  - A small high quality RCT by Marsh et al. (2015)[53] found no statistically significant difference between four techniques for securing peripheral venous catheters in terms of catheter failure. Tissue adhesive in addition to standard polyurethane dressing was associated with minor side effects of a skin tear, rash or blister in three people.
- Ultrasound guided access:
  - A low quality SR by Stolz et al. (2015)[54] found ultrasound-guided peripheral venous access for people of any age with difficult venous access had higher success rates than traditional techniques but was not significantly different for other outcomes.

Table 13: Evidence table for peripheral access device and flushing

Study	Participants	Intervention	Comparator	Outcomes	Quality
Bertolino et al. 2012[52] RCT	214 adults admitted to medical wards expected to require intravenous therapy for more than five days. Setting: single hospital in Northern Italy.	Flushing peripheral cannulas with 3ml of 100 IU heparin/ml of normal saline (N=107). Cannula size was chosen by the nurse from 18, 20 or 22G and the catheter was flushed at least two times per day. As per hospital policy, the catheter was changed after three days.	Flushing peripheral cannulas with 3ml of normal saline (N=107). Cannula size was chosen by the nurse from 18, 20 or 22G and the catheter was flushed at least two times per day. As per hospital policy, the catheter was changed after three days.	**Outcomes:** Phlebitis occurred less frequently in the heparin group (26.2% of cases versus 52.3% in the saline group, odds ratio [OR] 0.32, 95% CI 0.18 to 0.57; p<0.001). Catheter occlusion occurred less often in the heparin group (21.5% versus 43.9%, OR 0.35, 95% CI 0.18 to 0.57; p=0.001). The heparin group required fewer cannulas despite the same average length of hospital stay (2 versus 3, OR 0.79, 95% CI 0.67 to 0.94; p=0.006). The median time each cannula was patent for was longer for the heparin group (72 hours versus 62 hours, OR 0.79, 95% CI 0.70 to 0.89; p<0.001). **Safety:** No episodes of bleeding or heparin-induced thrombocytopenia occurred in the heparin group. One case of blood stream infection with Klebsiella oxytoca occurred in the heparin group.	**High quality RCT** The adults had a range of medical conditions so the results are generalisable to a diverse patient population. People were excluded if they were at risk of bleeding.

Study	Participants	Intervention	Comparator	Outcomes	Quality
Daud et al. 2013[8] SR RCT=3 Non-RCT=3	120 critically ill adults with peripheral arterial catheters that have intra-arterial pressure monitoring. Setting: single ICU.	Administration set (the tubing attached to the peripheral arterial catheter) changed every four (N=19) or eight days (N=39).	Administration set changed every 2 days (N=62).	**Outcomes:** In the Luskin et al. 1986 RCT, 2/39 (5.1%) of patients who had an administration set for between four to eight days had an infusate colonisation compared to none in the group who had it changed every two days, but this was not significant (p>0.05). Infusion-related blood stream infection was 1/58 (1.7%) for AS changed every four to eight days and 0/62 for those having it changed every two days (p=NR).	**High quality SR** Based on three small RCTs
	30 critically ill adults with peripheral arterial catheters that have intra-arterial pressure monitoring. Setting: single hospital, multiple ICUs.	Group 1: change of flush solution and pressure-monitoring tubing every 24 hours (N=NR). Group 2: change of flush solution every 24 hours and tubing every 48 hours (N=NR). Group 3: change of flush solution and tubing every 48 hours (N=NR).	All groups compared with each other.	**Outcomes:** In the Covey et al. 1988 RCT, there was no catheter-related blood stream infection or infusion-related blood stream infection in any of the three groups. **Safety:** NR	
	76 critically ill adults and children with peripheral arterial catheters that have intra-arterial pressure monitoring. Setting: single hospital.	Administration set changed every 72 hours (N=38).	Administration set changed every 48 hours (N=38).	**Outcomes:** The McLane et al. 1998 RCT, found stopcock colonisation was 3/26 (11.5%) for administration set change every 48 hours and 10/23 (43.5%) when changed every 72 hours (p<0.01). There was no infusate colonisation or catheter-related blood stream infection in either group. **Safety:** NR	

Study	Participants	Intervention	Comparator	Outcomes	Quality
González López et al. 2014[46] RCT	642 adults on general medical and surgical wards. Setting: single hospital.	COS peripheral intravenous catheter (N=584 catheters).	MOS peripheral intravenous catheter (N=599 catheters).	**Outcomes:** MOS catheters were significantly more likely to be inserted with fewer attempts (76.3% first time for MOS versus 66% for COS; p=0.001). COS catheters stayed in place for longer, median indwell time 137.1 hours versus 96 hours for MOS (p=0.001). **Safety:** MOS was less likely to cause a rupture of the vein during insertion (4.4% of MOS cases versus 12% for COS cases; p<0.001). Phlebitis rate was significantly lower with COS (12% of COS cases versus 17% of MOS cases, p=0.004). Bacterial colonisation and catheter-related infection rates were similar in both groups. There were no needlestick injuries in either group.	**Medium quality RCT** Nurses were more familiar with using MOS catheters which may have biased results.
Marsh et al. 2015[53] RCT	85 adults admitted to general medical or surgical wards. Setting: single hospital.	One of three securement methods: tissue adhesive (TA) with SPU (N=21); bordered polyurethane dressing (BPU) (N=20); sutureless securement device (SSD) with an SPU (N=23).	Standard polyurethane dressing (SPU) (N=21).	**Outcomes:** There was no statistically significant difference between the techniques in terms of catheter failure. **Safety:** Three people in the TA group had minor side effects of a skin tear, rash or blister.	**High quality RCT** All groups received additional securement with non-sterile tape and tubular elastic bandage which may have biased the results. The study size was too small to show any statistical difference.
Rickard et al. 2012[36] RCT	3,283 adults expected to have a peripheral venous catheter for longer than 4 days. Setting: three hospitals.	Clinically indicated replacement of peripheral catheter (N=1593).	Routine peripheral catheter replacement on day three (N=1690).	**Outcomes:** The average mean length of time that catheters stayed in without the clinical need for removal was 99 hours compared to 70 hours when removed on day three regardless of clinical need. Each group required a similar number of hours of intravenous therapy, but the group in which the catheter was changed based on clinical need used a fifth less catheters: clinical need average 1.7 catheters compared to 1.9 catheters, difference of 0.21 catheters (95% CI 0.13 to 0.29; p<0.0001). **Safety:** Phlebitis occurred at 7% in both groups and there were no serious adverse events.	**High quality RCT**

Study	Participants	Intervention	Comparator	Outcomes	Quality
Stolz et al. 2015[54] SR and Meta-analysis Six RCTs One non-RCT	People of any age with difficult peripheral venous access. Setting: surgical suite, emergency department, ICU.	Ultrasound-guided peripheral venous access (N=NR).	Traditional peripheral venous access (N=NR).	**Outcomes:** Ultrasound-guided peripheral venous access was more successful than traditional techniques (OR 3.96, 95% CI 1.75 to 8.94) but was not significantly different for time to cannulation or number of punctures. **Safety:** NR	**Low quality SR** There were considerable differences in each study according to the participant characteristics.

12: Subcutaneous infusion

The RCN search for evidence regarding the safety and effectiveness of performing subcutaneous infusions included evidence for: subcutaneous infusion (hypodermoclysis); subcutaneous injection; use in community settings; site access; insertion of; administration and maintenance. The search identified one SR[57] which included one low quality RCT, and three individual RCTs[55, 56, 58] which were of low or medium quality. Details are provided in Table 14.

There was limited evidence from two of the RCTs to answer the following specific RCN research question:[39, 40]

- What is the effect of different devices on patient safety and outcomes; for example, peripheral cannula vs steel winged infusion devices?
    - One small RCT of medium quality by Connolly et al. (2011)[55] found that subcutaneous fluid administration with hyaluronidase, an enzyme that improves fluid delivery, was less painful with smaller needles such as 24G/0.5in compared to larger 20G/1in needles. The needle used for subcutaneous fluid administration was less likely to fail if held in place with plastic tape or a transparent semipermeable membrane (TSM) dressing compared to double-chevron tape with cloth.
    - One low quality RCT by Lamblet et al. (2011)[56] found that use of retractable fixed needles for subcutaneous injections of insulin reduced the risk of bruising compared to using a fixed needle and syringe. No other safety outcomes were reported.

No evidence covered the following specific research questions identified by the RCN:

- What is the effect of electronic devices for this procedure on patient safety and outcomes?
- What is the effect of site selection on patient safety and outcomes?
- What is the effect of site management on patient safety and outcomes?
- What is the effect of solution tonicity on patient safety and outcomes?
- What is the effect of electrolytes used (for example, sodium chloride, dextrose saline, dextrose 5%) on patient safety and outcomes?

Other results from the literature identified were:

- Rate of injection:
    - Slow subcutaneous injection of heparin over 30 seconds may be less painful than fast injection over 10 seconds according to the one low quality RCT identified by a high quality SR by Akbari et al. (2014)[57].
- Route of infusion:
    - One small low quality RCT by Mannan et al. (2010)[58] found that subcutaneous injections of morphine in the first four hours after gastrectomy were less effective at pain relief than intravenous patient controlled analgesia with morphine. After four hours, both routes were similarly effective. The subcutaneous group used slightly less morphine over the 24 hour study period which may have affected the results. Both routes had similar incidences of side effects such as vomiting, low blood pressure and itching.

Table 14: Evidence table for subcutaneous infusions

Study	Participants	Intervention	Comparator	Outcomes	Quality
Akbari 2014[57] SR	100 adults on neurology, cardiology or orthopaedic wards. 1 RCT, all people had both intervention and comparator. Setting: single hospital in Turkey.	Slow subcutaneous heparin injection in the abdomen over 30 seconds (N=50).	Fast subcutaneous heparin injection in the abdomen over 10 seconds (N=50).	**Outcomes:** Slow injection was significantly less painful, on the visual analogue scale of 0mm (no pain) to 100mm (very severe pain). The mean pain score for slow injection was 13.9 ± 17.1mm versus 20.6 ± 22.3mm for the fast injection (p<0.001). **Safety:** Slow injections caused significantly less bruising by 48 hours afterwards, mean bruising size 18.76 ± 9.32mm2 versus 109.2 ± 468.66mm2 (p=0.033).	**High quality SR** Only 1 small RCT identified so results should be viewed with caution.
Connolly 2011[55] RCT	100 healthy adults in a phase IV trial of different catheter size, material and securement on ease of giving hyaluronidase with subcutaneous fluids. Hyaluronidase is an enzyme that aids fluid delivery by reducing tissue resistance to fluid flow. Setting: single research institute.	One of nine different combinations of devices including: Catheter gauge/length 24/0.75in, 20/1in or 27/9mm subcutaneous button. Teflon or polyurethane Securement with double-chevron tape with cloth, plastic tape or TSM (transparent semipermeable membrane) dressing.	Each combination was assessed against one another (N=10 to 12 per group).	**Outcomes:** Catheter kinking, dislodgement or pull-out was low (17% to 27% of participants) but only occurred when securement was done with double-chevron tape with cloth. **Safety:** Pain was most common with the larger needle: 20/1in catheter (50% to 75% of participants reported pain) compared to those with the 24/0.75in catheter (20% to 36% of participants had pain) or the 27-gauge SC button (27% had pain). Other side effects reported across groups were erythema and swelling but there were no clear patterns. No infusion site rash or pruritus was reported in any group.	**Medium quality RCT** Small numbers of study participants and all were healthy. This may impact the reliability of the results and applicability to people who are unwell.
Lamblet 2011[56] RCT	240 adults attending an Emergency Care Unit or the medical-surgical unit. Setting: single hospital in Sao Paulo.	Subcutaneous injection of 100IU of insulin using a retractable fixed 27G/0.5in needle with 1ml syringe. (N=120)	Subcutaneous injection of 100IU of insulin using a fixed 26G/0.5in needle with 1ml syringe. (N=120)	**Outcomes:** Bruising was significantly less likely with the retractable needle technique (0.07mm versus 0.76mm; p<0.029) when assessed after 24 hours. **Safety:** NR	**Low quality RCT** Pain was also assessed but the results were not separated from a much larger sample of 1000 patients who had intramuscular injections, so are not reported here.

Study	Participants	Intervention	Comparator	Outcomes	Quality
Mannan 2010[58] RCT	50 adults in the first 24 hours after elective gastrectomy. Setting: single hospital.	Regular subcutaneous injections of morphine on demand, 0.1mg/kg body weight through 22G venflon. (N=25)	Intravenous patient-controlled analgesia using morphine, 1mg available every 10mins. No background level of morphine was given except for 2mg IV boluses every 15 minutes after surgery until pain relieved. (N=25)	**Outcomes:** Visual analogue scores for pain were significantly higher for the subcutaneous group for each of the first four hours after surgery ($p<0.05$), but they were comparable thereafter. Of note, average pain scores remained below 35, on a scale of 0mm (no pain) to 100mm (very severe pain). The subcutaneous group used slightly less morphine: on average 11.68mg ± 1.46mg morphine in the 24 hours compared to 12.64mg ± 1.35mg in the intravenous group ($p=0.028$). **Safety:** There was no significant difference between the groups for the following side effects: • vomiting: 8% of participants in the subcutaneous group compared to 10% in the intravenous route • hypotension: 8% of participants in the subcutaneous group compared to 10% in the intravenous route • pruritus: 10% of both groups.	**Low quality RCT** The study is of small size, reducing the strength of confidence in the results.

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Appendix A: Systematic review quality appraisals

Table 15: Systematic review AMSTAR quality appraisal

Study	Was an a priori design provided?	Was there duplicate study selection and data extraction?	Was a comprehensive literature search performed?	Was the status of publication used as one of the inclusion criteria?	Was a list of studies (included and excluded) provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies assessed and documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	Was the likelihood of publication bias assessed?	Was the conflict of interest included?	Overall rating: Low (≤6 yes) Medium (7-8 yes) High (≥9 yes)
Akbari 2014[57]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Chopra 2013[14]	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Medium
Daud 2013[8]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	High
Dreesen 2013[37]	No	No	Yes	No	No	Yes	Yes	Yes	No	No	No	Low
Hayek 2011[31]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	Medium
Ker 2015[50]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Lai 2013[18]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Lopez-Briz 2014[11]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Mitchell 2013[15]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	Medium
Moureau 2015[3]	Yes	Yes	Yes	Yes	No	No	Yes	No	No	No	No	Low
Mustafa 2013[5]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
O'Horo 2014[33]	Yes	Yes	Yes	No	No	Yes	No	No	Yes	No	No	Low
Palmer 2013[41]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	No	Medium
Ray-Barruel 2014[47]	Yes	No	Yes	No	No	Yes	No	No	Yes	No	No	Low
Stolz 2015[54]	Yes	Yes	Yes	No	No	Yes	No	No	Yes	Yes	No	Low
Snaterse 2010[32]	No	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Medium
Tabak 2014[4]	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Medium
Ullman 2013[35]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Ullman 2015[2]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Wang 2010[17]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	Yes	Medium
Zhao 2014[12]	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	No	Medium

Appendix B: RCT quality appraisals

Table 16: Cochrane risk of bias quality assessment for RCTs

Study	Random sequence generation?	Allocation concealment?	Blinding of participants and personnel?	Blinding of outcome assessment?	Incomplete outcome data?	Selective reporting?	Other sources of bias?	Overall rating: Low (≥4 high risk) Medium (3 high risk) High (≤2 high risk)
Antonelli 2012[19]	Low risk	Low risk	High risk	Low risk	High risk	Low risk	Low risk	High quality
Bell 2012[30]	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	High quality
Bertolino 2012[52]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	High quality
Caparas 2014[25]	Unclear risk	High risk	High risk	High risk	Low risk	Low risk	High risk	Low quality
Caparas Jan 2014[51]	High risk	High risk	High risk	High risk	Low risk	Low risk	High risk	Low quality
Casaer 2011[38]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	High quality
Connolly 2011[55]	High risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	Medium quality
Doig 2013[39]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	High quality
Edwards 2014[7]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	High quality
Fenik 2013[27]	Low risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	Medium quality
Fragou 2011[28]	Low risk	High risk	High risk	High risk	High risk	Low risk	Low risk	Low quality
González López 2014[46]	Low risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	Medium quality
Itkin 2014[20]	Low risk	High risk	High risk	Low risk	High risk	Low risk	Low risk	Medium quality
Jaschke 2014[9]	High risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	Low quality
Justo Meirelles 2011[40]	High risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	Low quality
Klek 2013[42]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	High quality
Lamblet 2011[56]	Low risk	Low risk	High risk	High risk	Low risk	High risk	High risk	Low quality
Lim 2012[26]	Low risk	High risk	High risk	Low risk	Low risk	Low risk	High risk	Medium quality
Loftus 2012[48]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	High quality
Mannan 2010[58]	High risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	Low quality
Marsh 2015[53]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	High quality
Marsteller 2012[34]	Low risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	Medium quality
Ong 2010[21]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	High quality
Pittiruti 2014[22]	High risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	Low quality

Study	Random sequence generation?	Allocation concealment?	Blinding of participants and personnel?	Blinding of outcome assessment?	Incomplete outcome data?	Selective reporting?	Other sources of bias?	Overall rating: Low (≥4 high risk) Medium (3 high risk) High (≤2 high risk)
Power 2014[23]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk	High quality
Raurell-Torreda 2014[6]	High risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	Low quality
Reades et al. 2011[49]	Unclear risk	High risk	High risk	High risk	Low risk	High risk	Low risk	Low quality
Rickard 2012[36]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	High quality
Schindler 2010[24]	High risk	High risk	Low risk	High risk	Low risk	Low risk	High risk	Low quality
Siqueira 2011[45]	High risk	High risk	High risk	High risk	Low risk	Low risk	High risk	Low quality
Stauss 2012[10]	Low risk	High risk	High risk	High risk	Low risk	Low risk	High risk	Low quality
Theilla 2012[43]	Low risk	High risk	High risk	Low risk	Low risk	Low risk	High risk	Medium quality
Timsit 2012[16]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	High quality
Umpierrez 2012[44]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	High quality
Van der Meersch 2014[29]	Low risk	High risk	High risk	High risk	Low risk	Low risk	High risk	Low quality
Worth 2014[13]	High risk	High risk	High risk	High risk	Low risk	Low risk	Low risk	Low quality

Appendix C: Excluded studies

Excluded studies at full text, grouped by section.

Section 1: Add on devices

Out of scope – non-RCT

Central Venous Catheter Protective Connector Caps Reduce Intraluminal Catheter-Related Infection. Ramirez, Chuck; Lee, Antonina M.; Welch, Ken. *Journal of the Association for Vascular Access*, 2012 Winter; 17 (4): 210-3.

> Background: Central line-associated blood stream infection (CLABSI) rates in adult care intensive care units have been decreasing across the board. However, we continued to see just a few infections in patients whose catheters are in for more than four days. Therefore, we looked at infections associated with intraluminal contamination to help reduce our infection rate. Methods: A protective cap trial was developed and implemented in two intensive care units. All of the central venous catheter and intravenous tubing access valves were covered with a protective cap saturated with alcohol. This intervention eliminated the need to wipe off intravenous access points with an alcohol swab. The study was done as a nonrandomized prospective trial occurring March 1, 2011 through February 29, 2012. Results: During 2010, there were 4 CLABSI-related infections. By the end of the trial, we had incurred one catheter-associated blood stream infection. CLABSI rate reduced from 1.9 in 2010 to 0.5 during the one-year trial period. Conclusions: The implementation of the port protector cap system resulted in lower infection rates compared with an alcohol swab technique. Our results indicate that consistent use of the caps in tandem with strict compliance does influence CLABSI rates.

Excluded at Full Text – Guideline: the systematic review performed for the guideline is by Mustafa et al. 20135 and is included in the this report.

Canadian Society of Nephrology guidelines for the management of patients with ESRD treated with intensive hemodialysis. Nesrallah GE; Mustafa RA; MacRae J et al. *American Journal Of Kidney Diseases: The Official Journal Of The National Kidney Foundation*, 2013 Jul; Vol. 62 (1): 187-98.

> Intensive (longer and more frequent) hemodialysis has emerged as an alternative to conventional hemodialysis for the treatment of patients with end-stage renal disease. However, given the differences in dialysis delivery and models of care associated with intensive dialysis, alternative approaches to patient management may be required. The purpose of this work was to develop a clinical practice guideline for the Canadian Society of Nephrology. We applied the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach for guideline development and performed targeted systematic reviews and meta-analysis (when appropriate) to address prioritized clinical management questions. We included studies addressing the treatment of patients with end-stage renal disease with short daily (≥5 days per week, <3 hours per session), long (3-4 days per week, ≥5.5 hours per session), or long-frequent (≥5 days per week, ≥5.5 hours per session) hemodialysis. We included clinical trials and observational studies with or without a control arm (1990 and later). Based on a prioritization exercise, six interventions of interest included optimal vascular access type, buttonhole cannulation, antimicrobial prophylaxis for buttonhole cannulation, closed connector devices, and dialysate calcium and dialysate phosphate additives for patients receiving intensive hemodialysis. We developed six recommendations addressing the interventions of interest. Overall quality of the evidence was very low and all recommendations were conditional. We provide detailed commentaries to guide in shared decision making. The main limitation was the very low overall quality of evidence that precluded strong recommendations. Most included studies were small single-arm observational studies. Three randomized controlled trials were applicable, but provided only indirect evidence. Published information for patient values and preference was lacking. In conclusion, we provide six recommendations for the practice of intensive hemodialysis. However, due to very low-quality evidence, all recommendations were conditional. We therefore also highlight priorities for future research.

Section 2: Arterial catheters

Excluded at Full Text – condition specific

Chen B-L, Li J, Chen Y-Y, et al. A novel external catheter fixation method for chemotherapy using inferior epigastric arterial catheterization for cervical cancer. Chen B-L, Li J, Chen Y-Y, et al. *International Journal of Nursing Practice*. 2015;21(S2):150-6.

> The aim of this randomized controlled study was to investigate the effects of a novel external catheter fixation method for chemotherapy using inferior epigastric arterial catheterization for cervical cancer. Patients diagnosed with cervical cancer were randomly divided into a control group (n=32) and a treatment group (n=33). Patients in the control group underwent a traditional fixation method using a haemostat, elastic band and abdominal bandage. Patients in the treatment group underwent an improved fixation method using an indwelling needle and membrane cover. We used a visual analogue scale (VAS) to evaluate each patient's comfort score and also recorded the incidence of needlestick injury and the length of injection time in each group. The VAS scores measured before and after chemotherapy in the treatment group were lower than in the control group. The incidence of needlestick injury in the treatment group was significantly lower than in the control group. The length of injection time in treatment group was significantly lower than in the control group. Compared with the traditional fixation method, the improved

fixation method not only increased patient comfort but also reduced both the risk of needlestick injury and the length of injection time. This improved technique deserves increased clinical use.

Section 3: Blood sampling

None out of scope

Section 4: Central venous catheter devices

Out of scope – non-RCT: lack of randomisation after one month

Hemodialysis Catheter Outcomes Pilot Study: No Dressing Coverage With Prescribed Showering. Evans, Elizabeth C; Hain, Debra; Kear, Tamara M; Dork, Leslie A; Schrauf, Christine. *Nephrology Nursing Journal*. 2014; 41(1): 53-65,72.

This six-month prospective, multi-site study incorporated no dressing coverage over hemodialysis central venous catheter exit sites and compared the outcomes of two groups of patients receiving incenter hemodialysis: a shower group and a non-shower group. Outcomes included exit site infection rates, tunnel infection rates, and catheter-related blood stream infection rates. The study enrolled 40 patients – 31 patients in the shower group and nine patients in the non-shower group. The study was initially designed as a randomized controlled study, but after a month of enrolling patients, most patients insisted on being in the shower group. Results for both groups demonstrated infection rates that were not statistically different and were below levels reported in other studies. The qualitative satisfaction in ability to shower by patients in this study was an additional important finding.

Excluded at second sift – condition specific

Concentrated citrate locking in order to reduce the long-term complications of central venous catheters: a randomized controlled trial in patients with hematological malignancies. Boersma RS; Jie KS; Voogd AC; Hamulyak K; Verbon A; Schouten HC, *Supportive Care In Cancer: Official Journal Of The Multinational Association Of Supportive Care In Cancer* [Support Care Cancer], ISSN: 1433-7339, 2015 Jan; Vol. 23 (1), pp. 37-45.

Purpose and Methods: Central venous catheter (CVC)-related thrombosis and infections are frequently occurring complications in patients with hematological malignancies. At present, heparin is most often used as a locking solution. Trisodium citrate (TSC) had been shown to be a very effective antimicrobial catheter locking in hemodialysis patients. We performed a prospective randomized phase III multicenter trial to determine the efficacy of TSC as a locking solution compared to heparin in preventing CVC-related thrombosis and infections in patients with hematological malignancies. Results: Thirty-four episodes of CVC-related blood stream infections (CVC-BSI) occurred in the 108 patients who were randomized to locking with heparin compared with 35 episodes in the 99 patients who were randomized to locking with TSC (P = 0.654). We did find seven times more CVC-BSI with gram-negative rods in CVCs locked with heparin (P = 0.041). The cumulative incidence of symptomatic thrombosis was 10% in the heparin group and 5% in the TSC group (hazard ratio 0.525; 95% confidence interval 0.182-1.512). Conclusion: This study shows that locking with TSC in patients with hematological malignancies significantly reduced the incidence of CVC-BSI with gram-negative rods. However, the incidence of CVC-BSI with coagulase-negative staphylococcus or CVC-related thrombosis was not reduced by TSC locking.

Excluded at second sift – not nursing focussed

A randomised, controlled trial comparing the long-term effects of peripherally inserted central catheter placement in chemotherapy patients using B-mode ultrasound with modified Seldinger technique versus blind puncture. Li J; Fan YY; Xin MZ; Yan J; Hu W; Huang WH; Lin XL; Qin HY, *European Journal Of Oncology Nursing*: The Official Journal Of European Oncology Nursing Society [Eur J Oncol Nurs], ISSN: 1532-2122, 2014 Feb; Vol. 18 (1), pp. 94-103.

Objective: To compare the effects of peripherally inserted central venous catheter (PICC) placement using B-mode ultrasound with the modified Seldinger technique (BUMST) versus the blind puncture. Methods: One hundred chemotherapy patients were recruited to participate in a randomised, controlled trial in Guangzhou, China. Fifty were assigned to the experimental group (using BUMST), and 50 were assigned to the control group (blind puncture). Demographic and background data, data related to PICC placement, complications after PICC placement, the patients' degree of comfort (determined via a questionnaire), and patients' costs for PICC maintenance were collected to compare the effects of the two methods. T-tests and chi-square tests were used to analyse the data; $p < 0.05$ was accepted as statistically significant. Results: Nighty-eight of the 100 PICCs were successfully inserted (50 in the experimental group and 48 in the control group). Compared with the control group, the experimental group had a lower rate of unplanned catheter removal (4.0% vs. 18.7%; $p = 0.02$), a lower incidence of mechanical phlebitis (0% vs. 22.9%; $p < 0.001$), a lower incidence of venous thrombosis (0% vs. 8.3%; $p = 0.037$), and a higher incidence of catheter migration (32% vs. 2.1%; $p < 0.001$). Compared with the control group, the experimental group experienced significantly less severe contact dermatitis ($p = 0.038$), had improved comfort at one week, one month, two months, and three months after PICC placement ($p < 0.001$), and had lower costs for PICC maintenance at two months, three months and when the catheter was removed ($p < 0.05$). Conclusions: Using B-mode ultrasound with MST for PICC placement reduced complications and patients' costs for PICC maintenance and improved patients' degree of comfort; thus, this procedure should be more widely used. The clinical trial registration number: ChiCTR-TRC-12002749.

Excluded at full text – RCT included in the SR by Lopez-Briz et al. 201411

Heparin or 0.9% sodium chloride to maintain central venous catheter patency: A randomized trial. Schallom ME; Prentice D; Sona C; Micek ST; Skrupky LP; *Critical Care Medicine*, 2012 Jun; 40 (6): 1820-6.

Abstract: OBJECTIVE: To compare heparin (3 ml, 10 units/ml) and 0.9% sodium chloride (NaCl, 10 ml) flush solutions with respect to central venous catheter lumen patency. DESIGN: Single-center, randomized, open label trial. SETTING: Medical intensive care unit and Surgical/Burn/Trauma intensive care unit at Barnes-Jewish Hospital, St. Louis, MO. PATIENTS: : Three hundred forty-one patients with multilumen central venous catheters. Patients with at least one lumen with a minimum of two flushes were included in the analysis. INTERVENTIONS: Patients were randomly assigned within 12 hrs of central venous catheter insertion to receive either heparin or 0.9% sodium chloride flush. MEASUREMENTS AND MAIN RESULTS: The primary outcome was lumen nonpatency. Secondary outcomes included the rates of loss of blood return, inability to infuse or flush through the lumen (flush failure), heparin-induced thrombocytopenia, and catheter-related blood stream infection. Assessment for patency was performed every eight hrs in lumens without continuous infusions for the duration of catheter placement or discharge from intensive care unit. Three hundred twenty-six central venous catheters were studied yielding 709 lumens for analysis. The nonpatency rate was 3.8% in the heparin group (n = 314) and 6.3% in the 0.9% sodium chloride group (n = 395) (relative risk 1.66, 95% confidence interval 0.86-3.22, p = .136). The Kaplan-Meier analysis for time to first patency loss was not significantly different (log rank = 0.093) between groups. The rates of loss of blood return and flush failure were similar between the heparin and 0.9% sodium chloride groups. Pressure-injectable central venous catheters had significantly greater rates of nonpatency (10.6% vs. 4.3%, p = .001) and loss of blood return (37.0% vs. 18.8%, p <.001) compared to nonpressure-injectable catheters. The frequencies of heparin-induced thrombocytopenia and catheter-related blood stream infection were similar between groups. CONCLUSION: 0.9% sodium chloride and heparin flushing solutions have similar rates of lumen nonpatency. Given potential safety concerns with the use of heparin, 0.9% sodium chloride may be the preferred flushing solution for short-term use central venous catheter maintenance.

Excluded at full text – secondary analysis of 2 RCTs

Jugular versus femoral short-term catheterization and risk of infection in intensive care unit patients: causal analysis of two randomized trials. Timsit, Jean-François; Bouadma, Lila; Mimoz, Olivier; Parienti, Jean-Jacques; Garrouste-Orgeas, Maïté; Alfandari, Serge; et al. *American Journal of Respiratory and Critical Care Medicine*: 2013; 188(10): 1232-1239.

Rationale: When subclavian access is not possible, controversy exists between the internal jugular and femoral sites for the choice of central-venous access in intensive care unit patients. Objectives: To compare infection and colonization rates of short-term jugular and femoral catheters. Methods: Using data from two multicenter studies, we compared femoral and internal jugular for the risks of catheter-related blood stream infection, major catheter-related infection, and catheter-tip colonization. We also compared the rates of dressing disruption and skin colonization. We used marginal structural models with inverse probability of treatment weighting to adjust on indication bias. Measurements and Main Results: We included 2,128 patients (2,527 catheters and 19,481 catheter-days). We found no difference in catheter-related blood stream infection (internal jugular 1.0 vs. fem- oral 1.1 per 1,000 catheter-days; hazard ratio [HR], 0.63 [0.25-1.63]; P = 0.34), major catheter-related infection (internal jugular 1.8 vs. femoral 1.4 per 1,000 catheter-days; HR, 0.91 [0.38-2.18]; P = 0.34), and colonization (internal jugular 11.6 vs. femoral 12.9 per 1,000 catheter-days; HR, 0.80 [0.25-1.63]; P = 0.15). However, colonization was higher with femoral for female (HR, 0.39 [0.24-0.63]; P < 0.001) and, at the significance limit, catheter maintained for more than 4 days (HR, 0.73 [0.53-1.01]; P= 0.05). The absence of benefit of internal jugular before Day 5 was related to a higher skin colonization at the internal jugular site for catheters removed before Day 5. After the fourth day, dressing disruption became more frequent with femoral catheters and may explain the subsequent risk of catheter colonization. Differences in cutaneous and catheter colonization between internal jugular and femoral was suppressed by the use of chlorhexidine-impregnated dressings. Differences in cutaneous and catheter colonization between internal jugular and femoral was suppressed by the use of chlorhexidine-impregnated dressings. Conclusions: Femoral and internal jugular accesses lead to similar risks of catheter infection. Internal jugular might be preferred for female, nonchlorhexidine-impregnated dressings users, and when catheters are left in place more than four days. Both sites are acceptable when a subclavian approach is not feasible.

Excluded at full text – SR updated by Ullman et al. 20152

Webster JG, D.; O'Riordan E.; Sherriff, K.; Rickard, C.;. Gauze and tape and transparent polyurethane dressings for central venous catheters. *The Cochrane database of systematic reviews.* 2011(Issue 11).

Background: Central venous catheters (CVCs) facilitate venous access, allowing the intravenous administration of complex drug treatments, blood products and nutritional support, without the trauma associated with repeated venepuncture. However, CVCs are

associated with a risk of infection. Some studies have indicated that the type of dressing used with them may affect the risk of infection. Gauze and tape, transparent polyurethane film dressings such as Tegaderm® and Opsite®, and highly vapour-permeable transparent polyurethane film dressings such as Opsite IV3000®, are the most common types of dressing used to secure CVCs. Currently, it is not clear which type of dressing is the most appropriate. Objectives: To compare gauze and tape with transparent polyurethane CVC dressings in terms of catheter-related infection, catheter security, tolerance to dressing material and dressing condition in hospitalised adults and children. Search Methods: For this third update, we searched The Cochrane Wounds Group Specialised Register (10 May 2011); The Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library 2011, Issue 2), Ovid MEDLINE (1950 to April Week 4 2011); Ovid MEDLINE (In-Process & Other Non-Indexed Citations, May 11, 2011); Ovid EMBASE (1980 to 2011 Week 18); and EBSCO CINAHL (1982 to 6 May 2011). Selection criteria: All randomised controlled trials (RCTs) evaluating the effects of dressing type (e.g. gauze and tape versus transparent polyurethane dressings) on CVC-related infection, catheter security, tolerance to dressing material and dressing condition in hospitalised patients. Data collection and analysis: Two review authors independently assessed trial quality and extracted data. We contacted study authors for missing information. Main results: Six studies were included in earlier versions of the review. In this update two of the previously included papers have been excluded and two new trials have been added. Of these six trials, four compared gauze and tape with transparent polyurethane dressings (total participants = 337) and two compared different transparent polyurethane dressings (total participants = 126). Catheter-related bloodstream infection was higher in the transparent polyurethane group when compared with gauze and tape; OR 4.19 (95%CI 1.02 to 17.23) however these small trials were at risk of bias so this evidence is graded low quality. There was no evidence of a difference between highly permeable polyurethane dressings and other polyurethane dressings in the prevention of catheter-related bloodstream infection (low quality evidence). No other significant differences were found. Author's conclusions: We found a four-fold increase in the rate of catheter related blood stream infection when a polyurethane dressing was used to secure the central venous catheter however this research was at risk of bias and the confidence intervals were wide indicating high uncertainty around this estimate; so the true effect could be as small as 2% or as high as 17-fold. More, better quality research is needed regarding the relative effects of gauze and tape versus polyurethane dressings for central venous catheter sites.

Section 5: Flow control devices

Out of scope – non-RCT

Amount of accidental flush by syringe pump due to inappropriate release of occluded intravenous line. Kawakami H; Miyashita T; Yanaizumi R; Mihara T; Sato H; Kariya T; Mizuno Y; Goto T. *Technology And Health Care*: Official Journal Of The European Society For Engineering And Medicine ISSN: 1878-7401, 2013; 21 (6): 581-6.

Background: An unintended bolus is delivered by the syringe pump if intravenous line occlusion is released in an inappropriate manner. Objective: The aim of this study was to measure the amount of flushed fluid when an occlusion is inappropriately released and to assess the effect of different syringe pump settings (flow rate, alarm setting, size of syringe and syringe pump model) on the flushed amount. Methods: After the stopcock was closed, infusions were started with different model syringe pumps (Terufusion® TE312 and TE332S), different syringe sizes or at different alarm settings. After the occlusion alarm sounded, the occlusion was released and the amount of fluid emerging from the stopcock was measured. Results: The bolus was significantly lower when the alarm was set at a low-pressure setting. The bolus was significantly lower with a 10-ml than a 50-ml syringe. A significant difference was seen only when a 50-ml syringe was used (TE312: 1.99 ± 0.16 ml vs. TE332S: 0.674 ± 0.116 ml, alarm High, $p < 0.001$). Conclusion: To minimize the amount of accidentally injected medication, a smaller syringe size and a low alarm setting are important. Using a syringe pump capable of reducing the inadvertently administered bolus may be helpful.

Excluded at full text – condition specific

Subcutaneous compared with intravenous administration of amifostine in patients with head and neck cancer receiving radiotherapy: Final results of the GORTEC 2000-02 phase III randomized trial. Bardet E, Martin L, Calais G, et al. *Journal of Clinical Oncology*. 2011;29(2):127-33.

Purpose: To compare compliance with and efficacy of intravenous (IV) and subcutaneous (SC) amifostine for the treatment of patients undergoing radiotherapy for head and neck cancer. Patients and Methods: Patients with newly diagnosed squamous cell carcinoma of the head and neck, who were eligible for radiotherapy and who were not receiving concurrent chemotherapy, were randomly assigned to receive either IV amifostine (200 mg/m2 daily for 3 minutes, 15 to 30 minutes before irradiation) or SC amifostine (500 mg; two sites; 20 to 60 minutes before irradiation). The primary end point was late xerostomia at one year as indicated by unstimulated and stimulated salivary flow rates, a patient benefit questionnaire score, and Radiation Therapy Oncology Group (RTOG) late toxicity grade. Results: Results for IV (n = 143) versus SC (n = 148) administration were as follows. There was no significant difference in compliance (69% for IV v 71% for SC) in patients receiving a full dose of amifostine. Reasons for dose reduction

were acute toxicity (25% for IV v 27% for SC; P = .51) and logistics (18% for IV v 9% for SC administration; P = .09). Acute toxicity differed significantly in terms of grade 1 to 2 hypotension (19% for IV v 8% for SC; P = .01), grade 1 to 2 skin rash (9% for IV v 21% for SC; P = .01), and local pain (0% for IV v 8% for SC; P = .003). The incidence of grade 2 or greater xerostomia was significantly higher for patients who received amifostine via SC administration (37% for IV v 62% for SC; P = .005) in the 127 patients (n = 67, IV; n = 60, SC) evaluable at one year but not at two or three years (36% for IV v 51% for SC administration; P = .19; 32% for IV v 41% for SC; P = .63). A generalized linear mixed-model analysis of all data revealed no significant difference in patient self-assessment of salivary function (P = .25), unstimulated or stimulated salivary flow rates (P = .054 and .82, respectively), or grade 2 or greater xerostomia (P = .23). Conclusion: SC amifostine administration was not significantly superior to IV amifostine administration in terms of patient compliance or efficacy.

Section 6: Infusion related blood stream infections

Out of scope at full text – not infusion related

A comparison of the efficacy of 70% v/v isopropyl alcohol with either 0.5% w/v or 2% w/v chlorhexidine gluconate for skin preparation before harvest of the long saphenous vein used in coronary artery bypass grafting. Casey, A; Itrakjy A; Birkett, C; et al. *American Journal of Infection Control*, 2015;43(8):816-20.

Chlorhexidine gluconate (CHG) is often recommended for skin antisepsis; however, the most efficacious concentration is currently unclear. Our objective was to compare the efficacy of 70% isopropyl alcohol (IPA) containing either 0.5% or 2% CHG for antiseptic skin preparation in patients undergoing coronary artery bypass grafting. METHODS: One hundred patients were randomized to one of the two CHG concentrations. The designated antiseptic was applied to the skin of the operative site of patients before long saphenous vein harvest. Bacterial counts on the skin incision site were determined at various time points to assess any immediate and persistent antimicrobial activity. The number of patients developing surgical site infection was also determined. RESULTS: The total numbers of microorganisms on the skin two minutes after skin antisepsis and after wound closure was lower with 2% CHG/70% IPA compared with 0.5% CHG/70% IPA (P = .033 and P = .016, respectively). Six of 41 patients in the 0.5% CHG/70%IPA group developed a superficial surgical site infection compared with 2 of 44 patients in the 2% CHG/70% IPA group (relative risk, 3.22; 95% confidence interval, 0.63-22.75; P = .147). CONCLUSIONS: Isopropyl alcohol (70%) containing 2% CHG compared with 0.5% CHG reduces the number of microorganisms detectable on a surgical patient's skin peri-operatively.

Out of scope at full text – not an SR

Reducing blood stream infections during catheter insertion. Petree C, Wright DL, Sanders V, et al. *Radiologic technology*. 2012;83(6):532-40.

Registered radiologist assistants (R.R.A.s) and other health care providers frequently are responsible for placing peripherally inserted central catheter (PICC) lines. Postprocedure blood stream infections are a potentially costly and medically serious complication. To determine the most effective methods for R.R.A.s and other health professionals to reduce blood stream infections related to PICC line insertion and management. Using specific inclusion criteria, the authors searched for scholarly reviewed articles related to PICC lines, infection, and adulthood. The search produced 2,237 articles, from which the authors selected 35 for review, in addition to 6 articles identified in the reference lists of articles not selected. The authors investigated 6 topics related to infection control in PICCs among non-immunocompromised adults: securement devices, staff education, needleless systems, site preparation, maximum sterile barriers, and antimicrobial patches. In the long run, proactive continuing education is less expensive than the cost of complications caused by postprocedure infections. Although further research is needed, specific strategies reported in the literature included prepping the skin using chlorhexidine and antimicrobial patches to reduce the microorganisms in the area. These steps should be followed by maximum sterile barriers. Needleless connectors and positive-pressure valves were found to be more effective than the alternatives, and proper securement with self-adhesive anchoring devices was found to be more effective than suturing for reducing blood stream infections.

Section 7: Infusion therapy parenteral nutrition

Out of scope – condition specific

Influence of the slow infusion of a soybean oil emulsion on plasma cytokines and ex vivo T cell proliferation after an esophagectomy.(includes abstract) Kagawa Y; Maeda T; Kato Y; Ueda I; Kudo T; Watanabe N; Kimura M; Minami S; Sakamoto T; Yamada H; et al. *JPEN – Journal of Parenteral & Enteral Nutrition*, 2013 Jan; 37 (1): 123-8.

Abstract: Background: Lipid emulsions have been suggested to reduce immune responses, particularly in severely stressed patients. The authors investigated the influence of the slow intravenous infusion of a soybean oil-based lipid emulsion on some immune parameters in patients who had undergone an esophagectomy for esophageal cancer. Methods: Thirty-two patients who had undergone an esophagectomy were randomly divided into a lipid emulsion (LPD)-treated group and a control group. All patients received parenteral feeding with a glucose-based solution. Patients in the LPD group received 100 ml of a 20% soybean oil emulsion for seven days after the esophagectomy in addition to the glucose-

based feeding. A slow infusion rate (0.09-0.12 g/kg/h) was adopted to take account of the intrinsic degradation of infused lipids. Immune responses were measured based on lymphocyte proliferation and serum concentrations of monocyte chemoattractant protein-1 (MCP-1), interleukin-6 (IL-6), and tumor necrosis factor-[alpha] (TNF-[alpha]). The authors also measured levels of rapid turnover proteins (ie, transferrin, prealbumin, and retinol-binding protein). Results: Phytohemagglutinin- and concanavalin A-stimulated lymphocyte proliferation significantly decreased after the esophagectomy, but no significant difference was seen between the LPD and control groups. No significant difference in changes in plasma concentrations of MCP-1, IL-6 and TNF-[alpha] occurred between the two groups either. Plasma concentrations of rapid turnover proteins did not differ between the groups. Conclusions: These results indicate that the lipid emulsion did not affect the immune parameters measured in patients who had undergone an esophagectomy when administered at a slow rate. JAPAN.

Out of scope – secondary analysis of an RCT

Role of Disease and Macronutrient Dose in the Randomized Controlled EPaNIC Trial: A Post Hoc Analysis.(includes abstract) Casaer MP; Wilmer A; Hermans G; Wouters PJ; Mesotten D; Van den Berghe G; *American Journal of Respiratory & Critical Care Medicine*, 2013 Feb 1; 187 (3): 247-55.

Abstract: Rationale: Early parenteral nutrition to supplement insufficient enteral feeding during intensive care (early PN) delays recovery as compared with withholding parenteral nutrition for 1 week (late PN). Objectives: To assess whether deleterious effects of early PN relate to severity of illness or to the dose or type of macronutrients. Methods: Secondary analyses of a randomized controlled trial (EPaNIC; n = 4,640) performed in seven intensive care units from three departments in two Belgian hospitals. In part 1, all patients were included to assess the effect of the randomized allocation to early PN or late PN in subgroups of patients with increasing-on-admission severity of illness. In part 2, observationally, the association of the amount and type of macronutrients with recovery was documented in those patient cohorts still present in intensive care on Days 3, 5, 7, 10, and 14. Measurements and Main Results: The primary end point was time to live discharge from the intensive care unit. For part 1, a secondary end point, acquisition of new infections, was also analyzed. All statistical analyses were performed by univariable and adjusted multivariable methods. In none of the subgroups defined by type or severity of illness was a beneficial effect of early PN observed. The lowest dose of macronutrients was associated with the fastest recovery and any higher dose, administered parenterally or enterally, was associated with progressively more delayed recovery. The amount of proteins/amino acids rather than of glucose appeared to explain delayed recovery with early feeding. Conclusions: Early combined parenteral/enteral nutrition delayed recovery irrespective of severity of critical illness. No dose or type of macronutrient was found to be associated with improved outcome. Clinical trial registered with www.clinicaltrials.gov (NCT 00512122). BELGIUM.

Out of scope – condition specific

Enteral and parenteral nutrition in the conservative treatment of pancreatic fistula: a randomized clinical trial. (English) By: Klek S; Sierzega M; Turczynowski L; Szybinski P; Szczepanek K; Kulig J, *Gastroenterology*. 2011 Jul; Vol. 141 (1), pp. 157-63.

Background& Aims: Postoperative pancreatic fistula is the most common and potentially life-threatening complication after pancreatic surgery. Although nutritional support is a key component of conservative therapy in such cases, there have been no well-designed clinical trials substantiating the superiority of either total parenteral nutrition or enteral nutrition. This study was conducted to compare the efficacy and safety of both routes of nutritional intervention.

Methods: A randomized clinical trial was conducted in a tertiary surgical center of pancreatic and gastrointestinal surgery. Seventy-eight patients with postoperative pancreatic fistula were treated conservatively and randomly assigned to groups receiving for 30 days either enteral nutrition or total parenteral nutrition. The primary end point was the 30-day fistula closure rate.

Results: After 30 days, closure rates in patients receiving enteral and parenteral nutrition were 60% (24 of 40) and 37% (14 of 38), respectively (P=.043). The odds ratio for the probability that fistula closes on enteral nutrition compared to total parenteral nutrition was 2.571 (95% confidence interval [CI]: 1.031-6.411). Median time to closure was 27 days (95% CI: 21-33) for enteral nutrition, and no median time was reached in total parenteral nutrition (P=.047). A logistic regression analysis identified only 2 factors significantly associated with fistula closure, ie, enteral nutrition (odds ratio=6.136; 95% CI: 1.204-41.623; P=.043) and initial fistula output of ≤200 mL/day (odds ratio=12.701; 95% CI: 9.102-47.241; P<.001).Conclusions: Enteral nutrition is associated with significantly higher closure rates and shorter time to closure of postoperative pancreatic fistula.

Out of scope – secondary analysis of an RCT

Enteral nutrition is associated with improved outcome in patients with severe sepsis. A secondary analysis of the VISEP trial. (English) By: Elke G; Kuhnt E; Ragaller M; Schädler D; Frerichs I; Brunkhorst FM; Löffler M; Reinhart K; Weiler N; German Competence Network Sepsis (SepNet), *Medizinische Klinik, Intensivmedizin Und Notfallmedizin* [Med Klin Intensivmed Notfmed], ISSN: 2193-6226, 2013 Apr; Vol. 108 (3), pp. 223-33.

Introduction: The optimal nutritional strategy remains controversial, particularly in severely

septic patients. Our aim was to analyze the effect of three nutritional strategies--enteral (EN), parenteral (PN), and combined nutrition (EN+PN)--on the outcome of patients with severe sepsis or septic shock. Patients and Methods: This secondary analysis of the prospective, randomized-controlled, multicenter "Intensive Insulin Therapy and Pentastarch Resuscitation in Severe Sepsis (VISEP)" trial only included patients with a length of stay in the intensive care unit (ICU) of more than seven days. Besides patient characteristics, data on nutrition therapy were collected daily for up to 21 days. Morbidity as measured by the mean Sequential Organ Failure Assessment (SOFA) score, incidence of secondary infections, renal replacement therapy, ventilator-free days and severe hypoglycemia, length of ICU stay, and mortality at 90 days were compared between the three nutritional strategies. Results: In all, 353 patients were included in the analysis with the majority (68.5 %) receiving EN+PN, 24.4 % receiving EN, and only 7.1 % receiving PN. Median caloric intake was 918 kcal/day (EN), 1,210 kcal/day (PN), and 1,343 kcal/day (EN+PN; p < 0.001). In the latter group, calories were predominantly administered via the parenteral route within the first week. The rate of death at 90 days was lower with EN than with EN+PN (26.7 % vs. 41.3 %, p = 0.048), as was the rate of secondary infections, renal replacement therapy, and duration of mechanical ventilation. In the adjusted Cox regression analysis, the effect on mortality [hazard ratio (HR) = 1.86, 95 % confidence interval (CI): 1.16-2.98, p = 0.010] and the rate of secondary infections (HR= 1.89, 95 % CI: 1.27-2.81, p = 0.002) remained different between EN and EN+PN. Conclusion: In patients with severe sepsis or septic shock and prolonged ICU stay, EN alone was associated with improved clinical outcome compared to EN+PN. This hypothesis-generating result has to be confirmed by a randomized-controlled trial in this specific patient population.

Out of scope – secondary analysis of an RCT

Role of disease and macronutrient dose in the randomized controlled EPaNIC trial: a post hoc analysis. (English) By: Casaer MP; Wilmer A; Hermans G; Wouters PJ; Mesotten D; Van den Berghe G. *American Journal Of Respiratory And Critical Care Medicine*. ISSN: 1535-4970, 2013 Feb 1; 187 (3), pp. 247-55.

Rationale: Early parenteral nutrition to supplement insufficient enteral feeding during intensive care (early PN) delays recovery as compared with withholding parenteral nutrition for 1 week (late PN). Objectives: To assess whether deleterious effects of early PN relate to severity of illness or to the dose or type of macronutrients. Methods: Secondary analyses of a randomized controlled trial (EPaNIC; n = 4,640) performed in seven intensive care units from three departments in two Belgian hospitals. In part 1, all patients were included to assess the effect of the randomized allocation to early PN or late PN in subgroups of patients with increasing-on-admission severity of illness. In part 2, observationally, the association of the amount and type of macronutrients with recovery was documented in those patient cohorts still present in intensive care on Days 3, 5, 7, 10, and 14. Measurements and Main Results: The primary end point was time to live discharge from the intensive care unit. For part 1, a secondary end point, acquisition of new infections, was also analyzed. All statistical analyses were performed by univariable and adjusted multivariable methods. In none of the subgroups defined by type or severity of illness was a beneficial effect of early PN observed. The lowest dose of macronutrients was associated with the fastest recovery and any higher dose, administered parenterally or enterally, was associated with progressively more delayed recovery. The amount of proteins/amino acids rather than of glucose appeared to explain delayed recovery with early feeding. Conclusions: Early combined parenteral/enteral nutrition delayed recovery irrespective of severity of critical illness. No dose or type of macronutrient was found to be associated with improved outcome. Clinical trial registered with www.clinicaltrials.gov (NCT 00512122).

Out of scope – condition specific and case-control

Use of home parenteral nutrition in patients with intra-abdominal desmoid tumors. Shatnawei A; Hamilton C; Quintini C; Steiger E; Kirby DF, *Nutrition In Clinical Practice*: Official Publication Of The American Society For Parenteral And Enteral Nutrition. ISSN: 1941-2452, 2010 Jun; 25 (3), pp. 290-5.

Background: Fistulae, small bowel obstruction (SBO), and malabsorption are complications of intra-abdominal desmoid (IAD) tumors that require home parenteral nutrition (HPN). HPN outcomes in patients with IAD tumors have not been previously reported. The aim of this study was to compare some of the nutrition parameters and complications of HPN in patients with IAD with a control group of patients on HPN. Methods: This was a case-control study of patients and randomly selected controls who required HPN because of fistulae, SBO, or malabsorption and were managed by the Cleveland Clinic Nutrition Support Team between 1990 and 2008. Variables included demographics, indications, number of episodes, duration of HPN, number of admissions and complications related to HPN, and nutrition parameters. Univariable and multivariable logistic regression analyses were used. Results: Eighteen of 1615 HPN patients (1.1%) had IAD. For the study, 58 patients were included: 14 with IAD and 44 controls. Four IAD patients did not have complete medical records. IAD patients had longer duration of HPN (P = .015), were younger (P = .028), and were more likely to receive HPN for malabsorption (P < .001). Body mass index (BMI), serum albumin level, protein intake provided at the beginning of HPN, energy intake provided at the start and end of HPN, mortality, and complications were

comparable between groups. At the end of HPN, IAD patients received significantly more protein and had lower serum albumin levels compared with controls. Conclusions: HPN for IAD patients maintained BMI but did not increase serum albumin concentration despite receiving more protein than controls. IAD patients did not have increased HPN-related complications.

Out of scope after second sift – RCT on enteral versus parenteral nutrition

Effect of Enteral Versus Parenteral Nutrition on Outcome of Medical Patients Requiring Mechanical Ventilation. Altintas, Neriman Defne; Aydin, Kadriye; Türkogglu, Melda Aybar; Abbasogglu, Osman; Topeli, Arzu; *Nutrition in Clinical Practice*, 2011 Jun; 26 (3): 322-9.

Out of scope after second sift – RCT on enteral versus parenteral nutrition

Perioperative nutrition in malnourished surgical cancer patients – A prospective, randomized, controlled clinical trial. Klek, Stanislaw; Sierzega, Marek; Szybinski, Piotr; Szczepanek, Kinga; Scislo, Lucyna; Walewska, Elzbieta; Kulig, Jan; *Clinical Nutrition*, 2011 Dec; 30 (6): 708-13.

Abstract: Summary: Background and aims: Malnourished surgical patients are supposed to benefit from perioperative nutrition. It is unclear, however, whether enteral intervention really surpasses the parenteral one, and whether the modification of standard formula matters. The aim of the study was to evaluate the clinical value of the route and type of perioperative nutritional support. Methods: A group of 167 malnourished patients (91 M, 76 F, mean age 61.4 years) operated between June 2001 and December 2008 was randomly assigned during postoperative period to four groups according to nutritional intervention: enteral and parenteral, standard or immunomodulating. All patients received parenteral nutrition before surgery for 14 days, which provided homogenous groups for the postoperative evaluation. The trial was designed to test the hypothesis that enteral nutrition and/or immunonutrition can reduce the incidence of postoperative complications. Results: The incidence of individual complications was comparable among all four groups ($p > 0.05$). Infectious complications occurred in 23 of 84 patients with standard diets and in 20 of 83 patients receiving immunomodulatory formula (odds ratio 0.84; 95% CI 0.42 to 1.69). There were no significant differences in infectious complications' ratio in patients receiving enteral (24/84 patients) and parenteral formulas (19/83 patients). Neither immunomodulating formulas nor enteral feeding significantly affected the length of hospitalization, overall morbidity and mortality rates. Conclusions: Results demonstrated that postoperative nutritional intervention generates comparable results regardless of the route and formula used and that preoperative intervention is of the utmost importance. The study was registered in the Clinical Trials Database – number: NCT 00558155. POLAND.

Out of scope after second sift – RCT on the composition of parenteral nutrition

Phase IV Prospective Clinical Study to Evaluate the Effect of Taurine on Liver Function in Postsurgical Adult Patients Requiring Parenteral Nutrition. Arrieta, Francisco; Balsa, José Antonio; de la Puerta, Cristina; Botella, José Ignacio; Zamarrón, Isabel; Elías, Elena; del Río, José Ignacio Pérez; Alonso, Paloma; Candela, Ángel; Blanco-Colio, Luis Miguel; et al.; *Nutrition in Clinical Practice*, 2014 Oct; 29 (5): 672-80.

Abstract: BACKGROUND: Taurine's role in bile acid metabolism and anti-inflammatory activity could exert a protective effect on hepatobiliary complications associated with parenteral nutrition (PN). In this study, the effects of two amino acid solutions, with and without taurine, on liver function administered to nonacutely ill postsurgical patients as part of a short-term PN regimen were prospectively compared. METHODS: Adult patients randomly received (double-blind) Tauramin 10% or a standard PN solution without taurine as the control (1.5 g amino acid/kg body weight [bw]/d; infusion rate of ≤4 mg glucose/kg bw/d) for a period of 5-30 days. μ-Glutamyl transpeptidase (GGT) and other indicators of liver function, glucose metabolism, lipid profile, inflammation markers, and treatment safety data were collected. RESULTS: Thirty-five patients receiving taurine PN and 39 receiving control PN were enrolled (intention-to-treat [ITT] population). Most patients (n = 62) discontinued after day 7 of follow-up (per-protocol [PP] population: n = 24 and n = 27, respectively). ITT patients with high GGT values after 5 days of PN comprised 68.6% and 64.1%, respectively. The mean change in GGT values with respect to the baseline values was 167 ± 192 and 157 ± 185 IU/L, respectively. Low-density lipoprotein (LDL) cholesterol levels after 7 days of PN were significantly decreased in the taurine PN group of PP patients (-2.83 ± 30.9 vs 23.9 ± 27.0 mg/dL for control PN; $P < .05$). None of the adverse events reported (taurine PN: n = 6; control PN: n = 7) were treatment related. CONCLUSION: PN solutions with and without taurine had similar effects on liver function parameters, except for an LDL reduction in PN with taurine, when administered to nonacutely ill postsurgical patients in the short term (5-7 days).

Out of scope after second sift – RCT on the composition of parenteral nutrition

Comparison of the effects of different intravenous fat emulsions in patients with systemic inflammatory response syndrome and sepsis. (English) By: Sungurtekin H; Degirmenci S; Sungurtekin U; Oguz BE; Sabir N; Kaptanoglu B, *Nutrition In Clinical Practice*: Official Publication Of The American Society For Parenteral And Enteral Nutrition [Nutr Clin Pract], ISSN: 1941-2452, 2011 Dec; Vol. 26 (6), pp. 665-71.

Background: In this study, the authors aimed to compare the effects that a medium- and long-chain triglyceride (MCT/LCT) fat infusion and a fish oil-based (omega-3) fat infusion for parenteral nutrition (PN) had on systemic

inflammation, cytokine response, and hepatic steatosis in mixed intensive care unit (ICU) patients.

Methods: This was a single-center, placebo-controlled, randomized clinical trial in a university hospital. Four patient groups, including systemic inflammatory response syndrome (SIRS) and sepsis patients, were assigned to receive PN employing the MCT/LCT fat infusion or the fish oil-based fat infusion over seven days. Blood biochemistry and liver steatosis were evaluated. Results: Twenty sepsis and 20 SIRS patients were included in this study. There was no statistically significant difference in terms of biochemical values and Acute Physiology and Chronic Health Evaluation II scores between the different feeding groups. Sepsis groups who received MCT/LCT revealed higher grades of liver steatosis by ultrasound on days 7 and 10 ($P < .05$). Tumor necrosis factor (TNF)-α and interleukin (IL)-6 values in sepsis group 1 (S1) were higher than in sepsis group (S2) on day 7, whereas IL-1 values were higher on days 3, 7, and 10 in group S1 than in group S2. Conversely, IL-10 values on days 3 and 7 were significantly higher in group S2. Conclusion: Fish oil-based fat emulsions might have anti-inflammatory and hepatoprotective effects in hyperinflammatory disease such as sepsis. TURKEY.

Out of scope after second sift – SR of guideline recommendations

Guidelines recommendations on care of adult patients receiving home parenteral nutrition: a systematic review of global practices. (English) By: Dreesen M; Foulon V; Vanhaecht K; De Pourcq L; Hiele M; Willems L, *Clinical Nutrition* (Edinburgh, Scotland) [Clin Nutr], ISSN: 1532-1983, 2012 Oct; Vol. 31 (5), pp. 602-8.

Background& Aims: Because home parenteral nutrition (HPN) in adult patients can give rise to a variety of complications, good guidance is necessary. To achieve this, clarity and consistency in guidelines are essential. The aim of this review is to identify and compare evidence-based guidelines, and to compile a list of main recommendations, according to their evidence-based grade. Methods: We searched Medline and the international guideline database for HPN guidelines, performed a content analysis of retrieved guidelines, and evaluated their quality. We then compiled a comparative table of guideline recommendations along with their assigned level of evidence. Summary Of Results: Six systematically developed evidence-based guidelines and one expert opinion-based standard for home care were retrieved. Of these guidelines, two were exclusively devoted to HPN. Although the guidelines generally covered the same topics, most did not provide information on intravenous medication, bone metabolic disease, and indications in patients with malignant disease. Moreover, we found grading discrepancies among various guidelines, as identical recommendations were often labelled with different grades. Conclusion: Our comparison of guidelines and standards for HPN revealed substantial differences among recommendations. Identification of these discrepancies and omissions should facilitate the development of more comprehensive and better justified guidelines in the future.

Out of scope at full text – guideline

Australasian Society for Parenteral and Enteral Nutrition guidelines for supplementation of trace elements during parenteral nutrition.(includes abstract) Osland, Emma J; Ali, Azmat; Isenring, Elizabeth; Ball, Patrick; Davis, Melvyn; Gillanders, Lyn; *Asia Pacific Journal of Clinical Nutrition*, 2014; 23 (4): 545-54.

Abstract: BACKGROUND: This work represents the first part of a progressive review of AuSPEN's 1999 Guidelines for Provision of Micronutrient Supplementation in Adult Patients receiving Parenteral Nutrition, in recognition of the developments in the literature on this topic since that time. METHODS: A systematic literature review was undertaken and recommendations were made based on the available evidence and with consideration to specific elements of the Australian and New Zealand practice environment. The strength of evidence underpinning each recommendation was assessed. External reviewers provided feedback on the guidelines using the AGREE II tool. RESULTS: Reduced doses of manganese, copper, chromium and molybdenum, and an increased dose of selenium are recommended when compared with the 1999 guidelines. Currently the composition of available multi-trace element formulations is recognised as an obstacle to aligning these guidelines with practice. A paucity of available literature and limitations with currently available methods of monitoring trace element status are acknowledged. The currently unknown clinical impact of changes to trace element contamination of parenteral solutions with contemporary practices highlights need for research and clinical vigilance in this area of nutrition support practice. CONCLUSIONS: Trace elements are essential and should be provided daily to patients receiving parenteral nutrition. Monitoring is generally only required in longer term parenteral nutrition, however should be determined on an individual basis. Industry is encouraged to modify existing multi-trace element solutions available in Australia and New Zealand to reflect changes in the literature outlined in these guidelines. Areas requiring research are highlighted.

Out of scope at full text – RCT of the indications for supplemental parenteral nutrition

The effect of L-alanyl-L-glutamine dipeptide supplemented total parenteral nutrition on infectious morbidity and insulin sensitivity in critically ill patients. Grau T; Bonet A; Miñambres

E; Piñeiro L; Irles JA; Robles A; Acosta J; Herrero I; Palacios V; Lopez J; et al.; Metabolism, Nutrition Working Group, SEMICYUC, Spain; *Critical Care Medicine*, 2011 Jun; 39 (6): 1263-8.

Abstract: OBJECTIVE: The aim of this study was to assess the clinical efficacy of alanine-glutamine dipeptide-supplemented total parenteral nutrition defined by the occurrence of nosocomial infections. Secondary parameters included Sequential Organ Failure Assessment score, hyperglycemia and insulin needs, intensive care unit and hospital length of stay, and six-month mortality. DESIGN: Multicenter, prospective, double-blind, randomized trial. SETTING: Twelve intensive care units at Spanish hospitals. PATIENTS: One hundred twenty-seven patients with Acute Physiology and Chronic Health Evaluation II score >12 and requiring parenteral nutrition for 5-9 days. INTERVENTION: Patients were randomized to receive an isonitrogenous and isocaloric total parenteral nutrition or alanine-glutamine dipeptide-supplemented total parenteral nutrition. Nutritional needs were calculated: 0.25 g N/kg(-1)/d(-1) and 25 kcal/kg(-1)/d(-1). The study group received 0.5 g/kg(-1)/d(-1) of glutamine dipeptide and the control total parenteral nutrition group a similar amount of amino acids. Hyperglycemia was controlled applying an intensive insulin protocol with a target glycemia of 140 mg/dL. MEASUREMENTS AND MAIN RESULTS: The two groups did not differ at inclusion for the type and severity of injury or the presence of sepsis or septic shock. Caloric intake was similar in both groups. Preprotocol analysis showed that treated patients with alanine-glutamine dipeptide-supplemented total parenteral nutrition had lesser nosocomial pneumonia, 8.04 vs. 29.25 episodes-[0/00] days of mechanical ventilation ($p = .02$), and urinary tract infections, 2.5 vs. 16.7 episodes-[0/00] days of urinary catheter ($p = .04$). Intensive care unit, hospital, and 6-month survival were not different. Mean plasmatic glycemia was 149 ± 46 mg/dL in the alanine-glutamine dipeptide-supplemented total parenteral nutrition group and 155 ± 51 mg/dL in the control total parenteral nutrition group ($p < .04$), and mean hourly insulin dose was 4.3 ± 3.3 IU in the alanine-glutamine dipeptide-supplemented total parenteral nutrition group and 4.7 ± 3.7 IU in control total parenteral nutrition group ($p < .001$). Multivariate analysis showed a 54% reduction of the amount of insulin for the same levels of glycemia in the alanine-glutamine dipeptide-supplemented total parenteral nutrition group. CONCLUSIONS: Total parenteral nutrition supplemented with alanine-glutamine in intensive care unit patients is associated with a reduced rate of infectious complications and better glycemic control.

Out of scope at full text – RCT of outcomes for supplemental parenteral nutrition

Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomised controlled clinical trial. (English) By: Heidegger CP; Berger MM; Graf S; Zingg W; Darmon P; Costanza MC; Thibault R; Pichard C. *Lancet* 2013 Feb 2; Vol. 381 (9864), pp. 385-93.

Background: Enteral nutrition (EN) is recommended for patients in the intensive-care unit (ICU), but it does not consistently achieve nutritional goals. We assessed whether delivery of 100% of the energy target from days 4 to 8 in the ICU with EN plus supplemental parenteral nutrition (SPN) could optimise clinical outcome.

Methods: This randomised controlled trial was undertaken in two centres in Switzerland. We enrolled patients on day 3 of admission to the ICU who had received less than 60% of their energy target from EN, were expected to stay for longer than five days, and to survive for longer than seven days. We calculated energy targets with indirect calorimetry on day 3, or if not possible, set targets as 25 and 30 kcal per kg of ideal bodyweight a day for women and men, respectively. Patients were randomly assigned (1:1) by a computer-generated randomisation sequence to receive EN or SPN. The primary outcome was occurrence of nosocomial infection after cessation of intervention (day 8), measured until end of follow-up (day 28), analysed by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00802503. Findings: We randomly assigned 153 patients to SPN and 152 to EN. 30 patients discontinued before the study end. Mean energy delivery between day 4 and 8 was 28 kcal/kg per day (SD 5) for the SPN group (103% [SD 18%] of energy target), compared with 20 kcal/kg per day (7) for the EN group (77% [27%]). Between days 9 and 28, 41 (27%) of 153 patients in the SPN group had a nosocomial infection compared with 58 (38%) of 152 patients in the EN group (hazard ratio 0•65, 95% CI 0•43-0•97; p=0•0338), and the SPN group had a lower mean number of nosocomial infections per patient (-0.42 [-0.79 to -0.05]; p=0.0248). Interpretation: Individually optimised energy supplementation with SPN starting four days after ICU admission could reduce nosocomial infections and should be considered as a strategy to improve clinical outcome in patients in the ICU for whom EN is insufficient.

Out of scope at full text – enteral administration of glutamine

The effects of intravenous, enteral and combined administration of glutamine on malnutrition in sepsis: a randomized clinical trial.(includes abstract) Koksal, Guniz Meyanci; Erbabacan, Emre; Tunali, Yusuf; Karaoren, Gulsah; Vehid, Suphi; Oz, Huseyin; *Asia Pacific Journal of Clinical Nutrition*, 2014; 23 (1): 34-40.

Abstract: Our aim was to compare the effects of intravenous, enteral, and enteral plus intravenous supplemented glutamine on plasma transferrin, nitrogen balance, and creatinine/height index in septic patients with malnutrition. Blood and urine samples were collected for transferrin, urea and creatinine measurements. Samples, SOFA score and protein-calorie intake values were repeated on

days 7 and 15. Patients (n:120) were randomly divided into four groups. Group I received 30 g/day IV glutamine, group II received 30 g/day enteral glutamine, group III received 15 g/day IV and 15 g/day enteral glutamine. Group IV received only enteral feeding as a control group. Transferrin levels decreased in group IV ($p<0.01$ 0-7 days, $p<0.01$ 7-15 days, $p<0.01$ 0-15 days). Nitrogen balance levels were highest in group IV when compared with group I ($p<0.05$, $p<0.001$), group II ($p<0.001$), and group III ($p<0.05$, $p<0.001$) on days 7-15. Creatinine/height indexes increased in group I ($p<0.001$), group II ($p<0.001$), group III ($p<0.001$), and group IV ($p<0.05$) on day 15. In group III the creatinine/height index was higher than in groups I and II ($p<0.05$). In group IV, creatinine/height index was lower than in group I ($p<0.01$) and group II ($p<0.001$). Protein-calorie intake in group IV was higher than others on day 7 ($p<0.05$). SOFA scores of group IV were higher than the other groups on day 15 ($p<0.05$). This study demonstrated, that combined route of gln supplementation resulted in the most positive outcome to transferrin, creatine/height index and nitrogen balance (on days 7 and 15) during the catabolic phase of septic patients with malnutrition. TURKEY

Section 8: Infusion therapy phlebitis

Out of scope – secondary analysis of an RCT

Risk factors for peripheral intravenous catheter failure: a multivariate analysis of data from a randomized controlled trial. Wallis MC; McGrail M; Webster J; Marsh N; Gowardman J; Playford EG; Rickard CM, *Infection Control And Hospital Epidemiology* ISSN: 1559-6834, 2014 Jan; Vol. 35 (1), pp. 63-8.

Objective: To assess the relative importance of independent risk factors for peripheral intravenous catheter (PIVC) failure. Methods: Secondary data analysis from a randomized controlled trial of PIVC dwell time. The Prentice, Williams, and Peterson statistical model was used to identify and compare risk factors for phlebitis, occlusion, and accidental removal. Setting: Three acute care hospitals in Queensland, Australia. Participants: The trial included 3,283 adult medical and surgical patients (5,907 catheters) with a PIVC with greater than 4 days of expected use. Results: Modifiable risk factors for occlusion included hand, antecubital fossa, or upper arm insertion compared with forearm (hazard ratio [HR], 1.47 [95% confidence interval (CI), 1.28-1.68], 1.27 [95% CI, 1.08-1.49], and 1.25 [95% CI, 1.04-1.50], respectively); and for phlebitis, larger diameter PIVC (HR, 1.48 [95% CI, 1.08-2.03]). PIVCs inserted by the operating and radiology suite staff had lower occlusion risk than ward insertions (HR, 0.80 [95% CI, 0.67-0.94]). Modifiable risks for accidental removal included hand or antecubital fossa insertion compared with forearm (HR, 2.45 [95% CI, 1.93-3.10] and 1.65 [95% CI, 1.23-2.22], respectively), clinical staff insertion compared with intravenous service (HR, 1.69 [95% CI, 1.30-2.20]); and smaller PIVC diameter (HR, 1.29 [95% CI, 1.02-1.61]). Female sex was a nonmodifiable factor associated with an increased risk of both phlebitis (HR, 1.64 [95% CI, 1.28-2.09]) and occlusion (HR, 1.44 [95% CI, 1.30-1.61]).

Conclusions: PIVC survival is improved by preferential forearm insertion, selection of appropriate PIVC diameter, and insertion by intravenous teams and other specialists.

Trial Registration: The original randomized controlled trial on which this secondary analysis is based is registered with the Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au; ACTRN12608000445370).

Out of scope – condition specific

Very early administration of progesterone for acute traumatic brain injury. Wright DW; Yeatts SD; Silbergleit R; Palesch YY; Hertzberg VS; Frankel M; Goldstein FC; Caveney AF; Howlett-Smith H; Bengelink EM; Manley GT; Merck LH; Janis LS; Barsan WG; NETT Investigators, *The New England Journal Of Medicine* ISSN: 1533-4406, 2014 Dec 25; Vol. 371 (26), pp. 2457-66.

Background: Traumatic brain injury (TBI) is a major cause of death and disability worldwide. Progesterone has been shown to improve neurologic outcome in multiple experimental models and two early-phase trials involving patients with TBI. Methods: We conducted a double-blind, multicenter clinical trial in which patients with severe, moderate-to-severe, or moderate acute TBI (Glasgow Coma Scale score of 4 to 12, on a scale from 3 to 15, with lower scores indicating a lower level of consciousness) were randomly assigned to intravenous progesterone or placebo, with the study treatment initiated within 4 hours after injury and administered for a total of 96 hours. Efficacy was defined as an increase of 10 percentage points in the proportion of patients with a favorable outcome, as determined with the use of the stratified dichotomy of the Extended Glasgow Outcome Scale score at six months after injury. Secondary outcomes included mortality and the Disability Rating Scale score. Results: A total of 882 of the planned sample of 1140 patients underwent randomization before the trial was stopped for futility with respect to the primary outcome. The study groups were similar with regard to baseline characteristics; the median age of the patients was 35 years, 73.7% were men, 15.2% were black, and the mean Injury Severity Score was 24.4 (on a scale from 0 to 75, with higher scores indicating greater severity). The most frequent mechanism of injury was a motor vehicle accident. There was no significant difference between the progesterone group and the placebo group in the proportion of patients with a favorable outcome (relative benefit of progesterone, 0.95; 95% confidence interval

[CI], 0.85 to 1.06; P=0.35). Phlebitis or thrombophlebitis was more frequent in the progesterone group than in the placebo group (relative risk, 3.03; CI, 1.96 to 4.66). There were no significant differences in the other prespecified safety outcomes. Conclusions: This clinical trial did not show a benefit of progesterone over placebo in the improvement of outcomes in patients with acute TBI. (Funded by the National Institute of Neurological Disorders and Stroke and others; PROTECT III ClinicalTrials.gov number, NCT00822900).

Out of scope at full text – Re-publish of the results of the RCT by Rickard et al. 201236

Routine versus clinically indicated replacement of peripheral catheters. Ullman, Amanda J 1 ; Keogh, Samantha; Marsh, Nicole; Rickard, Claire M. *British Journal of Nursing*. 2015; 24 (2), S14.

Currently the US Centers for Disease Control and Prevention (CDC) state that peripheral intravenous catheters do not need to be replaced more frequently than every 72 to 96 hours to reduce the risk of infection and phlebitis in adults. Here, Ullman et al examine the effect of extension of peripheral intravenous catheter dwell time beyond 3 days with replacement of catheters only for clinical reasons.

Section 9: Intraosseous access

None out of scope

Section 10: Midline catheters

None out of scope

Section 11: Peripheral access device and flushing

Out of scope – not an SR

Guidelines on timing in replacing peripheral intravenous catheters. Ho, Ken HM1; Cheung, Daphne SK1 Student and Instructor I, School of Continuing and Professional Studies, The Chinese University of Hong Kong, Hong Kong, China. *Journal of Clinical Nursing*, Volume. 2012; 21(11-12), 1499-1506.

Aims. To design clinical guidelines on timing for replacing peripheral intravenous catheters, in an attempt to decrease complications and lower related expenditures. Background. Intravenous therapy is a common intervention for patients in hospitals and some other clinical settings. However, the currently available international and local guidelines have come under criticism. There is a need to develop evidence-based guidelines to benefit patients as well as to save on the resources of health care systems. Design. A discursive paper. Methods. The evidence-based health care of Dawes et al. (BioMed Central Medical Education5, 2005, 1) was adopted to guide the development of this guideline. Cochrane Library Database was searched with four keywords: (1) Intravenous, (2) Infusion, (3) Infection, and (4) Timing, which identified one SYSTEMATic review. Guideline on timing for replacing peripheral intravenous catheters was proposed based on the SYSTEMATic review. Further recommendation for application in clinical settings and quality management are given. An algorithm on the replacement of peripheral intravenous catheters was included. Conclusion. Clinically indicated replacement was suggested over routine replacement because the former results in lower health care expenditures without involving any extra risks of complications. Relevance to clinical practice. These guidelines are simple and easy to follow in a clinical environment. An algorithm is given to enhance the usage of these guidelines by clinicians.

Section 12: Subcutaneous infusion

Out of scope – condition specific

Comparative Effectiveness of Continuous Subcutaneous Insulin Infusion Using Insulin Analogs and Multiple Daily Injections in Pregnant Women with Diabetes Mellitus: A Systematic Review and Meta-Analysis. Ranasinghe, Padmini D. 1 ; Maruthur, Nisa M.; Nicholson, Wanda K.; Yeh, Hsin-Chieh; Brown, Todd; Suh, Yong; Wilson, Lisa M.; Nannes, Elisabeth B.; Berger, Zack; Bass, Eric B.; Golden, Sherita. *Journal of Women's Health*. 2015; 24 (3) 237-249.

Abstract. We systematically reviewed the effectiveness and safety of continuous subcutaneous insulin infusion (CSII) with insulin analogs compared with multiple daily injections (MDI) in pregnant women with diabetes mellitus. We searched Medline®, Embase®, and the Cochrane Central Register of Controlled Trials through May 2013. Studies comparing CSII with MDI in pregnant women with diabetes mellitus were included. Studies using regular insulin CSII were excluded. We conducted meta-analyses where there were two or more comparable studies based on the type of insulin used in the MDI arm. Seven cohort studies of pregnant women with type 1 diabetes reported improvement in hemoglobin A1c (HbA1c) in both groups. Meta-analysis showed no difference in maternal and fetal outcomes for CSII versus MDI. Results were similar when CSII was compared with MDI with insulin analogs or regular insulin. Studies had moderate to high risk bias with incomplete descriptions of study methodology, populations, treatments, follow up, and outcomes. We conclude that observational studies reported similar improvements in HbA1c with CSII and MDI during pregnancy, but evidence was insufficient to rule out possible important differences between CSII and MDI for maternal and fetal outcomes. This highlights the need for future studies to examine the effectiveness and safety of CSII with insulin analogs and MDI in pregnant women with diabetes mellitus.

Out of scope – condition specific

Clinical effectiveness and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes: systematic review and economic evaluation. Cummins E; Royle P; Snaith A; Greene A; Robertson L; McIntyre L; Waugh N; Health *Technology Assessment*, 2010; 14 (11): 1-208.

BACKGROUND: The National Institute for Health and Clinical Excellence (NICE) was reviewing its previous guidance on continuous subcutaneous insulin infusion (CSII). The review provided an assessment of evidence which had been published since the previous NICE appraisal (TA 151) in 2007. OBJECTIVES: To examine the clinical effectiveness and cost-effectiveness of using CSII to treat diabetes. To update the previous assessment report by reviewing evidence that has emerged since the last appraisal, and to take account of developments in alternative therapies, in particular the long-acting analogue insulins, which cause fewer problems with hypoglycaemia. DATA SOURCES: A systematic review of the literature and an economic evaluation were carried out. The bibliographic databases used were MEDLINE and EMBASE, 2002 to June 2007. The Cochrane Library (all sections), the Science Citation Index (for meeting abstracts only) and the website of the 2007 American Diabetes Association were also searched. REVIEW METHODS: The primary focus for type 1 diabetes mellitus (T1DM) was the comparison of CSII with multiple daily injection (MDI), based on the newer insulin analogues, but trials of neutral protamine Hagedorn (NPH)-based MDI that had been published since the last assessment were identified and described in brief. For type 2 diabetes mellitus (T2DM), all trials of MDI versus CSII were included, whether the long-acting insulin was analogue or not, because there was no evidence that analogue-based MDI was better than NPH-based MDI. Trials that were shorter than 12 weeks were excluded. Information on the patients' perspectives was obtained from four sources: the submission from the pump users group - Insulin Pump Therapy (INPUT); interviews with parents of young children who were members of INPUT; some recent studies; and from a summary of findings from the previous assessment report. Economic modelling used the Center for Outcomes Research (CORE) model, through an arrangement with the NICE and the pump manufacturers, whose submission also used the CORE model. RESULTS: The 74 studies used for analysis included eight randomised controlled trials (RCTs) of CSII versus analogue-based MDI in either T1DM or T2DM, eight new (since the last NICE appraisal) RCTs of CSII versus NPH-based MDI in T1DM, 48 observational studies of CSII, six studies of CSII in pregnancy, and four systematic reviews. The following benefits of CSII were highlighted: better control of blood glucose levels, as reflected by glycated haemoglobin (HbA1c) levels, with the size of improvement depending on the level before starting CSII; reduction in swings in blood glucose levels, and in problems due to the dawn phenomenon; fewer problems with hypoglycaemic episodes; reduction in insulin dose per day, thereby partly off-setting the cost of CSII; improved quality of life, including a reduction in the chronic fear of severe hypoglycaemia; more flexibility of lifestyle – no need to eat at fixed intervals, more freedom of lifestyle and easier participation in social and physical activity; and benefits for the patients' family. The submission from INPUT emphasised the quality of life gains from CSII, as well as improved control and fewer hypoglycaemic episodes. Also, there was a marked discrepancy between the improvement in social quality of life reported by successful pump users, and the lack of convincing health-related quality of life gains reported in the trials. With regard to economic evaluation, the main cost of CSII is for consumables, such as tubing and cannulas, and is about 1,800-2,000 pounds per year. The cost of the pump, assuming 4-year life, adds another 430-720 pounds per annum. The extra cost compared with analogue-based MDI averages 1,700 pounds. Most studies, assuming a reduction in HbA1c level of 1.2%, found CSII to be cost-effective. LIMITATIONS: The most important weakness of the evidence was the very small number of randomised trials of CSII against the most modern forms of MDI, using analogue insulins. CONCLUSIONS: Based on the totality of evidence, using observational studies to supplement the limited data from randomised trials against best MDI, CSII provides some advantages over MDI in T1DM for both children and adults. However, there was no evidence that CSII is better than analogue-based MDI in T2DM or in pregnancy. Further trials with larger numbers and longer durations comparing CSII and optimised MDI in adults, adolescents and children are needed. In addition, there should be a trial of CSII versus MDI with similar provision of structured education in both arms. A trial is also needed for pregnant women with pre-existing diabetes, to investigate using CSII to the best effect.

Out of scope – condition specific

Subcutaneous versus intravenous insulin therapy for glucose control in non-diabetic trauma patients. A randomized controlled trial.(includes abstract) Aron, A.; Wang, J.; Collier, B.; Ahmed, N.; Brateanu, A.; *Journal of Clinical Pharmacy & Therapeutics*, 2013 Feb; 38 (1): 24-30.

Abstract: What is known and Objective: Hyperglycaemia in trauma patients admitted to the intensive care unit (ICU) is associated with increased morbidity and mortality. Our pilot study is a prospective randomized controlled trial comparing the impact of two glucose control regimens on outcomes in non-diabetic trauma patients admitted with hyperglycaemia to the ICU. Methods: Trauma patients with blood glucose levels (BGLs) ≥7•8 mm within the first 48 h of the hospital admission were randomized to receive intermittent SQ or continuous IV insulin to maintain BGLs between 4•4 and 6•1 mm. We excluded diabetics on the basis of history, or a glycosylated haemoglobin ≥6% on admission. We compared the effect of SQ vs. IV insulin therapy on the ICU length of stay (ILOS). Results and Discussion: A total of 58 patients were included in the study. The SQ and IV groups were comparable in terms of age, gender, injury severity, revised trauma,

Glasgow coma scores and type of trauma (blunt vs. penetrating). There was no significant difference between the two treatment groups in the ILOS (3 vs. 2 days, P = 0•084), hospital length of stay (8 vs. 6, P = 0•09), ventilator support days (6 vs. 3, P = 0•98), requirement for blood transfusion (P = 0•66), rates of infections (P = 0•70), acute kidney injury (P = 0•99) and mortality (P = 0•61). What is new and Conclusion: There was no difference between SQ and IV insulin therapy in the ILOS in non-diabetic trauma patients.

Out of scope – condition specific

Patients' preferences for subcutaneous trastuzumab versus conventional intravenous infusion for the adjuvant treatment of HER2-positive early breast cancer: final analysis of 488 patients in the international, randomized, two-cohort PrefHer study. Pivot X; Gligorov J; Müller V; Curigliano G; Knoop A; Verma S; Jenkins V; Scotto N; Osborne S; Fallowfield L; PrefHer Study Group, *Annals Of Oncology*: Official Journal Of The European Society For Medical Oncology / ESMO, ISSN: 1569-8041, 2014 Oct; Vol. 25 (10), pp. 1979-87.

Background: Patients with HER2-positive early breast cancer (EBC) preferred subcutaneous (s.c.) trastuzumab, delivered via single-use injection device (SID), over the intravenous (i.v.) formulation (Cohort 1 of the PrefHer study: NCT01401166). Here, we report patient preference, health care professional satisfaction, and safety data pooled from Cohort 1 and also Cohort 2, where s.c. trastuzumab was delivered via hand-held syringe. Patients and Methods: Patients were randomized to receive four adjuvant cycles of 600 mg fixed-dose s.c. trastuzumab followed by four cycles of standard i.v. trastuzumab, or vice versa. The primary endpoint was overall preference proportions for s.c. or i.v., assessed by patient interviews in the evaluable ITT population. Results: A total of 245 patients were randomized to receive s.c. followed by i.v. and 243 received i.v. followed by s.c. (evaluable ITT populations: 235 and 232 patients, respectively). s.c. was preferred by 415/467 [88.9%; 95% confidence interval (CI) 85.7-91.6; P < 0.0001; two-sided test against null hypothesis of 65% s.c. preference]; 45/467 preferred i.v. (9.6%; 95% CI 7-13); 7/467 indicated no preference (1.5%; 95% CI 1-3). Clinician-reported adverse events occurred in 292/479 (61.0%) and 245/478 (51.3%) patients during the pooled s.c. and i.v. periods, respectively (P < 0.05; 2 × 2 CT); 16 patients (3.3%) in each period experienced grade 3 events; none were grade 4/5. Conclusions: PrefHer revealed compelling and consistent patient preferences for s.c. over i.v. trastuzumab, regardless of SID or hand-held syringe delivery. s.c. was well tolerated and safety was consistent with previous reports, including the HannaH study (NCT00950300). No new safety signals were identified compared with the known i.v. profile in EBC. PrefHer and HannaH confirm that s.c. trastuzumab is a validated and preferred option over i.v. for improving patients' care in HER2-positive breast cancer. Clinicaltrialsgov Registration Number: NCT01401166.

Out of scope – condition specific

An open-label trial of a sumatriptan auto-injector for migraine in patients currently treated with subcutaneous sumatriptan. Landy SH; Tepper SJ; Wein T; Schweizer E; Ramos E, *Headache*, ISSN: 1526-4610, 2013 Jan; Vol. 53 (1), pp. 118-25.

Objective: To assess the ability of patients, during an acute migraine attack, to successfully self-inject a single dose of sumatriptan using a novel sumatriptan auto-injector (Alsuma(®)), and to evaluate the safety, tolerability, and effectiveness of this sumatriptan auto-injector during an acute migraine attack. Background: This sumatriptan auto-injector is a single-use system for the rapid subcutaneous delivery of 6 mg of sumatriptan succinate in the acute management of migraine pain. This auto-injector was developed to address the clinical need for an easy-to-use and rapid-to-administer system that did not require any assembly during the time of an ongoing attack. Methods: This was an open-label, phase 3 trial conducted at 10 sites in the USA. Male or female adults, ages 18-60 years old, were eligible for study entry if they met International Headache Society criteria for migraine with or without aura, with at least two attacks per month, and if they reported use of subcutaneous injectable sumatriptan on at least two occasions within the previous two months. During the onset of a migraine attack of moderate-to-severe intensity, patients were asked to administer a 6-mg subcutaneous dose of sumatriptan using the auto-injector. Patients returned to the study site within 72 hours of the migraine for the post-treatment assessment visit. Results: A total of 63 patients met entry criteria and received a dose of study medication (the intent-to-treat sample). Sixty-one patients (96.8%) reported injection in the thigh, and two patients (3.2%) reported injection in the arm. On the patient questionnaire, 100% of patients (95% confidence interval [CI] 94.3-100%) "agreed" or "agreed strongly" that the written instructions for the auto-injector were clear and easy to follow (30.2% "agreed"; 69.8% "agreed strongly"); 95.2% of patients (95% CI 86.7-99.0%) found that the auto-injector was easy to use (36.5% "agreed"; 58.7% "agreed strongly"), and 65.1% of patients (95% CI 52.0-76.7%) stated that they preferred the new auto-injector to the traditional auto-injector that they were using prior to study entry (42.9% "agreed"; 22.2% "agreed strongly"). Headache response rate at two hours was 93.7% (95% CI 84.5-98.2%), and pain-free rate at two hours was 60.3% (95% CI 47.2-72.4%). Pain-free rates at 2 hours were similarly high (58.3%; 95% CI 36.6-77.9%) in the subgroup of patients reporting severe baseline headache pain. Only one patient reported use of rescue medication after use of the auto-injector, a single oral dose of sumatriptan 100 mg on the same day. The most frequent adverse event was injection site bruising, reported by 15.9% of patients, and

rated in all instance as mild in intensity. The second most frequent adverse event was injection site pain, reported by 6.3% of patients, and rated as mild by all patients except one, who rated it as moderate in intensity. Conclusion: The majority of injection-experienced patients reported the pre-assembled, single-use sumatriptan auto-injector to be an easy-to-use, preferred treatment for an acute migraine attack. The study found the auto-injector to be safe and well tolerated, with levels of injection site reactions that were mild and infrequent.

Out of scope – condition specific

Consequences of delayed pump infusion line change in patients with type 1 diabetes mellitus treated with continuous subcutaneous insulin infusion. Thethi TK; Rao A; Kawji H; Mallik T; Yau CL; Christians U; Fonseca V, *Journal Of Diabetes And Its Complications*, ISSN: 1873-460X, 2010 Mar-Apr; Vol. 24 (2), pp. 73-8.

Objective: To systematically investigate the effect of lack of adherence to the recommended change in insulin pump infusion line use beyond 48 h and determine whether the type of insulin made a difference. Research Design and Methods: This was a double-blind, randomized, crossover trial with 20 patients with diabetes mellitus I using insulins aspart and lispro without a line change for up to 100 h. Using retrospective continuous glucose monitoring, we analyzed the average glucose over the day. Changes in serum 1,5-anhydroglucitol, carboxymethyllysine, and free 15-F(2t) isoprostane were also studied.

Results: From Day 2 to Day 5 of the pump line use, the daily average glucose level increased from 122.7 to 163.9 mg/dl (P<.05), fasting glucose from 120.3 to 154.5 mg/dl (P<.05), postprandial glucose from 114.6 to 172.1 mg/dl (P<.05), and the daily maximum glucose from 207.7 to 242.8 dl (P<.05 for the trend). Time period that the glucose was >180 mg/dl increased from 14.5% to 38.3% (P<.05). Loss of control occurred despite increase in total daily insulin dose from 48.5+/-11.8 to 55.3+/-17.9 U (P=.05). There was no difference in loss of control between insulin types, and biomarkers measured did not change significantly.

Conclusions: The insulin pump infusion should be changed every 48 h in patients using continuous subcutaneous insulin infusion (CSII), to avoid loss of glycemic control. In the short-term, this loss of glycemic control has no impact on oxidative stress and glycation.

Appendix D: Manufacturers' submissions out of scope

Table 17: Manufacturers' submissions out of scope

Title	Author(s)	Year	Reason out of scope
Hypodermoclysis: a literature review to assist in clinical practice	Bruno VG	2013	Not a systematic review
Flushing and Locking of Venous Catheters: Available Evidence and Evidence Deficit	Goosens GA	2015	Not a systematic review
Heparin Locking for Central Venous Catheters	Hadaway L	2006	Not a systematic review
Accepted but Unacceptable: Peripheral IV catheter failure	Helm, RE; Klausner JD; Klemperer JD et al.	2015	Not a systematic review
Retrospective comparative audit of two peripheral IV securement dressings	Jackson A	2012	Non-RCT
A Time and Motion Study of Peripheral Venous Catheter Flushing Practice Using Manually Prepared and Prefilled Flush Syringes	Keogh S, Marsh N, Higgins N et al.	2014	Non-RCT
Stage One: Warning. Risk of death or severe harm due to inadvertent injection of skin preparation solution	Patient Safety Alert: NHS England	2015	Guideline
Risk of infection due to medical interventions via central venous catheters or implantable venous access port systems at the middle port of a three-way cock: luer lock cap vs. luer access split septum (Q-Syte)	Pohl F; Hartmann W; Holzmann T et al.	2014	Non-RCT
Fluid dispersal from safety cannulas: An in vitro comparative test	Rosenthal VD; Hughes G.	2015	Non-RCT
Registration of Blood Exposure Accidents in the Netherlands by a Nationally Operating Call Center	Schneeberger PM; Meiberg AE; Warmelts RN et al.	2012	Non-RCT
Strategies to Prevent Central Line-Associated Blood stream Infections in Acute Care Hospitals: 2014 Update	Society for Healthcare Epidemiology of America	2014	Guideline
The Science and Fundamentals of Intraosseous Vascular Access	Vidacare Science and Clinical Team	2013	Not a systematic review
Needlestick injuries: causes, preventability and psychological impact	Wicker S; Stirn AV; Rabenau HF et al.	2014	Non-RCT
Injection device-related risk management toward safe administration of medications: experience in a university teaching hospital in The People's Republic of China	Zhu L; Li W; Song P et al.	2014	Non-RCT

Section 3: Phase two of the evidence review (clinical practice)

Contents

Section 3 authors – Toni McIntosh and Anda Bayliss

Introduction

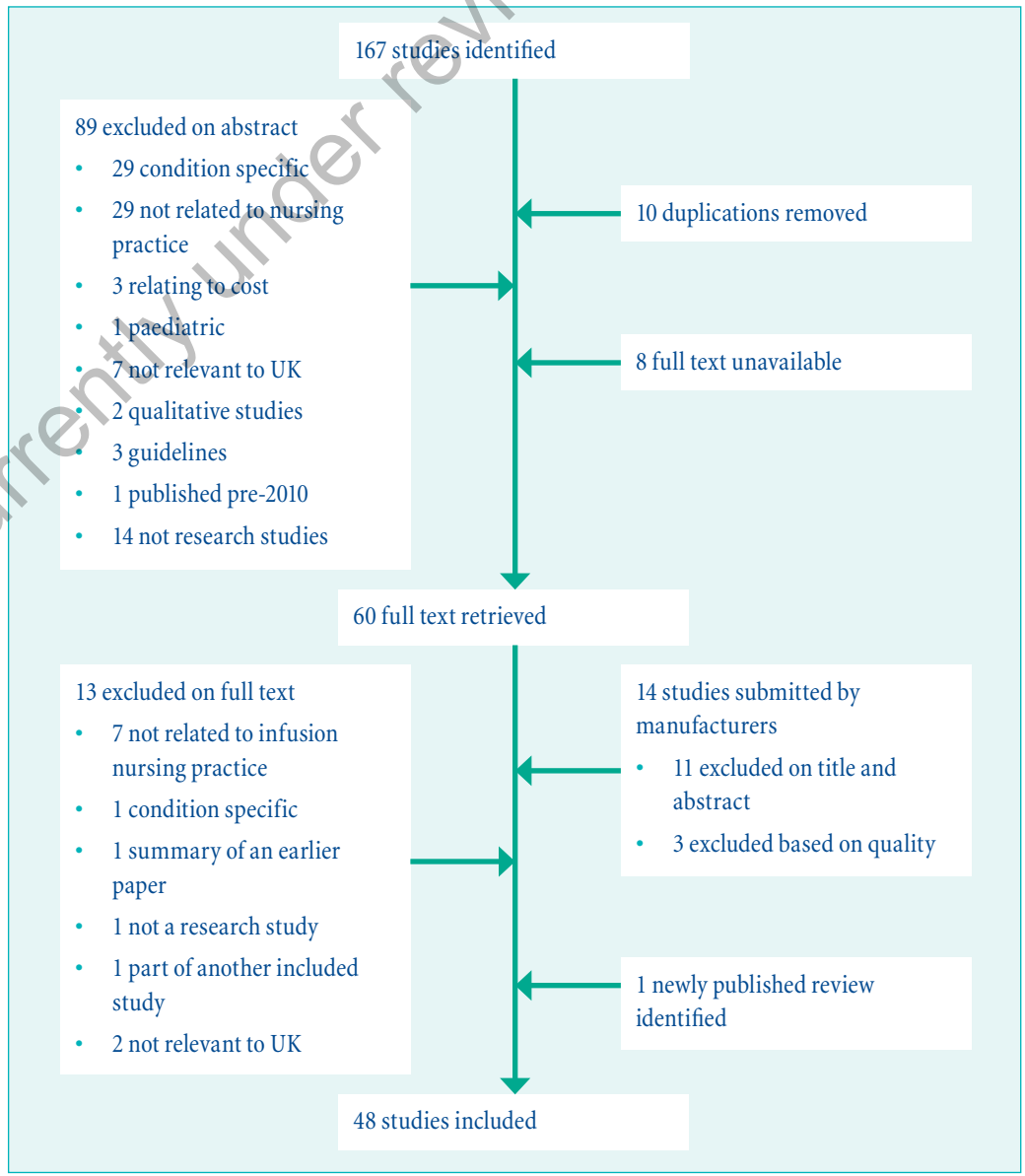
This section reports the results of a review of the quantitative (and some review) studies identified from the initial search, which were excluded from Phase 1 of the review, on the basis of not being randomised controlled trials (RCTs) or systematic reviews (SRs). It is widely understood that RCTs provide the gold standard of evidence to inform practice, however in nursing research it is often impractical or unethical to conduct RCTs. Therefore, well designed non-RCT studies can provide valuable information to add to the evidence base and to inform policy and practice.

Methods

Identification of relevant studies

A systematic approach was employed to identify studies for inclusion and extract all relevant data. The search had already been carried out by the RCN and once all relevant SRs and RCTs had been identified for separate analysis, the remaining 167 studies were screened for relevance based on the title and abstract. Only research reporting studies with a quantitative design or review, published from 2010 onwards, related to nursing practice and infusion therapy for adults, non-condition specific and being relevant to the UK were included (see Section 1 for detail on the search strategy). On the basis of the above, 99 studies were discarded during the initial sift, including ten duplications. Studies which could not be retrieved electronically or from the RCN library were excluded on the basis of time; as a result, 60 full text articles were obtained for further screening and analysis. All full text articles were screened for relevance using the predetermined inclusion and exclusion criteria, leading to the exclusion of 13 further studies at this stage (see Appendix B). During the review period, 14 studies were submitted by manufacturers that were not included in the first phase of the review and were subsequently considered for inclusion in the second phase reported in this paper. All were excluded at this stage (see Appendix C [i]). One additional literature review was identified that had just been published and was deemed suitable for inclusion. As a result, 48 studies were included in the final review (see Figure 1). The number of studies that resulted from the search and inclusion process in each of the 12 areas previously determined as relevant to nursing practice in infusion therapy is presented in Table 1.

Figure 1: Flow chart of studies included and excluded at each stage of the sift



i Identification of published guidance relevant to the RCN's *Infusion therapy standards* was conducted in parallel outside this review by the expert panel and any such guidance found in the course of the review was passed on to the panel.

Table 1: Areas of infusion therapy included in the review

Section	Number of studies
Add on devices	2
Arterial catheters	0
Blood sampling	8
Central venous access devices	3
Flow control devices	1
Infusion-related bloodstream infections	15
Infusion therapy phlebitis	4
Intraosseous access	3
Midline catheters	5
Parenteral nutrition	4
Peripheral access devices and flushing	3
Subcutaneous infusions	0

Quality appraisal

The included papers were appraised for quality using an in-house critical appraisal tool, adapted from the EPPI Centre REPOSE Guidelines[47]. This tool included seven areas relating to the study design, sampling, data collection and analysis, and reporting of findings. Each appraisal statement was equally weighted. Papers were scored on each area and an overall quality score assigned (high, medium or low) depending on the number of criteria met, as demonstrated below (see Appendix D):

- 7-6 criteria met or partially met = HIGH
- 5-4 criteria met or partially met = MEDIUM
- 3-0 criteria met or partially met = LOW.

Quality appraisal was conducted by one researcher, with a second researcher independently appraising a sample from each area. No major discrepancies were found between researchers. No studies were excluded on account of quality at this stage, however quality and design are considered when discussing the strength of the evidence in the synthesis.

Data extraction and mapping

A standardised data extraction form was used to extract relevant data from each of the studies. Again, this process was undertaken by a single researcher with a second researcher checking a sample. Data extracted included the country of origin, sample and setting, aim of the study, methods and key findings. Data extraction tables are displayed in the results section below, in their corresponding sections. Once all relevant data had been extracted, studies were mapped in order to provide an overview of the evidence in each area (see Table 2).

Table 2: Summary findings and gaps in the evidence

Section	Evidence	Gaps
Add on devices	One high quality study[54] including an observational clinical survey and lab assessment of disinfection procedures found scrubbing the IV connector hub for at least 5s with 70% isopropyl alcohol pledget significantly reduced bacterial contamination of the hub. One low quality prospective cohort study[38] found that changing from a positive pressure needleless connector to two negative displacement devices and then to an intraluminal protection device over a three year period, led to the elimination of central line-associated bloodstream infections (CLABSI) in a 36-bed long-term acute care hospital.	No evidence was found on the effect on patient safety and outcomes of: • changing add-on devices with each cannula or administration set replacement • changing add-on devices when integrity of either product is compromised.
Arterial catheters	No evidence found in this area	No evidence was found on the effect on patient safety and outcomes of: • different line flushing frequencies for arterial catheters • flushing arterial catheters with saline vs heparinised solutions • using different arteries for cannulation
Blood sampling	One high quality prospective cohort study[23] demonstrated similar haematology, biochemistry and coagulation parameter results between blood samples obtained from a PVC compared with venepuncture. Significant differences were only found in venous blood gas results. 1 high quality quasi experimental study[29] compared lab values of blood samples obtained via CVC compared with venepuncture and found that while some results produced significant differences, these differences were not clinically significant. One high quality quasi experimental study[25] found that drawing blood samples from heparinised PICCs produced similar coagulation test results, except for INR. One medium quality quasi experimental study[11] found that there was no significant difference in activated partial thromboplastin time (aPTT; a coagulation parameter) results when specimens are collected from a CVC compared with venepuncture in patients receiving continuous heparin infusions. However values were significantly prolonged if samples were taken from a port used to deliver heparin. One high quality quasi experimental study[13] demonstrated acceptable rejection rates due to haemolysis in blood samples taken from IV starts in the emergency department. Two high quality quasi experimental studies investigated different blood sampling methods. One found non-wire ports resulted in reduced contamination rates compared to wire ports[33], and the other found the 'Holdex' tube holder was more effective than a standard holder at reducing erythrocyte injury[35]. One high quality quasi experimental study[3] found that 1ml is an adequate waste volume to provide an undiluted blood sample.	No evidence was found for: • venepuncture interventions to reduce fear, pain and anxiety • the effect of site selection for an infusion cannula on patient safety and outcome • the impact of different infusion device flushing before blood sampling • best practice for different devices.

Section	Evidence	Gaps
Central venous access devices	One high quality retrospective cohort study[4] found no significant differences in infection rates between self-administered outpatient parenteral antimicrobial therapy, compared with administration in a hospital or clinic setting. One high quality prospective cohort study[41] examined risk factors for upper extremity deep vein thrombosis (UEDVT) in patients with peripherally inserted central venous catheters (PICCs) and found a statistically significant association between UEDVT and hypertension, obesity, an increase in PICC arm circumference and oedema. One medium quality quasi experimental study[42] found implementing an evidence-based practice intervention related to CVC flushing, resulted in significant improvement in nurses' knowledge and flushing technique.	No evidence was found on the effect on patient safety and outcomes of different line flushing frequencies
Flow control devices	1 low quality narrative review[39] described connector design features which facilitate scrubbing and flushing and improve outcomes. These features included a smooth, tight-fitting septum, low intra-luminal fluid pathway volume, a straight fluid pathway, no dead space, no reflux with connection or disconnection, and fail safe back-up systems.	No evidence was found for: • prognostic factors (for example, age, condition, therapy, care setting) affecting selection of different manual flow control devices on patient outcomes • how different frequencies of flow rate monitoring of different manual flow control devices affect patient outcomes • the effect of electronic devices which generate flow through positive pressure or low pressure devices on patient safety and outcomes.

Section	Evidence	Gaps
Infusion related bloodstream infection	One medium quality retrospective cohort study[1] found that the most common organism causing bloodstream infection in patients with PICCs was Candida glabrata, and that a higher infection rate was observed in the ICU setting. The study hospital also experienced an increase in PICC use with the withdrawal of an IV specialist service for the placement of difficult PVCs. Two medium quality quasi experimental studies[16,22] demonstrated a decrease in CLABSI rates as a result of a post-insertion maintenance bundle including hand hygiene[16,22], aseptic technique during use of connectors[16], dressing changes[16,22], regular assessment of the need for the catheter[16,22], scrubbing the hub for 10-15s before access[16,22], daily inspection of insertion site and site care if dressing wet or soiled[22]. One medium quality prospective cohort study[24] found self-reported compliance with five evidence-based CLABSI reduction practices was associated with reduced CLABSI rates. The practices included hand hygiene, chlorhexidine skin preparation, full barrier precautions, avoidance of femoral line placement, and removal of unnecessary lines. Avoidance of femoral site and removal of unnecessary lines had the strongest independent effects. One medium quality and one low quality prospective cohort study[46,30] demonstrated a decrease in CLABSI rates as a result of a step-wise multimodal intervention. 1 medium quality prospective cohort study[53] demonstrated the effectiveness of various device-related interventions over a three year period on the reduction of CLABSI. These included a change to positive displacement needleless connectors, enforcement of maximal barrier precautions on insertion, implementation of a chlorhexidine gluconate (CHG)-impregnated disk, change to a clear connector, and implementation of a 'scrub the hub' campaign. One high quality observational cohort study using historical controls[14], one low quality prospective observational study[30], and two low quality quasi experimental studies[36,43] demonstrated significant reductions in CLABSI rates with the introduction of daily CHG bathing for patients. One high quality quasi experimental study[28] found the use of a silver coated needleless connector reduced CLABSI rates by 32% compared with a standard needleless connector. One medium quality prospective cohort study[48] and one medium quality quasi experimental study[55] demonstrated significant decreases in CLABSI rates with the introduction of a lead nurse to standardise and facilitate good practice. One medium quality case-control study[49] explored patient- and device-related risk factors for bloodstream infections (BSI) in patients with PICCs and found the following to be associated with BSI: congestive heart failure, intra-abdominal perforation, history of C. diff, recent chemotherapy, presence of tracheostomy tube, and use of a multi lumen catheter. History of COPD and PICC placement in oncology, orthopaedics or surgery proved to be protective factors. One low quality literature review[39] identified a need for research into the effectiveness of interventions to reduce CLABSI rates in the non-ICU setting.	No evidence was found on the management of infusion-related blood stream infections.

Section	Evidence	Gaps
Infusion therapy parenteral nutrition	One medium quality prospective cohort study[19] found the most frequent cause of spurious bloodwork in parenteral nutrition (PN) patients was the failure to clamp the PN infusion prior to blood collection, or too short a time between clamping and drawing. One high quality case control study[37] found the strongest risk factor for candidemia infection in elderly hospitalised adults was duration of PN. Other factors included presence of other invasive devices such as CVC or urinary catheter and concurrent use of antibiotics. One medium quality prospective cohort study[51] found that previous immunosuppressive therapy and patient age were independent predictors of 30-day mortality in patients with PN catheter-related BSI. Catheter removal within 48h and appropriate antibiotic therapy were protective factors. One low quality audit[40] found a 2% CHG transparent antimicrobial dressing eliminated infection in PN patients compared with a standard dressing.	No evidence was found for: • the effect of different frequencies of change of parenteral nutrition administration sets and add- on devices on patient safety and outcomes • the performance of nutrition screening tools to assess nutritional status • the effect of different ways of monitoring for metabolic related complications and electrolyte imbalances and catheter-related complications on patient safety and outcomes.
Infusion therapy phlebitis	One medium quality prospective cohort study[9] found the likelihood of phlebitis increased with duration of catheter, highest after 96h. Phlebitis was more likely when the catheter was placed in the dorsum of the hand compared with the antecubital fossa or forearm. One high quality RCT[50] found no significant differences in complication rates, time to first complication, infections or duration of IV therapy when peripheral venous catheters (PVCs) were replaced routinely compared with replacement on clinical indication. One medium quality quasi experimental study[52] found patients receiving vancomycin compared with other antibiotics had no significant differences in incidence of phlebitis. They did, however, have increased venepunctures, number of attempts and time spent re-siting catheters. Patients receiving vancomycin were also more likely to end the study with a CVC. One high quality quasi experimental study[44] demonstrated a 48% reduction in peripheral vein phlebitis as a result of a quality improvement intervention including education and training of health care staff, a catheter maintenance bundle and surveillance of PVC-related adverse events.	No evidence was found on the impact of different phlebitis severity/degrees on patient safety and outcomes.
Intraosseous access devices	One high quality quasi experimental study[32] and one low quality observational study[5] demonstrated that success rate was significantly higher, and procedure time significantly lower for intraosseous (IO) access compared with CVC. A survey included as part of the observational study[5] showed that CVC remains the preferred choice for both second and third attempts at IV access, with IO selected only if a fourth attempt is required. One medium quality literature review[20] found that while IO is a safe and effective method of gaining access when IV access is unobtainable, IO is rarely used and guidance often not followed. The proximal tibia appears to be the favoured access site and the EZ-IO the most popular device.	No evidence was found on the effect on patient safety and outcomes of: • different durations of intraosseous access device • different durations of intraosseous ports • different intraosseous devices • site management after removal.

Section	Evidence	Gaps
Midline catheters	One high quality literature review[2] discusses advantages and disadvantages of midline catheters along with insertion and management issues. Advantages include avoidance of repeated cannulation; increased vessel diameter which reduces the incidence of complications such as chemical phlebitis; toleration of isotonic solutions and high flow rates; reduced infection rate compared with other vascular devices. Disadvantages include high risk of extravasation; not recommended for dextrose solutions >10%; risk of mechanical phlebitis. Insertion and management issues include the requirement for a thorough clinical and vascular assessment prior to insertion. One high quality literature review[21] concluded that pH alone is not an evidence-based indication for CVC placement over midline catheter placement. One high quality prospective cohort study[7] found low levels of pain and distress were reported during positioning of PICC or midline catheters, with the devices resulting in significant improvement of global quality of life. One low quality descriptive study[15] found no relationships between infusates or dwell time and complications. One low quality prospective pilot study[12] reported the success of a novel, resident-driven programme for the placement of ultrasound-guided midline catheters in critically ill patients.	No evidence was found on the effects on patient safety and outcomes of: • different flushing frequencies • flushing lines with saline versus heparinised solutions • use of different veins • effect of site selection
Peripheral access devices and flushing	One low quality audit[17] demonstrated the reduction of health care associated infections (HCAI) in an underperforming hospital as a result of the implementation of a change initiative relating to the use of peripheral venous catheters. One medium quality quasi experimental study[34] found two 20-g IV catheters are significantly faster than a single 18-g IV catheter. Both were markedly slower than infusion rates observed in in vitro testing and based on manufacturer data. One low quality retrospective case control study[31] identified risk factors associated with the development of infection in patients with PVC. These included >24h continuous infusion, insertion in the lower extremity, use of infusion pumps and hospitalisation for neurological or neurosurgical conditions.	No evidence was found on the effects on patient safety and outcomes of: • different line flushing frequencies for peripheral access devices • use of different veins • effect of site selection.
Subcutaneous infusions	No evidence found in this area.	No evidence was found on the effects on patient safety and outcomes of: • electronic devices for this procedure • site selection • site management • solution tonicity • electrolytes used (for example, sodium chloride, dextrose saline, dextrose 5%.

Study characteristics

The majority of studies were carried out in the US (N=28). Five studies originated in the UK, eight in Europe, three in Australia, one in Canada and three in Asia. Studies carried out beyond the UK were only included if, following a judgement of comparability of settings, results could be attributed to nursing practice in the UK.

Most of the studies were conducted in the hospital setting (N=38). Of these, eight studies included only ICU patients, with only three focussing exclusively on the non-ICU setting. Three took place in the emergency department and one study included only elderly patients. Other settings included outpatients (N=1), palliative care patients at home or in a hospice (N=1) and healthy volunteers (N=2). In addition, five reviews were included which were not context-specific.

The most common outcome measured was infection rates (N=23). This could be attributed to the high number of studies originating in the US, where reduction of catheter-related bloodstream infections (CRBSI) is a priority based on the cost to health services. Studies which focussed specifically on cost-effectiveness were excluded from this review; however as the reduction of CRBSI also improves patient care and outcomes, all studies which reported outcomes unrelated to cost were included in the review. Most studies reported patient-related outcomes; however, two focussed on outcomes related to nursing knowledge and practice.

The majority of studies (N=43) were primary research, employing quasi experimental methods as well as cohort and case control studies. Five literature reviews were also included. One RCT was included in this study, which was not appraised in phase one of the review. Several of the studies reported the results of practice improvement initiatives, using audits pre- and post-intervention. Nineteen studies were rated high quality, 17 were rated medium quality, and 12 were rated low quality during the quality appraisal process. The number of studies found in each of the 12 areas ranged from zero to 15 (see Table 1).

Data synthesis

After mapping the studies, results were synthesised to provide an overall appraisal of the evidence in each area. Due to the diversity of study designs and outcomes, it was difficult to combine data; therefore, results are presented in the form of a narrative synthesis. A framework developed by the US Infusion Nurses Society (2016)[26] was used to identify the strength of the evidence by volume and design (see Appendix A). Levels range from I-V, with Level I indicating the strongest level of evidence. As this review excludes SRs and RCTs, with the exception of one RCT which was not included in phase one of the review, the highest evidence level reported is Level III, which is obtained from several studies with quasi-experimental designs focussed on the same question.

Results

Add on devices

The RCN search for add on devices included use and management of the following: traffic lights; three-way taps; extension sets; stop cocks; cap connectors; needle free; 'Savy' systems; bio connectors. No evidence was found to answer the specific RCN question:

- What is the effect on patient safety and outcomes of changing add-on devices with each cannula or administration set replacement or when integrity of either product is compromised?

Some evidence was found at Levels IV and V, according to the Infusion Nurses Society classification[26], to suggest scrubbing the intravenous connector hub with alcohol for at least five seconds reduces the risk of contamination of the hub. One high quality study, which contained both a clinical survey and laboratory assessment[54], found that scrubbing the connector hub for at least five seconds with 70% isopropyl alcohol pledget significantly reduced bacterial contamination of the hub under both laboratory and clinical conditions. Three further studies which reported the results of quality improvement interventions (reported in the *Infusion-related bloodstream infections* section) included scrubbing the hub as part of a multimodal intervention which resulted in significantly reduced infection rates[16,22,53].

One low quality prospective cohort study[38] provides weak evidence at Level V that an intraluminal protection device is more effective at reducing CLABSI than a positive pressure needleless connector, negative displacement split septum, or negative pressure mechanical valve device. This study reported the results of a three-year quality improvement programme with little controlling for potential confounding variables, therefore the results cannot be attributed with confidence solely to the change of connector device.

Table 3: Evidence table for add on devices

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
38. Lynch (2012)	US	All patients admitted to a 36-bed LTAC hospital with catheter inserted (N=27,500 catheter days).	To describe how the hospital achieved 0 CLABSI over a three year period by changing the type of needleless connector.	Comparison of CLABSI rates from different time periods when different connectors were used.	Changing from a positive pressure needleless connector to negative displacement devices (split septum followed by negative pressure mechanical valve), to an intraluminal protection device led to the elimination of CLABSI over a three year period.	1 (low)
54. Rupp et al. (2012)	US	All adult inpatients at a 689-bed academic health care centre with vascular catheter (N=363)/150 sterile needleless connectors for lab assessment.	To define the optimum vascular catheter connector valve disinfection practices under lab and clinical conditions.	Prospective observational clinical survey and lab assessment of disinfection procedures.	In both settings, bacterial contamination was significantly reduced after scrubbing the connector valve with alcohol for at least 5s.	7 (high)

Arterial catheters

No relevant studies were identified in this area which meant no evidence was available to answer the following RCN questions during this phase of the review:

- What is the effect of site selection on patient safety and outcomes?
- What are the effects of different line flushing frequencies for arterial catheters on patient safety and outcomes?
- What are the effects of flushing lines with saline versus heparinised solutions for arterial catheters on patient safety and outcomes?
- What are the effects of different arteries being used in terms of patient safety and outcomes?

Blood sampling

The RCN searched for evidence on blood sampling for the following topics: venepuncture; blood sampling; blood collection; blood sampling/collection via vascular access devices; tubes; methods and preparation. No evidence was found to answer the following specific RCN questions:

- What is the impact of different methods for obtaining blood samples through the device on patient safety and outcomes? Push pull or missing method, discard method or reinfusion method.
- What interventions reduce fear, pain and anxiety in patients[ii] undergoing venepuncture?
- What is the effect of site selection for venepuncture on patient safety and outcome in patients with an infusion cannula?
- What is the impact on patient safety and outcomes of different infusion device flushing before blood sampling through the device?
- What is best practice for different devices?

Evidence was found in the following areas:

Accuracy of blood results

Several well designed studies provide evidence at Level III to suggest that blood samples taken from central or peripheral catheters provide similar blood results to those obtained via venepuncture. One high quality cohort study comparing blood samples taken from PVC and venepuncture[23] demonstrated similar haematology, biochemistry and coagulation parameter results. Significant differences were observed only in venous blood gas results.

A high quality quasi experimental study compared lab values of blood samples obtained from CVC with those obtained via venepuncture[29], and found no significant differences in results for white blood cell and platelet counts, sodium or glucose levels. Significant differences were observed in haemoglobin, potassium and creatinine levels, however the authors suggest that these differences do not reach clinical significance according to biases set by NCCLS EP9-A2 guidelines.

Another high quality quasi experimental study conducted amongst patients with heparinised PICCs[25] found that samples obtained from the heparinised PICC produced similar coagulation test results to those obtained via venepuncture. Only INR results were significantly different.

A medium quality quasi experimental study compared activated partial thromboplastin time (aPTT) results when specimens were collected from a CVC compared with venepuncture in patients receiving continuous heparin infusions[11]. No significant differences were found in this coagulation parameter, however values were significantly prolonged if samples were taken from the port used to deliver heparin.

In addition, a high quality cohort study carried out in the emergency department compared rejection rates due to haemolysis amongst blood samples obtained from IV starts with those taken from existing IV access or venepuncture[13]. The level of haemolysis was 1.1% from IV starts compared with 0.8% from existing access and 0.1% from venepuncture. However all results were below the 2% level cited as a benchmark by the American Society of Clinical Pathology.

All of these studies differed in their methods and outcome measures. However the results collectively suggest that in the majority of instances, IV catheter access provides a valid method of obtaining a blood sample.

Reducing contamination

There is evidence at Level IV to suggest drawing 1ml of waste prior to blood sampling is sufficient to provide an undiluted sample. One high quality quasi experimental study compared the results of blood samples after drawing various waste amounts[3], and identified 1ml as the statistically significant stabilising point for both sodium and glucose. This suggests drawing larger waste volumes is not required, however further studies are needed to confirm these results.

There is also evidence at Level IV to suggest that device selection can lead to improved outcomes. One high quality prospective cohort study compared samples from wire hubs and non-wire hubs[33] and found contamination occurred in 19% of wire hubs compared with 5% of non-wire hubs, while true-positive cultures were observed in similar proportions.

Another high quality quasi experimental study compared the Holdex® tube holder with a standard tube holder using a cross-over design[35] and found the Holdex® holder resulted in lower concentrations of potassium and cell-free haemoglobin, indicators of erythrocyte injury.

ii The patient perspective was explored through another review in this series of reviews for the development of the RCN *Infusion therapy standards*; no interventions to reduce fear, pain and anxiety in patients were identified there either. One study identified in the current review and presented later assessed distress and pain perceived by palliative care patients during the positioning of a PICC or MC7, however it did not address interventions to reduce distress.

Table 4: Evidence table for blood sampling

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
3. Baker et al. (2013)	US	60 healthy adults	To establish the minimum waste volume required to produce an undiluted blood sample	Samples obtained at baseline and following the extraction of various waste volumes. Sodium and glucose levels recorded using repeated measures.	1ml of waste was established as the statistically significant stabilising point for both sodium and glucose.	7 (high)
11. Dailey et al. (2014)	US	66 patients receiving continuous heparin infusion.	To determine if there is a difference in aPTT results between specimens collected from a CVC versus venepuncture in patients receiving continuous heparin infusions.	Simultaneous blood samples were obtained from each subject using CVC and venepuncture and aPTT results were compared.	Overall, mean aPTT difference (peripheral – CVC) was not statistically significant. However when samples were taken from a port used to deliver heparin, aTPP values were significantly prolonged.	5 (medium)
13. Dietrich (2014)	US	8,944 blood samples obtained by ED personnel and lab staff at a moderately sized hospital.	To show that acceptable rates of rejection due to haemolysis can be achieved using blood samples collected from IV starts in the ED setting.	Blood samples collected from IV starts in the ED were compared with those collected from existing vascular access devices or venepuncture, and levels of haemolysis were compared.	The level of haemolysis was 1.1% from IV starts compared with 0.8% from existing access and 0.1% from venepuncture. All results were below the 2% level cited as a benchmark by the American Society of Clinical Pathology.	6 (high)
23. Hambleton et al. (2014)	Spain	259 ED patients.	To evaluate the equivalence between analytic parameters from blood samples obtained from PVC compared with venepuncture.	Samples were collected from a saline solution lock device and venepuncture, and both samples analysed for haematology, biochemistry, venous blood gases and coagulation parameters.	No significant differences were found in any parameters except for venous blood gases (pH, PO2, PCO2).	7 (high)
25. Humphries et al. (2012)	US	30 hospitalised patients with heparinized PICCs	To test an evidence-based procedure of drawing blood samples for coagulation testing from heparinized PICCs compared with venepuncture.	Samples drawn from venepuncture and PICC and coagulation results compared.	All tests met agreement criteria, except for INR.	7 (high)

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
29. Jun et al. (2013)	Korea	27 ICU patients	To compare lab values of blood samples obtained via CVC compared with venepuncture.	Blood samples obtained from CVC and venepuncture and lab results compared.	No significant differences in the results for white blood cell and platelet counts, sodium or glucose levels. Haemoglobin, potassium and creatinine levels differed significantly but the differences were not clinically meaningful according to biases set by NCCLS EP9-A2 guidelines.	7 (high)
33. Levin et al. (2013)	Israel	139 ICU patients with CVC	To compare contamination rate and true-positive rates of blood cultures obtained at CVC insertion from wire ports and non-wire ports.	Proportions of blood cultures taken from wire and nonwire CVC hubs growing contaminants and true pathogens were compared.	Contamination occurred in significantly more wire hubs compared with non-wire hubs. True-positive findings were not significantly different.	7 (high)
35. Lippi et al. (2013)	Italy	60 ED patients	To investigate the effectiveness of the Holdex tube holder in preventing erythrocyte injury in samples collected from catheters.	Blood was collected using both standard and Holdex tube holders in each subject using a cross-over design, and haemolysis levels compared.	Concentrations of potassium and cell-free haemoglobin were higher in samples collected with BD Vacutainer One Use Holder compared with Holdex tube holder.	7 (high)

Central venous access devices

The RCN search was focussed on the management of central lines rather than insertion, but covered: central venous devices; tunnelled catheters; non-tunnelled catheters; catheter selection; catheter management and care of catheters. No evidence was found to address the following RCN questions:

- What are the effects on patient safety and outcomes of flushing lines with saline versus heparinised solutions for central venous catheter devices?
- What is the effect on patient safety and outcomes of site selection and different veins being used?
- What are the effects of different line flushing frequencies for central venous catheter devices on patient safety and outcomes?

Evidence was found in the following areas:

Infection rates

One high quality retrospective cohort study provides Level IV evidence to suggest that self-administration of outpatient parenteral antimicrobial therapy (OPAT) does not result in greater infection risk than administration in the hospital/clinic setting. This study looked at infection rates amongst patients who self-administered OPAT, compared with those who had the therapy administered in a hospital or clinic setting4.

Deep vein thrombosis

One high quality prospective cohort study examined risk factors for upper extremity deep vein thrombosis (UEDVT) in patients with PICCs[41]. Statistically significant associations were found between UEDVT and hypertension, obesity, an increase in PICC arm circumference and oedema, providing Level IV evidence for the importance of regular monitoring of the insertion site and surrounding area.

Practice improvement

One medium quality quasi experimental study found implementing an evidence-based practice intervention related to CVC flushing resulted in significant improvement in nurses' knowledge and flushing technique[42]. As the data was collected as a practice audit in a single-setting, the results cannot be generalised to all settings, however they do provide weak evidence (Level V) for the success of evidence-based practice-improvement interventions.

Table 5: Evidence table for central venous access devices

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
4. Barr et al. (2012)	UK	2,766 patients involved in a large scale OPAT service.	To investigate rates and predictors of IV access device complications in a large OPAT cohort.	Rates of line infections and other line events were compared between self-administered OPAT (S-OPAT) and clinic-administered OPAT (C-OPAT).	There were no statistically significant differences between infection rates in S-OPAT compared with C-OPAT. Multivariate analysis showed the only predictor of infection was length of IV course. For other line events there were no statistically significant differences between S-OPAT and C-OPAT, and the only predictor variables were line type and use of flucloxacillin.	6 (high)
41. Maneval and Clemence (2014)	US	203 acute care patients with PICCs in two acute care hospitals.	To examine risk factors associated with symptomatic upper extremity DVT (UEDVT) in patients with PICCs.	Prospective observational cohort study. Potential risk factors were identified in a prior literature review.	A statistically significant association was found between UEDVT and hypertension, obesity, an increase in PICC arm circumference and oedema.	6 (high)
42. Mathers (2011)	US	Nurses working in a 436-bed regional health care system (N=unclear).	To describe the implementation of evidence-based practice related to flushing CVCs.	Data collected pre- and post- implementation of an EBP intervention using questionnaires and a practice audit.	The programme resulted in a significant improvement in nurses' knowledge and also flushing technique.	4 (medium)

Flow control devices

The RCN searched for evidence on: infusion flow control devices; infusion pumps; accurate delivery of intravenous or infusion therapy; incidents and patient safety. No evidence was found to answer the following specific RCN questions:

- What prognostic factors (for example, age, condition, therapy, care setting) affect the selection of different manual flow control devices and their effect on patient outcomes?
- How do different frequencies of flow rate monitoring of different manual flow control devices affect patient outcomes?
- What is the effect of electronic devices which generate flow through positive pressure or low pressure devices on patient safety and outcomes?

A low quality literature review in this area[39] discussed how connector design can influence swabbing and flushing and affect outcomes. The review suggested a smooth, tight-fitting septum, low intra-luminal fluid pathway volume, a straight fluid pathway, no dead space, no reflux with connection or disconnection, and fail safe back-up systems facilitate scrubbing and flushing and improve outcomes. There is no evidence that this review was systematic or exhaustive, however it provides a weak rationale for further studies into the influence of connector design features on practice and infection risk.

Table 6: Evidence table for flow control devices

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
39. Macklin (2010)	US	Studies relating to connector design and care and maintenance practices.	To provide an overview of swabbing and flushing and how connector design can affect these practices and outcomes.	Narrative literature review	Connector design features which facilitate swabbing and flushing and improve outcomes include a smooth, tight-fitting septum; low intraluminal fluid pathway volume; straight fluid pathway; no dead space; no reflux with connection or disconnection; fail-safe back-up systems as suggested by leading infection control experts. Compliance may improve when a single IV connector is used for all catheters, and connector care should be individualised to the patient's condition.	2 (low)

Infusion related bloodstream infection

The RCN search covered: bloodstream infection prevention, management and catheter associated blood stream infection. There were no specific RCN questions for this section, however evidence was found in the following areas:

Pre-/post-insertion care bundles

Three medium quality practice improvement studies provide Level V evidence that CLABSI rates can be reduced as a result of a post-insertion maintenance bundle, including hand hygiene, aseptic technique, dressing changes, scrubbing the connector hub and monitoring and care of the insertion site[16,22,46].

Another two quality improvement studies of medium and low quality provide Level V evidence for reduced CLABSI rates as a result of a pre-insertion care bundle[24,30]. These studies included practices such as hand hygiene, skin preparation, barrier precautions, standardised insertion packs and guidance, and avoidance of femoral site.

One study, which used self-reported compliance with five evidence-based practices, found that avoidance of femoral site and removal of unnecessary lines had the strongest independent effects on infection rates[24]. Another study reported median time to infection as 7.5 days (ICU) and 13 days (non-ICU), suggesting that the majority of infections are in fact due to post-insertion care rather than the insertion procedure itself[30].

As these studies were all carried out as practice improvement initiatives at single-sites, this limits their generalisability; however they do provide evidence for the effectiveness of practice change initiatives consisting of several bundled interventions.

Chlorhexidine gluconate bathing

There is evidence at Level III for the effectiveness of daily chlorhexidine gluconate (CHG) bathing on the reduction of CLABSI. One high quality cohort study[14], one medium and three low quality quasi experimental studies[46,30,36,43] demonstrate that implementing this practice results in reduced infection rates. All of these studies introduced CHG bathing alongside other interventions as part of a practice improvement programme; therefore, further well-designed studies are required to strengthen the evidence for this practice.

Device-related factors

One study provides weak evidence that device-related factors can contribute to reduced CLABSI rates. This medium quality prospective cohort study[53] demonstrated reduced infection rates with a change to positive-displacement needleless connectors, implementation of a CHG-impregnated disk, and introduction of a clear connector device. However, these interventions took place alongside enforcement of maximal barrier precautions and a 'scrub the hub' campaign over a period of three years; it is therefore impossible to quantify the effect of the different device factors.

One high quality quasi experimental study compared a silver-coated needleless connector with a standard needleless connector using a cross-over design[28] and demonstrated significantly reduced infection rates with the silver-coated device, providing Level IV evidence for the effectiveness of this practice.

Introduction of a specialist nurse

Two quality improvement studies of medium quality demonstrated the effectiveness of introducing a lead nurse to reduce infection rates through standardising and facilitating good practice[48,55]. Both studies took place alongside other quality improvement measures but demonstrate Level V evidence for the potential impact of a specialist nurse dedicated to infection prevention in this area. One medium quality retrospective cohort study1 found that when a specialist IV nurse service was withdrawn, use of PICCs increased as the specialist nurse was no longer available to place difficult PVCs; prompting clinicians to seek central venous access sooner, and perhaps unnecessarily.

Risk factors for infusion-related bloodstream infection

One medium quality case-control study explored patient-and device-related risk factors for bloodstream infections in patients with PICCs[49]. This study found congestive heart failure, intra-abdominal perforation, history of C.difficile, recent chemotherapy, presence of a tracheostomy tube and use of a multi-lumen catheter increase the risk of infection. History of chronic obstructive pulmonary disorder and PICC placement in oncology, orthopaedics or surgery were found to be protective factors, although the reasons remain unclear. As this study was carried out on a single site, the generalisability of the results is limited, and also may suffer from the usual limitations of retrospective studies (selection bias and confounding factors); however, it provides limited evidence at Level IV for the existence of these risk factors.

Bloodstream infection in non-ICU settings

One low quality literature review[59] demonstrated that the much of the literature relating to CLABSI is focussed on the ICU setting, identifying a need for further research into the effectiveness of infection-reduction interventions in the non-ICU setting.

Table 7: Evidence table for infusion-related bloodstream infections

Reference	Country of origin	Sample / setting	Aim of study	Methods	Key findings	Quality
1. Ajenjo et al. (2011)	US	All patients with PICCs inserted in a large hospital (163 BSI episodes studied).	1. To determine the incidence of hospital-acquired PICC-BSI among adult inpatients; 2. To identify the microorganisms causing PICC-BSI; 3. To compare PICC use and BSI rates amongst ICU and non-ICU patients; 4. To assess the effect of changes in IV therapy service on PICC use and BSI rates.	Retrospective cohort study.	Overall BSI incidence was 3.13 per 1000 catheter days. Candida glabrata was the most commonly identified organism. A higher BSI rate was observed in ICU compared with non-ICU patients (overall more BSIs occurred in non-ICU patients). There was an increase in PICC use after the IV therapy service changes.	5 (medium)
14. Dixon and Carver (2010)	US	All patients admitted to a surgical ICU over a three month study period (N=144).	To assess the effectiveness of a quality-improvement protocol including chlorohexidine gluconate bathing on CLABSI incidence.	Observational cohort study using historical controls.	CLABSI rates fell by 73.7% over the three month study period. This reduction was maintained after the intervention period.	6 (high)
16. Dumyati et al. (2014)	US	All patient data from 37 non-ICU wards across six hospitals. Ward nurses were also surveyed to assess their knowledge (N=200 pre-intervention / 238 post-intervention).	To study the impact of a multimodal intervention on CLABSI incidence across multiple hospitals.	CLABSI rates recorded pre-, during- and post-intervention. Survey and audit also conducted amongst nurses to assess knowledge and compliance with care and maintenance.	CLABSI rates fell by 50% from pre-intervention to post intervention. The number of nurses reporting compliance with scrubbing procedures increased from 20% to 70% over the same time period.	5 (medium)
22. Guerin et al. (2010)	US	All patients admitted to an acute-care hospital (including ICU)	To assess the effect of a post-insertion care bundle on CLABSI incidence.	CLABSI rates were recorded pre- and post-intervention.	CLABSI rates fell from 5.7 per 1000 catheter days to 1.1 per 1000 catheter days following the intervention.	5 (medium)

Reference	Country of origin	Sample / setting	Aim of study	Methods	Key findings	Quality
24. Hsu et al. (2014)	US	Data from US national CLABSI prevention programme (N= 1071 adult ICU from 792 hospitals)	To examine self-reported compliance with CLABSI prevention measures and link compliance to CLABSI rates.	Data was analysed from a national CLABSI prevention programme. Adult ICUs participating in the programme submitted a self-reported measure of compliance, as well as CLABSI rates, on a monthly basis.	Consistent performance of all practices was associated with reduced CLABSI rates. Avoidance of the femoral site and removal of unnecessary lines had the strongest independent effects.	5 (medium)
28. Jacob et al. (2015)	US	All adults with non-haemodialysis lines admitted to two hospitals over a 20 month period (N= 15,845).	To compare a silver-coated needleless connector and a standard needleless connector on CLABSI rates.	Both connector types were used in two hospitals using a cross-over design, and infection rates compared.	Use of the silver coated connector reduced CLABSI rates by 32%	7 (high)
30. Klintworth et al. (2014)	Australia	All adults admitted to hospital with CVC (ICU and non-ICU) over a 20 month period	To assess the impact of a stepwise multi-modal intervention to reduce CLABSI rates.	CLABSI rates recorded pre- and post-intervention.	CLABSI rates in ICU decreased from 2.3 to 0.9 per 1000 CVC days. In non-ICU patients rates decreased from 2.5 to 1.3 per 1000 bed days. Median time to occurrence was 7.5 days (ICU) and 13 days (non-ICU) suggesting most cases are not due to insertion practice.	2 (low)
36. Lopez (2011)	US	All patients in a 24 bed ICU.	To assess the effect of compliance with maximal barrier precautions and daily chlorohexidine gluconate bathing on CLABSI rates.	CLABSI rates were compared before and after implementation of a quality improvement programme including compliance monitoring and daily chlorohexidine gluconate bathing.	CLABSI rate decreased by 96% between the pre-intervention and post-intervention period.	2 (low)
43. Medina et al. (2014)	US	All adults in medical/ surgical units (non-ICU).	To assess the effect of a quality improvement programme including daily chlorohexidine gluconate bathing, on CLABSI rates.	CLABSI rates were compared between pre- and post- intervention period.	Implementation of daily CHG bathing resulted in a 50% decrease in CLABSI rates.	2 (low)

Reference	Country of origin	Sample / setting	Aim of study	Methods	Key findings	Quality
46. Munoz-Price et al. (2012)	US	All patients admitted to three surgical ICUs (total 100 beds).	To determine the impact of three stepwise interventions on CLABSI rates.	CLABSI data collected at baseline and after three stages of intervention (1. 'Scrub the hub'; 2. Daily chlorhexidine baths; 3. Daily nursing rounds.)	Scrub the hub was associated with a reduction in CLABSI rates in 1 out of 2 units; The addition of CHG baths resulted in a further reduction in all units; Nursing rounds were only implemented in one unit, and resulted in a further reduction in CLABSI.	4 (medium)
48. O'Connor et al. (2012)	UK	All patients with CVCs in a large teaching hospital.	To describe a quality improvement programme implemented to reduce CLABSI.	CLABSI rates recorded at baseline and monthly throughout the programme which involved various interventions over a three year period.	CLABSI rates showed a sustained decline throughout the duration of the study.	4 (medium)
49. Pongruanporn et al. (2013)	US	Patients with PICCs in a tertiary care centre (162 with BSI and 485 controls).	To determine the patient- and device-specific risk factors for hospital acquired PICC-BSI.	Case control study. Each case matched with three controls without BSI.	Patient-associated risk factors included congestive heart failure, intra-abdominal perforation, history of C.diff, recent chemotherapy, presence of tracheostomy tube. Device associated risk factors related to use of multi lumen catheters. Protective factors included history of COPD and PICC placement in oncology, orthopaedics or surgery.	4 (medium)
53. Royer (2010)	US	All patients in a 350 bed acute hospital over 6.5 years (N > 78000 catheter days).	To assess the effectiveness of various bundle interventions on CLABSI rates.	Interventions were implemented over a 3.5 year period and CLABSI rates recorded on a six-monthly basis.	Each intervention resulted in a decrease in CLABSI rates.	4 (medium)

Reference	Country of origin	Sample / setting	Aim of study	Methods	Key findings	Quality
55. Thom et al. (2014)	US	All patients admitted to a surgical ICU over a 45 month period (N= 3257).	To assess the effect of implementing a unit-based quality nurse on CLABSI rates.	Data collected pre- and post-introduction of the nurse. A non-equivalent control group was included (different ICU).	The implementation of the quality nurse resulted in a significant reduction of CLABSI rates, even adjusting for rates in other ICUs in the same hospital.	5 (medium)
59. Whited and Lowe (2013)	US	Research studies involving CLABSI.	To explore the current literature on CLABSI and recommend additional research to focus on non-ICU population.	Literature review.	There is a need for research into the effectiveness of interventions to reduce CLABSI in the non-ICU setting. In the meantime interventions proven to be effective in ICU should be implemented more widely.	1 (low)

Infusion therapy parenteral nutrition

The RCN search covered: parenteral nutrition (PN); total parenteral nutrition (TPN); home PN; infection prevention and control; management of PN; sponges and PN and dedicated lines. No evidence was found to address the following RCN questions:

- What is the effect on patient safety and outcomes of different frequencies of change of PN administration sets and add-on devices?
- What is the performance of nutrition screening tools to assess nutritional status?
- What is the effect on patient safety and outcomes of different ways of monitoring for metabolic-related complications and electrolyte imbalances and catheter-related complications?

Evidence was found in the following areas:

Parenteral nutrition catheter-related bloodstream infection

One medium quality cohort study investigated the predictors of 30-day mortality in PN patients with catheter-related bloodstream infection[51]. This study found previous immunosuppressive therapy and patient age were identified as risk factors for mortality, whilst catheter removal within 48 hours and appropriate antibiotic therapy acted as protective factors. This study was carried out on a single site which limits the generalisability of the results; however, it does provide limited evidence at Level IV for the prompt removal of catheters and initiation of appropriate antibiotic therapy on the first sign of infection.

There is weak evidence that a 2% CHG transparent antimicrobial dressing reduces the risk of infection in PN patients compared with a standard dressing. However this study was a low quality audit comparing two dressings at a single site[40].

One high quality case-control study which focussed solely on elderly hospitalised adults[37], provides Level IV evidence that duration of PN, presence of other invasive devices, and use of antibiotics are risk factors for candidaemia infection in this population.

Blood sampling

There is evidence at Level IV that a failure to clamp the PN infusion prior to blood collection, or too short a time between clamping and drawing, results in spurious bloodwork in PN patients. These were the findings from one medium quality prospective cohort study[19], which monitored the results of bloodwork in PN patients and compared factors associated with blood collection with a control group.

Table 8: Evidence table for parenteral nutrition

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
19. Fairholm et al. (2011)	Canada	201 hospitalised patients receiving parenteral nutrition.	To determine the frequency of spurious blood work, unnecessary medical interventions and contributing factors.	All PN patients monitored over a year and episodes of spurious blood work identified. Subsequent medical interventions were tracked and factors associated with blood collection were assessed and compared with a control group (no spurious blood work).	34 patients had 63 instances of spurious blood work, which led to 23 medical interventions. Most frequent problem was failure to clamp PN infusion prior to blood collection, or too short a time between clamping and drawing.	4 (medium)
37. luzzati et al. (2013)	Italy	140 elderly hospitalised patients with candidemia and 280 matched controls (no candidemia).	To identify the incidence of and risk factors for candidemia amongst elderly hospitalised patients.	Case control study. Patients with candidemia were identified and various demographics and potential risk factors were compared against the controls.	Overall incidence of candidemia was 1.56 episodes per 10000 patient days per year. Strongest risk factor was duration of PN. Other factors included the presence of other invasive devices including CVC and urinary catheter, and use of antibiotics.	7 (high)
40. Madeo and Lowry (2011)	UK	All patients receiving PN at a 900-bed district hospital over a one year period (N=138).	To examine the effect of a 2% chlorhexidine gluconate transparent antimicrobial dressing on infection rates in PN patients.	Audit of infection rates. Standard dressing used for the first six months of the study and antimicrobial dressing used for second six months.	Eight infections were identified in the first six months, while none were identified in the second six months, during which time the antimicrobial dressing was in use.	2 (low)
51. Rodriguez-Pardo et al. (2014)	Spain	All adult patients diagnosed with PN-CRBSI over six years (N=263).	To describe the incidence, epidemiology and prognosis of PN-related CRBSI in hospitalised adults and evaluate the impact of catheter extraction within 48H on bacteraemia onset, on 30 day mortality.	Incidence of CRBSI recorded amongst PN patients and factors related to catheter management examined.	Previous immunosuppressive therapy and patient age were independent predictors of 30-day mortality. Catheter removal within 48H and appropriate antibiotic therapy were protective factors.	5 (medium)

Infusion therapy phlebitis

The RCN search covered: phlebitis; inflammation of the vein; definition of phlebitis; mechanical phlebitis; chemical phlebitis; infective phlebitis; causes of phlebitis; indications for phlebitis monitoring in peripheral access devices; midlines; central access devices; PICCs; incidence and prevalence of phlebitis. No evidence was found to answer the following RCN questions:

- What is the effect on patient safety and outcomes of monitoring vascular access sites for phlebitis?
- What is the impact of different phlebitis severity/degree on patient safety and outcomes?

Evidence was found in the following areas:

Risk factors for phlebitis

One medium quality prospective cohort study[9] provides evidence at Level IV for the existence of several risk factors for phlebitis. This study found that duration of catheter placement is related to the development of phlebitis, with incidence highest after 96 hours. The same study found placement of the catheter in the dorsum of the hand also increases risk of phlebitis, compared with placement in the antecubital fossa or forearm. However, the fact that this study was carried out at a single site limits the generalisability of these findings.

One high quality RCT compared replacement of catheters on clinical indication with routine replacement[50] and found no significant differences in complication rates. This provides Level III evidence for the replacement of catheters on clinical indication.

One medium quality prospective cohort study[52] found that whilst vancomycin does lead to increased venepunctures and time spent restarting catheters, it did not lead to increased incidence of phlebitis when administered through a PVC. This is in agreement with a high quality literature review[21] which proposed that pH alone is not an evidence-based indication for central line placement over midline catheter placement. Together, these studies provide Level IV evidence that vancomycin can safely be administered through PVC in some instances. However sample sizes in the study were small, therefore further research is required in order to determine the implications of administering vancomycin via this route.

One high quality improvement study which took place over six years[44] provides Level V evidence that the education of health care staff, along with a maintenance bundle and surveillance of catheter-related adverse events, can reduce the incidence of phlebitis. Interestingly, this study found that when expressed in relation to catheter days, there was in fact no significant reduction. This suggests that the impact of practice improvement interventions may be largely due to the removal of unnecessary devices.

Table 9: Evidence table for infusion therapy phlebitis

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
9. Cicolini et al. (2014)	Italy	All patients who received a new PVC in five hospitals (N= 1498.)	To evaluate whether PVC site of insertion influences risk of catheter-related phlebitis; and investigate potential predictors of phlebitis.	Prospective cohort study. The clinical course of each patient was followed and presence of phlebitis assessed every 24H.	Likelihood of phlebitis increased with duration on catheter; highest after 96H. Phlebitis was more likely when catheter placed in dorsum of hand compared with antecubital fossa or forearm.	5 (medium)
44. Mestre et al. (2013)	Spain	All patients who received a PVC in hospital during an eight year study period (N= 1631).	To evaluate an intervention to reduce PVP and PVC-related BSI.	Intervention took place over a six year period and data was collected for one month each year of the study.	PVP decreased by 48% during the intervention period (no difference when expressed per 1000 catheter days). PVC-related BSI and health care-acquired S. Aureus were also significantly reduced.	6 (high)
50. Rickard et al. (2010)	Australia	362 hospitalised patients with PVCs.	To assess the effect of routine re-site of PVCs compared with clinically-indicated re-site.	RCT. Patients randomised to have PVC replaced routinely (every three days) or on clinical indication.	There were no significant differences in complication rates, time to first complication, infections or duration of IV therapy. More PVCs were placed in the routine re-site group.	7 (high)
52. Roszell and Jones (2010)	US	153 surgical patients (49 vancomycin/104 other antibiotics).	To determine whether vancomycin IV therapy is associated with more PVC complications than other antibiotics.	Patients receiving vancomycin and patients receiving other antibiotics were compared with regards to incidence of phlebitis, number of repeat PVC insertions, number of attempts to get a successful insertion, nurses' time in the room for starting the catheter, delayed doses due to PVC venepuncture.	33% of patients receiving vancomycin ended the study with a CVC compared with 14% of patients receiving other antibiotics. The vancomycin group had increased venepunctures, number of attempts and time spent restarting catheters. There were no significant differences with regards to incidence of phlebitis.	4 (medium)

Intraosseous access

The RCN search covered: intraosseous access; intraosseous sampling from intraosseous sites; management of intraosseous infusion; evidence regarding the safety and effectiveness of intraosseous access. No evidence was found to address the following questions identified by the RCN:

- What is the effect of different durations of intraosseous access device on patient safety and outcomes?
- What is the effect of different durations of intraosseous ports on patient safety and outcomes?
- What is the effect of site management after removal of the intraosseous device?

Limited evidence was found to answer the following questions:

- What is the effect of site selection on patient safety and outcomes?

An exploratory literature review[20] found that proximal tibial access is associated with increased success compared with proximal humeral access, and also decreased risk of dislodgement. This route is also preferred by practitioners as reported in several studies.

- What is the effect of different intraosseous devices on patient safety and outcomes?

As part of one high quality quasi experimental study which compared intraosseous with central venous access[32] researchers randomised patients to two different IO devices (the battery driven EZ-IO system [Vidacare], and the springload driven Adult BIG Bone Injection Gun [WaisMed Ltd.]) to determine if device selection had an effect on success or procedure time. No significant differences were found.

In addition, evidence was found in the following areas:

One high and one low quality quasi experimental study[32,5] provide Level IV evidence that intraosseous access has a higher success rate and lower procedure time that central venous access. Nonetheless, intraosseous access remains the less favoured option compared with central venous catheters for obtaining venous access when peripheral access is unobtainable[5].

One medium quality literature review[20] provides further evidence that IO is a less favoured method of access despite receiving higher prominence in current guidelines. The review found that the proximal tibia is the favoured site and the EZ-IO the most popular device. The authors identified a need for further research, particularly in settings other than ED trauma centres and pre-hospital emergency care, to inform clinical practise.

Table 10: Evidence table for intraosseous access

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
5. Bloch et al. (2013)	US	Emergency medicine practitioners (number surveyed not stated/41 used for simulation part of study).	To investigate the use of IO in emergency medicine and compare IO access with alternative emergent vascular access techniques.	EM practitioners surveyed on their use of IO/preferred method of emergent vascular access for critically ill patients. 41 practitioners also took part in a simulation exercise where they were observed placing a simulated femoral line, ultrasound-guided IV and proximal tibia IO; Prior experience of performing technique, time to complete and errors were recorded.	Survey: CVC is the preferred choice for both second and third attempt at IV access. IO selected only if fourth attempt required. IO used less than 5% occasions where peripheral access was unobtainable in critically ill adults. Simulation: Time to place CVC was significantly longer than IO and also resulted in more errors.	2 (low)
32. Leidel et al. (2011)	Germany	40 critically ill patients for whom peripheral access was unobtainable.	To compare IO and CVC access in adults under resuscitation in the ED.	Patients for whom peripheral access couldn't be obtained, received both IO and CVC simultaneously, and success rate and procedure time compared. Two different IO devices were randomised to provide further comparison.	Success rates on first attempt were significantly higher and procedure time significantly lower for IO. No complications were observed in either group. There were no significant differences between IO devices.	7 (high)
20. Garside et al. (2015)	UK	Studies published relating to IO access in adults.	To present a detailed investigation critiquing contemporary practices of intraosseous (IO) vascular access in adult patients.	Exploratory literature review.	IO is a viable alternative to IV access when the latter is unobtainable. Further research is required to determine best practice and devices in a wider context.	4 (medium)

Midline catheters

No evidence covered the following specific research questions identified by the RCN:

- What are the effects of different line flushing frequencies for midline catheters on patient safety and outcomes?
- What are the effects of flushing lines with saline versus heparinised solutions for midline catheters on patient safety and outcomes?
- What are the effects of different veins being used in terms of patient safety and outcomes?
- What is the effect of site selection on patient safety and outcomes?

Evidence was found in the following areas:

Appropriateness of midline catheters

One high quality literature review[2] provides Level IV evidence for the value of a thorough clinical and vascular assessment prior to midline catheter insertion. The modified integrated literature review discusses advantages and disadvantages of midline catheters as well as insertion and management issues.

Another high quality literature review[21] critically appraises all of the evidence relating to pH and the development of phlebitis, presented in a chronological order, providing Level IV evidence that pH alone is not an evidence-based indication for the placement of CVC over midline catheters.

Midline catheters in palliative care

One high quality prospective cohort study[7] provides Level IV evidence for the use of MC in palliative care. This study assessed distress and pain perceived by palliative care patients during the ultrasound-guided positioning of a PICC or midline catheter. Low or null levels of pain and distress were reported, whilst the catheter resulted in significant improvement in the patients' quality of life.

Complications

There is weak evidence to suggest that no relationships exist between infusates and dwell time, and midline catheter-related complications. This is the conclusion of a low quality descriptive study[15] which gathered data relating to patient demographics, catheter-related factors and incidence of complications.

Midline catheter insertion

One low quality pilot study[12] reported the success of a novel, resident-driven programme for the placement of ultrasound-guided midline catheters in critically ill patients, with successful placement achieved in 96.8% of patients and only minor complications encountered. However, the methods used and reporting lack sufficient rigour to allow generalisations to be made regarding the feasibility or appropriateness of implementing a similar programme in the UK.

Table 11: Evidence table for midline catheters

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
2. Alexandrou et al. (2011)	Australia	Published studies relating to midline catheters.	To review published manuscripts on the use of midline catheters and provide recommendations for clinical practice in acute care settings.	Modified integrated literature review.	The author discusses advantages and disadvantages of midline catheters along with insertion and management issues. Advantages include avoidance of repeated cannulation; increased vessel diameter which reduces the incidence of complications such as chemical phlebitis; toleration of isotonic solutions and high flow rates; reduced infection rate compared with other vascular devices. Disadvantages include high risk of extravasation; not recommended for dextrose solutions >10%; risk of mechanical phlebitis. Insertion and management issues include the requirement for a thorough clinical and vascular assessment prior to insertion; best practice is discussed with regards to insertion and management.	6 (high)
7. Bortolussi et al. (2015)	Italy	48 palliative care patients in home or hospice setting.	To evaluate distress and pain perceived by patients during positioning of PICC or midline catheter.	Interviews were used to assess pain and distress on insertion and quality of life was measured before and after using a validated tool.	Low levels of pain and distress were reported during the procedure. Significant improvement was reported in global quality of life.	7 (high)

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
12. Deusch et al. (2014)	US	31 surgical ICU patients.	To report the success of a novel, resident-driven programme for the placement of ultrasound-guided midline catheters in critically ill patients.	Prospective pilot study: midline catheters were placed in patients and procedural details including time to cannulation, complications and cost were recorded.	Successful placement was achieved in 96.8% of patients. An average of 1.3 attempts with a median 13 mins were required for placement. Only minor complications were encountered.	3 (low)
15. Dumont et al. (2014)	US	345 patients with midline catheters in a community hospital.	To report the incidence of complications from midline catheters; average dwell time; relationships between infusates, dwell time, patient characteristics and complications.	Data was gathered on patient demographics, infusates, insertion site, type of catheter, dwell time and complications.	Mean dwell time was 6.9 days. 10.7% of patients had some form of complication (phlebitis or infiltration); only two patients were diagnosed with catheter-related BSI. No relationships were found between infusates or dwell time and complications.	1 (low)
21. Gorski et al. (2015)	US	Published studies relating to medication pH and the development of infusion thrombo-phlebitis.	To critically evaluate the evidence for pH of intermittently delivered IV medications and the development of infusion thrombo-phlebitis.	Narrative literature review (evidence presented in chronological order).	On the basis of the review, the authors conclude that pH alone is not an evidence-based indication for central line placement over midline catheter placement.	6 (high)

Peripheral access devices and flushing

The RCN search focused on finding the evidence for the most effective and safe frequency and solution for flushing peripheral access devices. There was no evidence found to answer the following RCN questions:

- What are the effects on patient safety and outcomes of flushing lines with saline versus heparinised solutions for peripheral access devices?
- What are the effects on patient safety and outcomes of different line flushing frequencies for peripheral access devices?
- What are the effects on patient safety and outcomes of different veins being used?
- What is the effect of site selection on patient safety and outcomes?

However evidence was found in the following areas:

Infusion rate

There is limited evidence at Level IV that two 18-g catheters provide a faster infusion than a single 20-g catheter. One medium quality quasi experimental study compared rates using both methods simultaneously on healthy volunteers[34]. The researchers found that two 18-g catheters provided a faster infusion than a single 20-g catheter, which is inconsistent with Poiseuille's Law, which suggests a larger diameter increases the flow rate. Moreover, both methods were markedly slower than rates observed in in vitro testing and based on manufacturers' data. While this study had several limitations, it highlights the need for more clinical data in this area, rather than basing judgements on scientific laws, in vitro testing or manufacturer data.

Infection

One low quality retrospective case-control study[31] provides weak evidence that more than 24 hours of continuous infusion, insertion in the lower extremity, use of infusion pumps and hospitalisation for neurological or neurosurgical conditions increase the risk of infection in patients with a PVC.

Best practice

One low quality audit carried out in an underperforming hospital[17], described the effectiveness of a change initiative relating to the use of PVC in reducing HCAIs. The initiative included the introduction of a new non-ported cannula, along with practice change. As the study period coincided with a period of widespread culture change brought about by a poor report from the Department of Health, it is not possible to generalise the results to other settings. However it does provide weak evidence for the widespread implementation of best practice, along with education and training, for the reduction of HCAI and improved patient outcomes.

Table 12: Evidence table for peripheral access devices and flushing

Reference	Country of origin	Sample/setting	Aim of study	Methods	Key findings	Quality
17. Easterlow et al. (2010)	UK	All hospitalised patients with PVC.	To assess the impact of a change initiative relating to the use of PVC on HCAI in an under-performing hospital.	Audit pre- and post-implementation of a change initiative which included introduction of a new non-ported cannula, along with practice change.	HCAI reduced over the course of the study.	1 (low)
34. Li et al. (2010)	US	18 Healthy volunteers	To determine if the infusion rate of a single 18-g IV was equivalent to the infusion rate of two 20-g IVs.	All subjects simultaneously received 500m normal saline via an 18-g IV in one arm, and two 20-g IVs in the other arm. Infusion times were compared.	Two 20-g IVs were significantly faster than a single 18-g IV. Both were markedly slower than rates observed in in vitro testing and based on manufacturer data.	5 (medium)
31. Lee et al. (2010)	Taiwan	46 patients with PVC-related soft tissue infection in acute hospital setting, 188 controls from same setting but with no infection.	To investigate risk factors for PVC-related soft tissue infections in hospital patients.	Retrospective case-control study.	Risk factors associated with the development of infection included >24h continuous infusion, insertion in the lower extremity, use of infusion pumps and hospitalisation for neurological or neurosurgical conditions.	3 (low)

Subcutaneous infusions

The RCN search for evidence regarding the safety and effectiveness of performing subcutaneous infusions included evidence for: subcutaneous infusion (hypodermoclysis); subcutaneous injection; use in community settings; site access; insertion of; administration and maintenance. No relevant studies were identified in this area which means no evidence was found to answer the following RCN questions:

- What is the effect of different devices on patient safety and outcomes; for example peripheral cannula versus steel winged infusion devices?
- What is the effect of electronic devices for this procedure on patient safety and outcomes?
- What is the effect of site selection on patient safety and outcomes?
- What is the effect of site management on patient safety and outcomes?
- What is the effect of solution tonicity on patient safety and outcomes?
- What is the effect of electrolytes used (for example, sodium chloride, dextrose saline, dextrose 5%) on patient safety and outcomes?

Discussion

As previously stated the studies that were examined varied widely with regards to design and outcome, therefore this review does not produce robust evidence for any single intervention or practice. This review deliberately targeted primary research studies that were not RCTs and secondary research studies that were not SRs, with a view to supplementing Phase One of the clinical review which included only RCTs and SRs. However the results of the studies do provide an overview of the evidence base in a wide area, a rationale for further research, and an indication of best practice in a variety of aspects of IV therapy.

Twelve aspects of infusion therapy were searched for evidence (add on devices; arterial catheters; blood sampling; central venous access devices; flow control devices; infusion-related bloodstream infection; infusion therapy parenteral nutrition; infusion therapy phlebitis; intraosseous access devices; midline catheters; peripheral access devices and flushing; subcutaneous infusions). The most researched area appeared to be bloodstream infections (15/48 studies) followed by blood sampling (8/48). The overall volume of studies per area was rather low with arterial catheters and subcutaneous infusions having no studies included. Moreover, within each area, studies addressed a variety of research questions.

The majority of primary research studies were conducted in hospital settings (38/43) and in the US (25/43). Other settings included outpatients, palliative care patients and healthy volunteers. In addition, five literature reviews were included which were not context-specific. Most studies focussed on patient-related outcomes, however two investigated outcomes related to nurses' knowledge or practice.

Based on the Infusion Nurses Society (2016) standards of evidence, most of the evidence is classified as Levels IV and V, due to the fact that no RCTs or SRs were included in this part of the review. However, the overall quality of studies, as assessed within the confines of this review, was high to medium, and no study was excluded on quality.

The most common outcome was catheter-related bloodstream infection rates. Other complications such as phlebitis, effective delivery of therapy and improvement in patient clinical condition were less well studied. There was also no evidence relating to management of complications or the impact on patient experience. Several interventions took place in the context of wider practice improvement initiatives which makes it difficult to quantify the effect of the intervention itself.

Implications for policy/practice

It is clear that pre- and post-insertion care bundles have the potential to significantly reduce catheter-related infection rates[16,22,24,30]. However, a care bundle is only effective if the practices are evidence-based and performed consistently at all times by all members of staff[27]. Therefore evidence from high quality studies must be gathered to identify the interventions which – when performed collectively – will have the largest impact on patient outcomes. The limited evidence available from the current review suggests that an effective pre-insertion care bundle would consist of hand hygiene, maximal barrier precautions, standardised insertion packs and guidance, and avoidance of the femoral site where possible. A post-insertion care bundle should include use of aseptic technique, scrubbing the connector hub prior to access, regular monitoring and care of the insertion site, and removal of any unnecessary lines. More well designed studies are required however to confirm these observations.

It appears from the limited evidence available from this review that blood samples can be obtained from IV access devices without significantly affecting the quality of the sample[11,13,23,25,29]. The only parameters which were found to be affected were venous blood gases[23] and INR[25]. As repeated venepuncture can be distressing for the patient and time consuming for nurses, sampling from IV starts or existing IV access devices should be considered for routine blood testing.

An important point to note is that if sampling from a heparinised PICC, the port used to deliver the heparin should be avoided[11]. It is also recommended that non-wire hubs should be used for sampling rather than wire hubs[33].

When sampling from IV access devices, it is widely accepted that a volume of blood should be drawn and discarded as waste, prior to obtaining the sample. The results of one study in this area suggest that 1ml is sufficient to produce an

undiluted sample[3]; therefore drawing excessive waste amounts is unnecessary. However further research is required to back up this study.

It is clear from several studies included in this review that quality improvement programmes have the potential to improve practice and outcomes[14,16,17,22,24,30,36,42,43,44,53]. The design of these studies makes it difficult to quantify the impact of any single intervention, however the collective results suggest a commitment to culture change and practice improvement can positively impact upon patient outcomes. In order to maximise the impact of these programmes, they must be evidence-based and widely enforced. Education and training should be provided to ensure all staff are aware of the rationale for the change as well as learning any new techniques. Evidence shows that regular monitoring and feedback can increase compliance rates[6,57].

Two studies demonstrated the effectiveness of employing a specialist nurse to improve practice with regards to infection prevention[48,55]. While such a specialist can provide standardisation and facilitation of good practice through education and monitoring, any such introduction would have to be considered at each individual trust in the light of local priorities and the financial situation.

Several studies identified risk factors for various complications relating to infusion therapy[9,31,37,41,49,51]. As many patients present with several co-morbidities, this reinforces the importance of taking a thorough history from each patient, as well as close and regular monitoring if a risk factor is identified.

One study found that replacement of catheters on clinical indication rather than routinely did not lead to increased complication rates[50]. Adopting this policy would both free up time for health care staff and reduce pain and discomfort for patients; however, if this practice is to be adopted, it is essential regular monitoring takes place in order to quickly identify early signs of complications.

The results of two studies suggest that obtaining intraosseous access is both quicker and more successful than placing a CVC in critically ill patients with no peripheral access[5,32]. However, intraosseous access is not routinely carried out[5,20]. In the light of these findings, health care professionals dealing with critically ill patients should be provided with education and training to increase their confidence and competence in placing intraosseous access devices.

One high quality study found that the placement of PICCs and midline catheters resulted in very little pain and distress to palliative care patients, and had a significant positive impact on global quality of life[7]. Therefore, midline catheters should be viewed as a viable treatment method in this population for the administration of fluid and nutrition, as well as intravenous medication. However, as with any intervention at end of life, the decision to insert such a device must be made on an individual basis, in partnership with the patient, carers and multidisciplinary team.

Finally, while simple in design and carried out on healthy volunteers, one study provides interesting data regarding the relative infusion rates of small and larger gauge catheters[34]. While scientific laws would suggest one 20-g catheter would provide a faster infusion than two 18-g catheters, the authors of this study found the opposite to be the case. Moreover, both methods were markedly slower than rates observed in in vitro testing and based on manufacturers' data. This reinforces the importance of basing clinical judgements on appropriate data obtained in clinical studies, rather than using scientific laws, in vitro testing or manufacturer data.

Limitations

This review has limitations relating both to the methods employed and the studies included. A high quality systematic review is understood to be the most reliable source of evidence to guide clinical practice[10]. The systematic review process, however, is time consuming, which is often at odds with the requirement to provide evidence to inform policy and practice in a timely manner. This review employs the methods of a rapid evidence assessment (REA), an established research method which could be viewed as a compromise between the expectation for a systematic review to be rigorous and comprehensive, and the requirement that results be available within a short time period[56]. When employing these methods there will always be a trade-off between completing the review quickly and ensuring it is rigorous and exhaustive; measures were taken at every stage to minimise bias and ensure the findings can be used with confidence to inform policy and practice.

The main difference between a SR and a REA is that the latter employs a more limited search strategy with a less exhaustive database search and no hand searching of current journals or search for 'grey literature', which is characteristic of a rigorous SR[8]. Watt and colleagues, however, found that restricting the search to the most productive databases did not impact adversely upon the REA as the additional number of relevant studies identified is generally very low[58]. The current study included only papers which could be retrieved electronically or from the RCN library; the number excluded due to inaccessibility was very low, and therefore unlikely to affect the quality of the final review.

An important consideration is that studies which are found more easily are often affected by publication bias[56]. Therefore when a list of studies was provided by several of the sponsors of the study, these were considered despite not being flagged up by the initial search. While none of these studies was included in the review after screening against inclusion and exclusion criteria, one review obtained at a later stage was included, ensuring that intraosseous evidence was considered in a systematic way.

Quality assessment and data extraction were conducted by only one researcher, however any difficult decisions were discussed with a second researcher, and the second researcher also checked

a random sample from each area in order to ensure there were no discrepancies.

In terms of the papers selected for review, as SRs and RCTs were extracted for separate review the studies in this review provide evidence at only Levels III to V (with Level I being the highest level according to the Infusion Nurses Society[26]). In health care research, however, it is increasingly being acknowledged that RCTs are unable to provide a complete evaluation[18]; specifically, it is often not practical or ethical to conduct RCTs in health care research. It is therefore important to include this section to ensure all studies which can contribute to the evidence base are identified and appraised.

The inclusion of a variety of research designs, which in turn looked at a range of outcome measures, makes it difficult to combine the data to come up with robust conclusions. No studies were excluded on the basis of quality, however, results have been considered with regards to quality, design and volume in order to provide a judgement on the reliability and validity of conclusions.

Conclusion

The results of this review provide an overview of the non-RCT evidence base in the area of infusion therapy. Due to the limitations discussed above with regards to the study designs and outcomes, it is not possible to draw robust conclusions from the findings. Therefore, the evidence provided here should be considered along with that obtained from the SRs and RCTs in Phase One of the review, in order to inform practice and policy development. Where there is no SR or RCT evidence, judgement must be based on the quality of the evidence provided and whether it is of sufficient strength on which to base recommendations. Using non-RCT evidence should be done with caution and it is recommended that further evidence or expert opinion be sought where there is any ambiguity.

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Appendix A: US infusion nursing standards of evidence (Infusion Nurses Society, 2016)

Strength of body of evidence	Evidence description*
I	Meta-analysis, systematic literature review, guideline based on randomised controlled trials (RCTs), or at least three well-designed RCTs.
I A/P	Evidence from anatomy, physiology and pathophysiology references as understood at the time of writing.
II	Two well-designed RCTs, two or more multicenter, well-designed clinical trials without randomization, or systematic literature review of varied prospective study designs.
III	One well-designed RCT, several well-designed clinical trials without randomization, or several studies with quasi-experimental designs focused on the same question. Includes two or more well-designed laboratory studies.
IV	Well-designed quasi-experimental study, case-control study, cohort study, correlational study, time series study, systematic literature review of descriptive and qualitative studies, or narrative literature review, psychometric study. Includes one well-designed laboratory study.
V	Clinical article, clinical/professional book, consensus report, case report, guideline based on consensus, descriptive study, well-designed quality improvement project, theoretical basis, recommendations by accrediting bodies and professional organisations, or manufacturer directions for use for products or services. Includes standard of practice that is generally accepted but does not have a research basis (for example, patient identification). May also be noted as Committee Consensus, although rarely used.
Regulatory	Regulatory regulations and other criteria set by agencies with the ability to impose consequences, such as the AABB, Centers for Medicare & Medicaid Services (CMS), Occupational Safety and Health Administration (OSHA), and state boards of nursing.

*Sufficient sample size is needed, with preference for power analysis adding to the strength of evidence.

Appendix B: Studies excluded on full text

Section 1: Add on devices

Excluded on full text – summary of paper published in 2009

Anderson B, Mitchell M and Williams K (2010) A comparison of heparin and saline flush to maintain patency in central venous catheters, *Nursing Times*, 106(6), pp. 15-16.

Abstract:
Summary of systematic review previously published in J Advanced Nursing. 2009. Oct. 65(10). p2007-21, on the effectiveness and safety of using heparin for flushing central venous access devices to prevent occlusion. The value of pressure caps, risk of heparin-induced thrombocytopenia, use of saline flushes and use of heparin-bonded catheters are discussed. [(BNI unique abstract) – 7 references].

Excluded on full text – not a research study

Hadaway L (2012) Needleless connectors for IV catheters, *American Journal of Nursing*, 112(11), pp. 32-44.

Abstract:
Needleless devices for connecting IV catheters, administration sets, and syringes were introduced in the early 1990s for the purpose of reducing the risk of needlestick injuries among health care providers. Although needleless connectors serve that purpose, their use has been associated with an increase in such complications as catheter-related bloodstream infection and catheter lumen occlusion. Complications may be related to design characteristics, user knowledge deficits, poor practices, or some combination thereof. Here, Hadaway describes the connectors in current use, how they differ in design and function, the potential complications associated with various models and practices, and the nursing interventions that can reduce the risk of these complications. [Publication – 46 references].

Arterial Catheters

No studies excluded on full text.

Blood Sampling

No studies excluded on full text.

Central venous access devices

Excluded on full text – literature review for Maneval and Clemence (2014) which is included

Clemence BJ and Maneval RE (2014) Risk factors associated with catheter-related upper extremity deep vein thrombosis in patients with peripherally inserted central venous catheters: literature review: part 1, *Journal of Infusion Nursing*, 37(3), pp. 187-196.

Abstract:
This is Part 1 of a two-part series of articles that report on the results of a prospective observational cohort study designed to examine the risk factors associated with symptomatic upper extremity deep vein thrombosis (UEDVT) in patients with peripherally inserted central catheters. This article provides an extensive review and critique of the literature that serves to explicate what is currently known about risk factors associated with catheter-related UEDVT. Risk factors such as anticoagulant use, cancer, infection, hypertension, catheter tip placement, and catheter size were identified most frequently in the literature as being associated with UEDVT development. Other risk factors-such as obesity, smoking history, surgery, and presence of pain or edema-were examined in a limited number of studies and lacked consistent evidence of their impact on UEDVT development. The subsequent study that evolved from the review of the literature investigates the relationship between identified risk factors and UEDVT development. [Publication].

Full text unavailable

Trerotola SO, Patel AA, Shlansky-Goldberg RD, Solomon JA, Mondschein JI, Stavropoulos SW, Soulen MC, Itkin M and Chittams J (2010) Short-term infection in cuffed versus noncuffed small bore central catheters: a randomized trial, *Journal of Vascular & Interventional Radiology*, 21(2), pp. 203-11.

Excluded on full text – not relevant to UK

Berenholtz SM, Lubomski LH, Weeks K, Goeschel CA, Marsteller JA, Pham JC, Sawyer MD, Thompson DA, Winters BD, Cosgrove SE, Yang T, Louis TA, Meyer LB, George CT, Watson SR, Albert-Lesher MI, St Andre JR, Combes JR, Bohr D, Hines SC, Battles JB and Pronovost PJ (2014) Eliminating central line-associated bloodstream infections: a national patient safety imperative, On the CUSP: Stop BSI program, Infection Control And Hospital Epidemiology, ISSN: 1559-6834, 35(1), pp. 56-62.

Abstract:
Background: several studies demonstrating that central line-associated bloodstream infections (CLABSIs) are preventable prompted a national initiative to reduce the incidence of these infections.

Methods: we conducted a collaborative cohort study to evaluate the impact of the national "On the CUSP: Stop BSI" program on CLABSI rates among participating adult intensive care units (ICUs). The program goal was to achieve a unit-level mean CLABSI rate of less than one case per 1,000 catheter-days using standardized definitions from the National Healthcare Safety Network. Multilevel Poisson regression modelling compared infection rates before, during, and up to 18 months after the intervention was implemented.

Results: a total of 1,071 ICUs from 44 states, the District of Columbia, and Puerto Rico, reporting 27,153 ICU-months and 4,454,324 catheter-days of data, were included in the analysis. The overall mean CLABSI rate significantly decreased from 1.96 cases per 1,000 catheter-days at baseline to 1.15 at 16-18 months after implementation. CLABSI rates decreased during all observation periods compared with baseline, with adjusted incidence rate ratios steadily decreasing to 0.57 (95% confidence intervals, 0.50-0.65) at 16-18 months after implementation.

Conclusion: coincident with the implementation of the national "On the CUSP: Stop BSI" program was

a significant and sustained decrease in CLABSIs among a large and diverse cohort of ICUs, demonstrating an overall 43% decrease and suggesting the majority of ICUs in the United States can achieve additional reductions in CLABSI rates.

Excluded on full text – not relevant to UK

Maki DG, Rosentha, VD, Salomao R, Franzetti F and Rangel-Frausto MS (2011) Impact of switching from an open to a closed infusion system on rates of central line-associated bloodstream infection: a meta-analysis of time-sequence cohort studies in four countries, *Infection Control and Hospital Epidemiology* 32(1), pp. 50-58.

Abstract:

Background: we report a meta-analysis of four identical time-series cohort studies of the impact of switching from use of open infusion containers (glass bottle, burette, or semirigid plastic bottle) to closed infusion containers (fully collapsible plastic containers) on central line-associated bloodstream infection (CLABSI) rates and all-cause intensive care unit (ICU) mortality in 15 adult ICUs in Argentina, Brazil, Italy, and Mexico.

Methods: all ICUs used open infusion containers for 6-12 months, followed by switching to closed containers. Patient characteristics, adherence to infection control practices, CLABSI rates, and ICU mortality during the two periods were compared by χ^2 test for each country, and the results were combined using meta-analysis.

Results: similar numbers of patients participated in two periods (2,237 and 2,136). Patients in each period had comparable Average Severity of Illness Scores, risk factors for CLABSI, hand hygiene adherence, central line care, and mean duration of central line placement. CLABSI incidence dropped markedly in all four countries after switching from an open to a closed infusion container (pooled results, from 10.1 to 3.3 CLABSIs per 1,000 central line-days; relative risk [RR], 0.33 [95% confidence interval {CI}, 0.24-0.46]; P <.001). All-cause ICU mortality also decreased significantly, from 22.0 to 16.9 deaths per 100 patients (RR, 0.77 [95% CI, 0.68-0.87]; P <.001).

Conclusions: switching from an open to a closed infusion container resulted in a striking reduction in the overall CLABSI incidence and all-cause ICU mortality. Data suggest that open infusion containers are associated with a greatly increased risk of infusion-related bloodstream infection and increased ICU mortality that have been unrecognized. Furthermore, data suggest CLABSIs are associated with significant attributable mortality.

Flow Control Devices

Full text unavailable

Woodward A (2013) Achievable temperatures of intravenous fluids delivered through a fluid warming device at differing clinically relevant flow rates, *The Dissector* 41(2), pp. 26-29.

Abstract:

The maintenance of normothermia during surgery is vital for good patient outcomes. Literature is reviewed and research conducted on the relative importance of the flow rate, viscosity and mass of the intravenous fluid, when it is passed through a fluid warming device to maintain body temperature and the implications for clinical practice. [Publication – 10 references].

Excluded on full text – not nursing related

McGuire R (2015) Assessing standards of vascular access device care, *British Journal of Nursing* 24(8), pp. S29-S35.

Abstract:

Vascular access devices (VADs) are essential in health care as they provide vital access for treatment including the infusion of medication, fluids, blood products and nutritional supplements. However, their invasive nature predisposes patients to potential complications, primarily bloodstream infections. This article examines the current standards of VAD care and assesses compliance with current guidelines (national and trust policy) in one hospital setting utilising a practice audit. The audit was conducted in a 500-bed district general hospital over six non-consecutive week days. The medical division where the audit took place had 13 wards with 288 beds. A total of 120 VADs were audited, averaging n=9.2 per ward (with a range of 4-18 on each ward). The results demonstrated a collective non-compliance rate of 48%. Although overall compliance was 52%, a poor standard of care was highlighted across the division for all components of the care elements. The post-insertion care of VADs is an essential component of a comprehensive strategy to prevent complications. Consequently, initiatives such as audit, education and feedback should be used in an effort to improve practice and maintain optimal care. [Publication – 40 references].

Infusion-related Bloodstream Infections

Excluded on full text – not relevant to infusion therapy practice

Krein SL, Fowler KE, Ratz D, Meddings J and Saint S (2015) Preventing device-associated infections in US hospitals: national surveys from 2005 to 2013, *BMJ Quality and Safety* 24(6), pp. 385-392.

Abstract:

Background: numerous initiatives have focused on reducing device-associated infections, contributing to an overall decrease in infections nationwide. To better understand factors associated with this decline, we assessed the use of key practices to prevent device-associated infections by US acute care hospitals from 2005 to 2013.

Methods: we mailed surveys to infection preventionists at a national random sample of ~600 US acute care hospitals in 2005, 2009 and 2013. Our survey asked about the use of practices to prevent the three most common device-associated infections: central line-associated bloodstream infection (CLABSI), ventilator-associated pneumonia (VAP) and catheter-associated urinary tract infection (CAUTI). Using sample weights, we estimated the per cent of hospitals reporting regular use (a score of 4 or 5 on a scale from 1 (never use) to 5 (always use)) of prevention practices from 2005 to 2013.

Results: the response rate was about 70% in all three periods. Use of most recommended

prevention practices increased significantly over time. Among those showing the greatest increase were use of an antimicrobial dressing for preventing CLABSI (25-78%, p<0.001), use of an antimicrobial mouth rinse for preventing VAP (41-79%, p<0.001) and use of catheter removal prompts for preventing CAUTI (9-53%, p<0.001). Likewise, a significant increase in facility-wide surveillance was found for all three infections. Practices for which little change was observed included use of antimicrobial catheters to prevent either CLABSI or CAUTI.

Conclusions: US hospitals have responded to the call to reduce infection by increasing use of key recommended practices. Vigilance is needed to ensure sustained improvement and additional strategies may still be required, given an apparent continuing lag in CAUTI prevention efforts. [Publication – 49 references].

Full text unavailable

Richardson J and Tjoelker R (2012) Beyond the central line-associated bloodstream infection bundle: the value of the clinical nurse specialist in continuing evidence-based practice changes, *Clinical Nurse Specialist: The Journal for Advanced Nursing Practice*, 26(4), pp. 205-211.

Abstract:
Purpose: the purpose of this project was to demonstrate the value of clinical nurse specialist (CNS)-led efforts to optimize patient outcomes through continued monitoring and management of a previously implemented evidence-based practice project.

Background: central line-associated bloodstream infections (CLABSIs) significantly impact patient morbidity/mortality and cost of care. In 2006, the critical care unit (CCU) of the Portland VA Medical Center implemented national recommendations for the prevention of CLABSIs through use of the Institute of Healthcare Improvement Central Line Bundle. This practice change was led by the CCU and infection control CNSs, and compliance in the completion of bundle items has remained consistently high (>90%). Although the CCU has maintained CLABSI rates below the national benchmark, it experienced a four-month period of increased incidence in late 2008. DESCRIPTION: : Clinical nurse specialists in CCU and infection control organized a "Hot Team" of nurses from multiple departments throughout the hospital to evaluate processes/data related to the recent increase in infections. Using national guidelines, the team focused on interdisciplinary implementation of strategies beyond the Central Line Bundle components. Consideration of cost and workflow patterns was critical to decision making.

Outcome: infection rates in CCU decreased from a high of 1.5 per 1000 line days down to 0 in June 2011, with the last CLABSI occurring in May 2010.

Conclusion: the formation and efforts of a CNS-led team of nurses has been successful in decreasing infection rates through implementation of multiple innovative strategies.

Implications: clinical nurse specialist surveillance, management, and leadership following project implementation are valuable strategies for continued optimal patient outcomes.

Excluded on full text – not nursing related

Weaver SJ, Weeks K, Pham JC and Pronovost PJ (2014) On the CUSP: Stop BSI: Evaluating the relationship between central line–associated bloodstream infection rate and patient safety climate profile, *American Journal of Infection Control* 42(S203-8).

Abstract:
Background central line–associated bloodstream infection (CLABSI) remains one of the most common and deadly hospital acquired infections in the United States. Creating a culture of safety is an important part of health care–associated infection improvement efforts; however, few studies have robustly examined the role of safety climate in patient safety outcomes. We applied a pattern-based approach to measuring safety climate to investigate the relationship between intensive care unit (ICU) patient safety climate profiles and CLABSI rates. Methods Secondary analyses of data collected from 237 adult ICUs participating in the On the CUSP: Stop BSI project. Unit-level baseline scores on the Hospital Survey on Patient Safety, a survey designed to assess patient safety climate, and CLABSI rates, were investigated. Three climate profile characteristics were examined: profile elevation, variability, and shape. Results Zero-inflated Poisson analyses suggested an association between the relative incidence of CLABSI and safety climate profile shape. K-means cluster analysis revealed 5 climate profile shapes. ICUs with conflicting climates and non-punitive climates had a significantly higher CLABSI risk compared with ICUs with generative leadership climates. Conclusions Relative CLABSI risk was related to safety climate profile shape. None of the climate profile shapes was related to the odds of reporting zero CLABSI. Our findings support using pattern-based methods for examining safety climate rather than examining the relationships between each narrow dimension of safety climate and broader safety outcomes like CLABSI.

Full text unavailable

Lissauer ME, Leekha S, Preas MA, Thom KA and Johnson SB (2012) Risk factors for central line-associated bloodstream infections in the era of best practice, *Journal of Trauma & Acute Care Surgery*, 72(5), pp. 1174-1180.

Abstract:
Background: best clinical practice aims to eliminate central line-associated blood stream infections (CLABSIs). However, CLABSIs still occur. This study's aim was to identify risk factors for CLABSI in the era of best practice.

Methods: critically ill surgical patients admitted over two years to the intensive care unit (ICU) for >=4 days were studied. Patients with CLABSI as cause for ICU admission were excluded. Patients who developed CLABSI (National Healthcare Safety Network definition) were compared with those who did not. Hand hygiene, maximal sterile barriers, chlorhexidine scrub, avoidance of femoral vein, and proper maintenance were emphasized. Variables collected included demographics,

diagnosis, and severity of illness using the Acute Physiology and Chronic Health Evaluation (APACHE) IV database and the hospital central data repository.

Results: of 961 patients studied, 51 patients (5.2%) developed 59 CLABSIs. Mean time from ICU admission to CLABSI was 26 days ± 26 days. The CLABSI group was more likely to be male (odds ratio [OR] 1.93, 95% confidence interval [CI] 1.02-3.68), more critically ill on ICU admission (APACHE IV score 85.2 ± 21.9 vs. 65.6 ± 23.2, $p < 0.01$), more likely admitted to the emergency surgery service (OR 1.92, 95% CI 1.02-3.61), and had an association with reopening of recent laparotomy (OR 2.08, 95% CI 1.10-3.94).

Conclusion: in the era of best practice, patients who develop CLABSI are clinically distinct from those who do not develop CLABSI. These CLABSIs may be due to deficiencies of the CLABSI definition or represent patient populations requiring enhanced prevention techniques.

Level of evidence: III, prognostic study.

Infusion therapy parenteral nutrition

Excluded on full text – not nursing related

Lee AM, Gabe SM, Nightingale JM and Burke M (2012) Oral health, dental prophylaxis and catheter related bloodstream infections in home parenteral nutrition patients: results of a UK survey and cohort study, *British Dental Journal*, 212 (2), pp. E4.

Abstract:
Background: concern that some catheter related bloodstream infections (CRBSI) arise from dental treatment in home parenteral nutrition (HPN) patients results in recommendation of antibiotic prophylaxis. Clinical guideline 64 is widely recognised and observed. There is a lack of consistent guidance for other patient groups viewed at risk from procedural bacteraemia.

Methods: (1) – an email survey of the British Association for Parenteral and Enteral Nutrition (BAPEN) HPN group, requesting physicians' opinions, observations and practises relating to oral health and CRBSI prevention; (2) – comparison of oral health parameters and dental treatment in relation to patient reported 12 month CVC infection history, using chi-square analysis to assess associations in 52 HPN patients.

Results: (1) – sixty-eight percent of the UK HPN Group responded. Fifty percent linked oral health/ dental treatment with the possibility of CRBSI, 39% were unsure. Sixty-one percent had recommended parenteral prophylactic antibiotics (82% IV, 18% IM), mainly following the historic infective endocarditis (IE) dental prophylaxis guidelines. Infection with streptococci, prevotella and fusobacteria caused most concern. Amoxicillin, metronidazole, co-amoxyclav and gentamycin were the most prescribed antibiotics. Thirty-six percent might delay HPN if oral health was poor; 57% had recommended dental examination and 25% dental extractions, to prevent or treat CRBSI; (2) – associations between patient recalled CVC infection and their current dental status, the interval since dental treatment or the prophylaxis received over the previous 12 months did not achieve significance.

Conclusions: opinion varies among UK HPN providers on the role of dental treatment and oral health in CRBSI and on prescribing prophylactic antibiotics for dental treatment. Prophylaxis guidance specific to this patient group is required.

Excluded on full text – condition specific

Teno JM, Gozalo PL, Mitchell SL, Kuo S, Rhodes RL, Bynum JP and Mor V (2012) Does feeding tube insertion and its timing improve survival? *Journal of the American Geriatrics Society*, 60(10), pp. 1918-1921.

Abstract:
To examine survival with and without a percutaneous endoscopic gastrostomy (PEG) feeding tube using rigorous methods to account for selection bias and to examine whether the timing of feeding tube insertion affected survival. Prospective cohort study. Thirty-six thousand four hundred ninety-two NH residents with advanced cognitive impairment from dementia and new problems eating studied between 1999 and 2007. Survival after development of the need for eating assistance and feeding tube insertion. Of the 36,492 NH residents (88.4% white, mean age 84.9, 87.4% with one feeding tube risk factor), 1,957 (5.4%) had a feeding tube inserted within one year of developing eating problems. After multivariate analysis correcting for selection bias with propensity score weights, no difference was found in survival between the two groups (adjusted hazard ratio (AHR) = 1.03, 95% confidence interval (CI) = 0.941.13). In residents who were tube-fed, the timing of PEG tube insertion relative to the onset of eating problems was not associated with survival after feeding tube insertion (AHR = 1.01, 95% CI =0.86-1.20, persons with a PEG tube inserted within 1 month of developing an eating problem versus later (four months) insertion). Neither insertion of PEG tubes nor timing of insertion affect survival. [Publication – 24 references].

Excluded on full text – not related to infusion therapy

Metheny NA and Meert KL (2014) Effectiveness of an electromagnetic feeding tube placement device in detecting inadvertent respiratory placement, *American Journal of Critical Care*, 23(3), pp. 240-248.

Abstract:
Background: use of technology capable of electromagnetically tracking advancement of a feeding tube on a monitoring screen during insertion may enable detection of deviation of the tube from the midline as it advances through the chest, possibly indicating entry of the tube into the right or left main bronchus.

Purposes: to describe (1) published peer-reviewed studies that report on the detection of malpositioned tubes inserted by an electromagnetic tube placement device, and (2) events reported to the US Food and Drug Administration's Manufacturer and User Facility Device Experience (MAUDE) database regarding

use of such a device.

Methods: an Ovid MEDLINE search was conducted to locate peer-reviewed studies published between 2007 and 2012 that referred to use of an electromagnetic tube placement device to detect inadvertent respiratory placements of feeding tubes. In addition, an online search of the MAUDE database was conducted for the years 2007 through 2012.

Results: the Ovid MEDLINE search yielded six studies that referred to respiratory placements; no cases of pneumothorax were reported. The MAUDE database search yielded 21 adverse events associated with use of an electromagnetic tube placement device (including 17 cases of pneumothorax and two deaths). As the MAUDE database relies on voluntary reports, this number should not be construed as the incidence of mal-positioned tubes during this period.

Conclusions: the ability of clinicians to place feeding tubes correctly by using an electromagnetic tube placement device varies. Thus, it is reasonable to question the wisdom of eliminating radiographic confirmation of tube position before starting feedings. [Publication – 22 references].

Excluded on full text – not related to infusion therapy

Taylor SJ, Allan K, McWilliam H and Toher D (2014) Nasogastric tube depth: the 'NEX' guideline is incorrect, *British Journal of Nursing*, 23(12), pp. 641-644.

Abstract:
Misplacing 17-23% of nasogastric (NG) tubes above the stomach (Rollins et al, 2012; Rayner, 2013) represents a serious risk in terms of aspiration, further invasive (tube) procedures, irradiation from failed X-ray confirmation, delay to feed and medication. One causal factor is that in the National Patient Safety Agency (NPSA) guidance to place a tube, length is measured from nose to ear to xiphisternum (NEX) (NSPA, 2011); NEX is incorrect because it only approximates the nose to gastro-oesophageal junction (GOJ) distance and is therefore too short. To overcome this and because the xiphisternum is more difficult to locate, local policy is to measure in the opposite direction; xiphisternum to ear to nose (XEN), then add 10 cm. The authors determined whether external body measurements can be used to estimate the NG tube length to safely reach the gastric body. This involved testing the statistical association of body length, age, sex and XEN in consecutive critically ill patients against internal anatomical landmarks determined from an electromagnetic (EM) trace of the tube path. XEN averaged 50 cm in 71 critically ill patients aged 53 ± 20 years. Tube marking and the EM trace were used to determine mean insertion distances at pre-gastro-oesophageal junction (GOJ) (48 cm), where the tube first turns left towards the stomach and becomes shallow on the trace; gastric body (62 cm), where the tube reaches the left-most part of the stomach; and gastric antrum (73 cm) at the midline on the EM trace. Using body length, age, sex and XEN in a linear regression model, only 25% of variability was predicted, showing that external measurements cannot reliably predict the length of tube required to reach the stomach. A tube length of XEN (or NEX) is too short to guarantee gastric placement and is unsafe. XEN +10 cm or more complex measurements will reach the gastric body (mid-stomach) in most patients, but because of wide variation, external measurements often fail to predict a safe distance. Only the EM trace or possibly direct vision can show in real time whether the tip has safely reached the gastric body. [Publication – 16 references].

Infusion therapy phlebitis

Full text unavailable

Mestre RG, Berbel BC, Tortajada LP, Gallemi SG, Aguilar RM, Caylà BJ, Rodríguez-Baño J and Martinez JA (2012) Assessing the influence of risk factors on rates and dynamics of peripheral vein phlebitis: an observational cohort study, *Medicina Clínica*, 139(5), pp. 185-191.

Abstract:
Background and objectives: to assess the influence of risk factors on the rates and kinetics of peripheral vein phlebitis (PVP) development and its theoretical influence in absolute PVP reduction after catheter replacement.

Methods: all peripheral short intravenous catheters inserted during one month were included (1201 catheters and 967 patients). PVP risk factors were assessed by a Cox proportional hazard model. Cumulative probability, conditional failure of PVP and theoretical estimation of the benefit from replacement at different intervals were performed.

Results: female gender, catheter insertion at the emergency or medical-surgical wards, forearm site, amoxicillin-clavulamate or aminoglycosides were independent predictors of PVP with hazard ratios (95 confidence interval) of 1.46 (1.09-2.15), 1.94 (1.01-3.73), 2.51 (1.29-4.88), 1.93 (1.20-3.01), 2.15 (1.45-3.20) and 2.10 (1.01-4.63), respectively. Maximum phlebitis incidence was reached sooner in patients with ≥2 risk factors (days 3-4) than in those with <2 (days 4-5). Conditional failure increased from 0.08 phlebitis/one catheter-day for devices with ≤1 risk factors to 0.26 for those with ≥3. The greatest benefit of routine catheter exchange was obtained by replacement every 60h. However, this benefit differed according to the number of risk factors: 24.8% reduction with ≥3, 13.1% with 2, and 9.2% with ≤1.

Conclusions: PVP dynamics is highly influenced by identifiable risk factors which may be used to refine the strategy of catheter management. Routine replacement every 72h seems to be strictly necessary only in high-risk catheters.

Intraosseous access devices

Full text unavailable

Gallo M, Lodini R, Destrebecq A, D'antuono A and Terzoni S (2014) Intraosseous access in emergency/urgency: review of the literature, SCENARIO: *Official Italian Journal of ANIARTI* 31 (2), pp. 35-40.

Midline catheters

Full text unavailable

Alexandrou E, Spencer TR, Frost SA, Mifflin N, Davidson, PM and Hillman KM (2014) Central venous catheter placement by advanced practice nurses demonstrates low procedural complication and infection rates-a report from 13 years of service, *Critical Care Medicine*, 42(3), pp. 536-543.

Abstract:
Objectives: to report procedural characteristics and outcomes from a central venous catheter placement service operated by advanced practice nurses.

Design: single-center observational study.
SETTING: A tertiary care university hospital in Sydney, Australia.

Patients: adult patients from the general wards and from critical care areas receiving a central venous catheter, peripherally inserted central catheter, high-flow dialysis catheter, or midline catheter for parenteral therapy between November 1996 and December 2009.

Interventions: none.

Measurements and main results: prevalence rates by indication, site, and catheter type were assessed. Nonparametric tests were used to calculate differences in outcomes for categorical data. Catheter infection rates were determined per 1,000 catheter days after derivation of the denominator. A total of 4,560 catheters were placed in 3,447 patients. The most common catheters inserted were single-lumen peripherally inserted central catheters (n = 1,653; 36.3%) and single-lumen central venous catheters (n = 1,233; 27.0%). A small proportion of high-flow dialysis catheters were also inserted over the reporting period (n = 150; 3.5%). Sixty-one percent of all catheters placed were for antibiotic administration. The median device dwell time (in d) differed across cannulation sites ($p < 0.001$). Subclavian catheter placement had the longest dwell time with a median of 16 days (interquartile range, 8-26 d). Overall catheter dwell was reported at a cumulative 63,071 catheter days. The overall catheter-related bloodstream infection rate was 0.2 per 1,000 catheter days. The prevalence rate of pneumothorax recorded was 0.4%, and accidental arterial puncture (simple puncture-with no dilation or cannulation) was 1.3% using the subclavian vein.

Conclusions: this report has demonstrated low complication rates for a hospital-wide service delivered by advance practice nurses. The results suggest that a centrally based service with specifically trained operators can be beneficial by potentially improving patient safety and promoting organizational efficiencies.

Peripheral access devices and flushing

Excluded on full text – not related to infusion therapy practice

Boyd S, Aggarwal I and Davey P (2011) Peripheral intravenous catheters: the road to quality improvement and safer patient care, *Journal of Hospital Infection*, 77(1), pp. 37-41.

Abstract:
Research in Scotland into the introduction of a peripheral venous catheter (PVC) care bundle as a tool for improving the management of PVCs as part of quality improvement. Performance for insertion and management of catheters and care bundle compliance were monitored over 25 weeks. [(BNI unique abstract) – 24 references].

Full text unavailable

Frigerio S, Di Giulio P, Gregori D, Gavetti D, Ballali S, Bagnato S, Guidi G, Foltran F and Renga G. (2012) Managing peripheral venous catheters: an investigation on the efficacy of a strategy for the implementation of evidence-based guidelines, *Journal of Evaluation in Clinical Practice*, 18(2), pp. 414-419.

Abstract:
Research in Italy to develop a revised protocol in accordance with guidelines concerning the management of peripheral venous catheters (PVCs). Characteristics of types of catheter and a comparison of PVC management and signs of infection at the insertion site before and after new protocol introduction are described. [ORIGINAL – 21 references].

Subcutaneous infusions

No studies excluded on full text.

Appendix C: Manufacturers' submissions excluded as out of scope

Title	Author(s)	Year	Reason out of scope
Hypodermoclysis: a literature review to assist in clinical practice	Bruno VG	2013	Not nursing related
Flushing and locking of venous catheters: available evidence and evidence deficit	Goossens GA	2015	Not a research paper
Accepted but unacceptable: peripheral IV catheter failure	Helm RE et al.	2015	Not a research paper
A time and motion study of peripheral venous catheter flushing practice using manually prepared and prefilled flush syringes	Keogh S et al.	2014	Study of adherence to protocol
Risk of infection due to medical interventions via central venous catheters or implantable venous access port systems at the middle port of a three-way cock: luer lock cap vs. luer access split septum system (Q-Syte)	Pohl F et al.	2014	Condition specific
Fluid dispersal from safety cannulas: an in vitro comparative test	Rosenthal VD and Hughes G	2015	Not relevant to current review (generation of blood droplets during catheter withdrawal)
Registration of Blood Exposure accidents in the Netherlands by a nationally operating call center	Schneeberger PM et al.	2012	Not relevant to UK nursing
Needlestick injuries: causes, preventability and psychological impact	Wicker S et al.	2014	Not relevant to current review (psychological impact of needlestick injuries)
A comparison of the efficacy of 70% v/v isopropyl alcohol with either 0.5% w/v or 2% w/v chlorhexedine gluconate for skin preparation before harvest of the long saphenous vein used in coronary artery bypass grafting	Casey A et al.	2015	Not related to infusion therapy
Stage One: warning. Risk of death or severe harm due to inadvertent injection of skin preparation solution	Patient Safety Alert: NHS England	2015	Guideline
Strategies to prevent central line–associated bloodstream infections in acute care hospitals: 2014 update	The Society for Healthcare Epidemiology of America	2015	Guideline
The science and fundamentals of intraosseous vascular access	Vidacare Corporation	2013	Guideline
Retrospective comparative audit of two peripheral IV securement dressings	Jackson A	2012	Audit of two dressings

Appendix D: Quality appraisal of selected papers using in-house appraisal tool

Study	Is there a convincing rational for overall research strategy and how it was designed to meet aims/ research questions, including comprehensive review of previous research and justification for collecting new primary data?	Is there good discussion of the research design strengths and weaknesses of data sources?	Does the study describe locations and population(s) of interest and how and why chosen to allow comparisons to be made?	Detailed description of data and collection methods used, explaining any limitations and methods to maximise inclusion/limit bias?	Explicit and appropriate analytic procedure for processing raw data into results/themes that could be repeated with a simply methodology?	Study reports findings on all variables or concepts investigated and includes discussion/ mention of any negative cases and outliers and confounding variables?	Conclusions presented are supported by study findings and previous research and theory (where appropriate)?	Overall rating of quality
Lynch (2012)	No	No	Yes	No	No	No	No	LOW
Rupp et al. (2012)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Baker et al. (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Dailey et al. (2014)	Yes	Yes	No	Yes	Yes	No	Yes	MEDIUM
Dietrich (2014)	No	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Hambleton et al. (2014)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Humphries et al. (2012)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Jun et al. (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Levin et al. (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Lippi et al. (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Barr et al. (2012)	No	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Maneval and Clemence (2014)	Yes	Yes	No	Yes	Yes	Yes	Yes	HIGH
Mathers (2011)	Yes	No	No	No	Yes	Yes	Yes	MEDIUM
Macklin (2010)	Yes	No	No	No	No	No	Yes	LOW
Ajenjo et al. (2011)	No	Yes	Yes	Yes	Yes	Yes	No	LOW
Dixon and Carver (2010)	Yes	Yes	Yes	No	Yes	Yes	Yes	HIGH
Dumyati et al. (2014)	Yes	No	Yes	No	Yes	Yes	No	MEDIUM

Study	Is there a convincing rational for overall research strategy and how it was designed to meet aims/ research questions, including comprehensive review of previous research and justification for collecting new primary data?	Is there good discussion of the research design strengths and weaknesses of data sources?	Does the study describe locations and population(s) of interest and how and why chosen to allow comparisons to be made?	Detailed description of data and collection methods used, explaining any limitations and methods to maximise inclusion/limit bias?	Explicit and appropriate analytic procedure for processing raw data into results/themes that could be repeated with a simply methodology?	Study reports findings on all variables or concepts investigated and includes discussion/ mention of any negative cases and outliers and confounding variables?	Conclusions presented are supported by study findings and previous research and theory (where appropriate)?	Overall rating of quality
Guerin et al. (2010)	Yes	Yes	Yes	No	No	Yes	Yes	MEDIUM
Hsu et al. (2014)	Yes	Yes	No	No	Yes	Yes	Yes	MEDIUM
Jacob (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Klintworth et al. (2014)	No	No	Yes	No	Yes	No	No	LOW
Lopez (2011	No	No	No	No	Yes	No	Yes	LOW
Medina et al. (2014)	Yes	No	Yes	No	No	No	No	LOW
Munoz-Price et al. (2012)	Yes	No	Yes	No	Yes	No	Yes	MEDIUM
O'Connor et al. (2012)	Yes	No	Yes	No	Yes	Yes	No	MEDIUM
Pongruanporn et al. (2013)	Yes	No	No	No	Yes	Yes	Yes	MEDIUM
Royer (2010)	Yes	No	Yes	No	No	Yes	Yes	MEDIUM
Thom et al. (2014)	Yes	Yes	Yes	No	Yes	No	Yes	MEDIUM
Whited and Lowe (2013)	Yes	No	No	No	No	No	No	LOW
Fairholm et al. (2011)	Yes	No	No	No	Yes	Yes	Yes	MEDIUM
Luzzati et al. (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Madeo and Lowry (2011)	No	No	No	Yes	No	No	Yes	LOW
Rodriguez-Pardo et al. (2014	Yes	No	Yes	No	Yes	Yes	Yes	HIGH

Study	Is there a convincing rational for overall research strategy and how it was designed to meet aims/ research questions, including comprehensive review of previous research and justification for collecting new primary data?	Is there good discussion of the research design strengths and weaknesses of data sources?	Does the study describe locations and population(s) of interest and how and why chosen to allow comparisons to be made?	Detailed description of data and collection methods used, explaining any limitations and methods to maximise inclusion/limit bias?	Explicit and appropriate analytic procedure for processing raw data into results/themes that could be repeated with a simply methodology?	Study reports findings on all variables or concepts investigated and includes discussion/ mention of any negative cases and outliers and confounding variables?	Conclusions presented are supported by study findings and previous research and theory (where appropriate)?	Overall rating of quality
Cicolini et al. (2014)	Yes	Yes	Yes	No	Yes	Yes	No	MEDIUM
Mestre et al. (2013)	Yes	Yes	Yes	No	Yes	Yes	Yes	HIGH
Rickard et al. (2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Roszell and Jones (2010)	Yes	No	No	No	Yes	Yes	Yes	MEDIUM
Bloch et al.(2013)	No	No	No	No	No	Yes	Yes	LOW
Leidel et al. (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Garside et al. (2015)	Yes	No	Yes	No	No	Yes	Yes	MEDIUM
Alexandrou et al. (2011)	Yes	Yes	Yes	Yes	Yes	No	Yes	HIGH
Borolussi et al. (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Deusch et al. (2014)	Yes	Yes	No	No	No	No	Yes	LOW
Dumont et al. (2014)	No	No	Yes	No	No	No	No	LOW
Gorski et al. (2015)	Yes	Yes	Yes	Yes	No	Yes	Yes	HIGH
Easterlow et al. (2010)	Yes	No	No	No	No	No	No	LOW
Li et al. (2010)	Yes	No	No	Yes	Yes	Yes	Yes	MEDIUM
Lee et al. (2010)	No	No	No	Yes	Yes	Yes	No	LOW

Section 4: Patient perspectives of infusion therapy

Section 4 authors – Lynne Currie and Anda Bayliss

Executive summary

The research question underpinning the rapid evidence review was "What are the facilitators and barriers identified from examining and including the patient perspective in the delivery of a range of infusion therapies"?

The review included 22 articles; 12 were rated high quality, four medium quality, and six low quality. The articles included in the review were subjected to a thematic analysis using an a priori framework, the Warwick Patient Experiences Framework or WaPEF (Staniszewska et al., 2014). The themes are patient-as-active participant; responsiveness of services (individualised approach); lived experience; continuity of care and relationships; communication; information; and support.

A number of facilitators and barriers were extrapolated from the articles reviewed and included reported behaviours, situations, perceptions and other constructs. Some were identified as both facilitator and barrier, and how these were perceived depended on individual patients and situations.

The greatest number of findings were mapped against lived experience (20/22 studies: 12 of high quality; three of medium quality; and five of low quality), followed by responsiveness of service (14/22 studies; six of high quality; four of medium quality; and four of low quality), support (14/22 studies: 11 of high quality; and three of low quality), communication (12/22 studies; eight of high quality; one of medium quality; and three of low quality), information (10/22; studies; six of high quality; one of medium quality; and three of low quality) and patient participation (2/22 studies; two of high quality). Table 7 presents the mapping of the evidence against the WaPEF themes, along with study reference number, number of studies per theme and quality ratings.

No findings were mapped against the theme continuity of care and relationships (0/22 studies). However, there is overlap between the themes and some of the findings mapped against responsiveness of services and patient participation could equally be interpreted as being linked to continuity of care and relationships.

Overall, the size of the evidence is small but the majority of the studies reviewed have been rated as high or medium quality. The coverage of infusion therapy range was limited with the majority of the papers (12 out of 22) focusing on dialysis treatment with only one, for example, looking at peripherally inserted catheters.

There was not an equal distribution of the studies across all the seven themes either. The majority of the findings (from 20 out of the 22 studies) were mapped against the theme of lived experience, with no study finding mapped against the theme of continuity of care and relationships and only two under patient participation.

It is not clear from the studies reviewed what the impact of the patient experience is on adherence to, quality, effectiveness and safety of the infusion therapy. The focus of the studies was on patient and carer perceptions, beliefs and fears and there was only limited exploration of possible ways to improve and alleviate them and their success in achieving that. There appear to be links between the experience of the treatment (clinical and as a service) and psychological state and mental health, but the presence of an effect and its direction were not clear.

In functional or operational terms, any move towards delivering infusion therapy services closer to home has implications for resource planning and management and nursing workload management. While treatments delivered closer to home will result in reduced travelling time for patients, they may conversely lead to greater travelling time for community, district, practice and specialist and advanced nurse practitioners, given the associated need for increased regular home visits to support patients and their families.

Infusion therapies delivered to patients closer to home will require adequate numbers of community, district, primary care and specialist and advanced nurse practitioners. However, in order to increase the uptake rates of patients choosing home treatments like dialysis, continued investment in hospital-based staff will not diminish. The need for clinical leadership and wider staff support has been described by Combes et al. (2015)[5], who identify the need for strong clinical leaders including renal clinical leads, highly visible and effective individual champions for home dialysis and home therapy nursing teams.

Extending the role and scope of community, district, general practice and specialist and advanced nurse practitioners to meet increased demand for more services closer to home may also require greater investment in continual professional development and support for these nurses to improve their skills and knowledge in order to ensure they are practising competently and safely.

Meeting increased demand from patients requiring a range of infusion therapy treatments closer to home may also require an extension to currently available nurse-led clinics or an increase in their numbers. Extended nurse-led clinics could become hubs for patients, carers and relatives, providing them with education and training support as well as formal information support and networking opportunities. Nurse-led clinics could also be the 'go to' place where patients, carers and relatives can access a range of tailored, format-friendly, relevant and timely information.

In addition training programmes may be required for non-specialist staff working in hospitals since Combes et al. (2015)[5] comment that many staff reported a lack of confidence in talking to patients about home treatment and reported receiving no recent training about home dialysis. The lack of training was reflected in patients' statements about how they felt their questions about treatment options were not addressed satisfactorily and how hospital staff failed to portray the benefits of home dialysis, resulting in a missed opportunity to encourage patients to consider home dialysis.

Meeting the communication needs of patients, carers and families to improve dialogue and shared

decision-making as a result of the increased demand for the provision of infusion therapy treatments closer to home will require improved channels of communication. In addition to face-to-face and telephonic communication; examples of new or improved communication channels could include greater utilisation of video-link consultations and social media interactions

Delivering infusion therapy closer to home may also need multi-professional interventions as the evidence reports on the multi-faceted impact of disease, treatment and associated coping mechanisms across the various life domains appear to interact. However, it is worth noting that while nine of the studies were from the UK, only five were of high quality, and the majority focused on dialysis treatment. As such this may affect the applicability of the findings in a UK context, whilst also suggesting a need for further research.

Introduction

Traditionally, the delivery of infusion therapy has taken place in hospitals but changes in demand have meant an increased focus on different routes of delivery including the community and patients' homes (Pearson et al., 2015). In 2015, following a discussion with key stakeholders, a decision was taken to update the Royal College of Nursing's (RCN) *Standards for Infusion Therapy* published in 2010. There is a requirement to develop standards for the delivery of infusion therapy in different settings which acknowledge the impact on service provision, nursing workloads, and the impact on the patient's experience. In response, it was agreed that a rapid evidence review would be undertaken by the Research and Innovation (Evidence) Team that would consider the available research evidence on patients' perceptions of infusion therapy. The review would supplement the rapid evidence review of clinical evidence being undertaken by an external contractor and by the RCN internal team to support publication of the updated RCN *Standards for Infusion Therapy*.

Following an overview of potential models for assessing the patients perspective (Asadi-Lari et al., 2004; Staniszewska et al., 2014) that could be used to map the findings from the review the authors agreed that The Warwick Patient Experiences Framework (WaPEF): patient-based evidence in clinical guidelines (Staniszewska et al., 2014) offered a suitable framework for organising and mapping the review results. The seven themes identified in the WaPEF are: patient-as-active participant; responsiveness of services (an individualised approach); lived experience; continuity of care and relationships; communication; information; and support. The WaPEF was developed using a thematic qualitative overview that utilised a systematic review approach, and the framework has informed the structure and content of the NICE Patient Experiences Guidelines (NICE, 2012).

Review question

To support the RCN in producing evidence-informed practice standards on infusion therapy for nurses and other relevant health care professionals across the UK, a rapid evidence review was undertaken to answer the following question:

> What are the facilitators and barriers identified from examining and including the patient perspective in the delivery of a range of infusion therapies?

Methods

Search strategy

A search to locate references relating to the patient experience of infusion therapy was carried out during September and October 2015. Three databases were searched; the British Nursing Index (BNI); CINAHL; and MEDLINE using the inclusion criteria listed below (these were the same as those used in the clinical evidence review for the *Standards for Infusion Therapy*).

Inclusion criteria

Publication date:	From 2010 to present
Geographical scope:	UK and OECD countries
Age range:	18+
Language:	English language
Study type:	All

Exclusion criteria

Neonates, infants, children

Searches were trialled in early September in order to establish appropriate terms for the patient experience element of the search, and to reflect differences in database structure and vocabulary. The appendix of the *Warwick Patient Experiences Framework* (Staniszewska et al., 2014) was also checked for any supplementary search terms. In addition, the first author searched for grey literature using Google Scholar and checked the reference lists of early retrieved articles for further papers. However, the search of grey literature produced no additional references to those identified by the library searches.

It is worth noting that research stakeholders need to understand the ways in which the availability of resources (or lack of resources) both in terms of money and time will impact on the integrity of a rapid evidence review (Toye et al., 2014).

Search terms

The database searches were undertaken by information specialists working in the RCN Library. The search terms used to capture patient experiences within each of the databases are listed in Table 1. These were combined with infusion set terms (which were the same as the ones used in the main infusions standards review) to produce an overall picture of the patients' perspective of a range of infusion therapies.

Table 1: Search terms used across BNI, CINAHL and MEDLINE

British Nursing Index:	CINAHL:	MEDLINE:
Patient experience terms "patient needs" or "patient experience*" or "patient satisfaction" or su(patients: empowerment) or su(nurse patient relations) or su(consumer satisfaction) or su(patients: attitudes and perceptions) or "patient* preference*" or user* preference*" or "carer* preference*" or "patient* expectation*" or "user* expectation*" or "carer* expectation*"	Patient experience terms "patient needs" or "patient experience*" or "patient empowerment" or MM"Patient Attitudes" or MM"Patient Satisfaction" or MM"Consumer Satisfaction" or MM"Nurse-Patient Relations") or "patient* preference*" or user* preference*" or "carer* preference*" or "patient* expectation*" or "user* expectation*" or "carer* expectation*"	Patient experience terms "patient needs" or "patient experience*" or "patient attitudes" or MH"Patient Satisfaction" or MM"Consumer Behavior" or MM"Nurse-Patient Relations" or MH"Patient Participation" or "patient* preference*" or user* preference*" or "carer* preference*" or "patient* expectation*" or "user* expectation*" or "carer* expectation*"
Infusion therapy terms "infusion therap*" or su(intravenous therapy) or "infusion pump*" or "peripheral access" or "central access" or central venous" or midline* or picc* or "vascular access" or parenteral or subcutaneous*	Infusion therapy terms ("infusion therap*" or MH"Intravenous Therapy+" or "infusion pump*" or MH"Infusion Devices+" or MM"Peripherally Inserted Central Catheters" or MM"Catheterization,Peripheral Central Venous" or MH"Vascular Access Devices+" or MH"Catheterization,Central Venous+" or MH"Central Venous Catheters+" or MM"Catheter Care,Peripherally Inserted Central" or MH"Infusions,Parenteral+" or MH"Infusions,Subcutaneous+")	Infusion therapy terms ("infusion therap*" or "intravenous therap*" or MH"infusion pumps" or "peripheral access" or "central access" or midline* or "picc line* or "vascular access" or MH"Infusions,Parenteral")

In addition, each of the following five topics was also investigated using the patient experience sets:

- parenteral nutrition
- chemotherapy infusions (intrathecal and intravenous)
- insulin (sub-cutaneous)
- blood transfusions
- renal transfusions (dialysis).

The search, which combined (a) patient perspective terms with (b) the infusion therapy terms or each of the additional sets (for example, parenteral nutrition or chemotherapy), produced six lists of references on patient experiences for each database.

Sifting process

The first sift removed all duplicate records and records identified as falling out of scope (see Box 1) and not relevant. Based on a further reading of the abstracts, the second sift identified a further number of records that were not relevant based on the inclusion and exclusion criteria. In addition, a further number of records were identified as being unobtainable due to limits to the projects budget and timeframe (see Table 2). A total of 42 records were obtained as full-text articles, and following a full reading of all 42, 20 were identified as falling out-of-scope in the third sift. Details of the 20 papers identified as falling out of scope at the third sift can be found in Appendix 1. The final review includes 22 articles.

Box 1: Scope of the review

Only papers in English
Only papers exploring patient experiences in OECD counties
Only articles examining the patient perspective
Excluding opinion/policy articles

Table 2: Study selection process

First sift:
• Number of records identified 466
• Number of duplicates identified 22
• Number of records identified as not relevant 354
• Number of records identified as relevant 90
Second sift:
• Number of records identified as unobtainable 21
• Number of records identified as not relevant 27
• Number of records requested as full text 42
Third sift (at full-text):
• Number of records identified as out of scope 20
• Number of records included in review 22

Quality appraisal of the evidence

Each single study/article was subjected to quality appraisal by the first author and a random selection was appraised by a second reviewer. Scores from each reviewer were compared and there was consensus on appraisal scores. The CASP appraisal tool (Critical Skills Appraisal Programme, 2013) was used to appraise the quality of the qualitative papers and has ten criteria. An in-house critical appraisal tool, adapted from the EPPI Centre REPOSE Guidelines (Newman and Elbourne, 2005) was used to appraise the quantitative/mixed method papers and has seven criteria. It was agreed that each appraisal statement would be equally weighted and the rating scale for high, medium and low was agreed by the review team – see Table 3.

Of the 15 qualitative papers included, nine were rated as high quality[1,2,3,4,10,11,13,21,2]; two as medium quality[6,18]; and four as low quality[7,8,14,19]. Of these 15 qualitative papers, the majority reported on dialysis treatment. From the seven quantitative/mixed methods papers, three were rated as high quality[5,9,6]; two as medium quality[15,17]; and two as low quality[12,20] (see Table 4).

Appendices 2 and 3 at the close of this section provide detailed information on the systematic quality appraisal of the 22 papers included in the review.

Table 3: Agreed quality appraisal ratings

CASP criteria (qualitative papers)
10-8 criteria met or partially met = HIGH
7-5 criteria met or partially met = MEDIUM
4-0 criteria met or partially met = LOW
IN-HOUSE criteria (quantitative/mixed methods papers)
7-6 criteria met or partially met = HIGH
5-4 criteria met or partially met = MEDIUM
3-0 criteria met or partially met = LOW

Table 4: Quality of evidence

Papers included in the review (n=22):
15 qualitative research papers quality assured against CASP criteria tool:
• 9 HIGH
• 2 MEDIUM
• 4 LOW
Seven quantitative/mixed method papers quality assurance against an in-house quality appraisal tool:
• 3 HIGH
• 2 MEDIUM
• 2 LOW

Size and context of evidence

Of the 22 two papers included in the review, 12 addressed patients' perceptions around a range of dialysis treatments (haemodialysis, peritoneal/home) delivered across a range of settings (see Table 5). Nine studies were from the UK[2,5,7,8,13,14,16,19,22]; the remainder were from Canada[15,20]; Norway[1,6]: Sweden[4,10]; USA[17,21]; Australia[11]; Germany[12]; Netherlands[9]; New

Zealand[18]; and international[3]. Thirteen papers covered patients receiving treatment in hospital, and nine papers covered patients receiving treatment in the home or a community setting.

Table 5: Context of evidence

• 12 papers explored patients' perceptions of dialysis treatment (haemodialysis and peritoneal/home dialysis)[1,2,3,5,8,9,10,11,15,18,20,22]
• Two papers explored patients' perceptions of subcutaneous insulin therapy[7,17]
• Two papers explored patients' perceptions of blood transfusions[14,21]
• One paper explored patients' perceptions of peripherally inserted catheters[13]
• One paper explored patients' perceptions of implantable port systems[12]
• One paper explored carers' perceptions of chemotherapy[16]
• One paper explored carers' perceptions of home enteral feeding[4]
• One paper explored patients' perceptions of using medical technologies[6]
• One paper explored patients' perceptions of community IV therapy[19]

Table 6: Evidence table (data extraction)

No	Study (first author, year. title, publication)	Country of origin	Sample/ participants/ setting	Aim/purpose of Study	Method(s)	Key findings	Quality	Implications for practice/research
1	Aasen et al (2011) Perceptions of patient participation amongst elderly patients with end-stage renal disease in a dialysis unit, *Scandinavian Journal Caring Science*, 26, pp. 612-69.	Norway	11 elderly patients with end stage renal disease (ESRD) receiving dialysis treatment in hospital.	To explore how elderly patients with ESRD who are undergoing treatment with HD perceive patient participation in a dialysis unit.	Qualitative – interviews.	Two discourses were identified. The first and dominant discourse was called the health teams' power and dominance. Both environmental conditions and the teams practice exercise power and control over patients. Patients trusted the health care team but some felt powerless and were afraid of what might happen if they refused to follow instructions. Most patients wanted dialogue about the future, and after years of treatment patient identity seemed to be threatened. Some patients struggled to be involved in decision-making about 'dry weight', blood access and time of treatment when these factors threatened their well-being and the quality of their daily lives. Elderly patients' right to participant in their treatment did not seem to be well incorporated into the social practices of HD units.	High	Need to change the social practice in dialysis units from a paternalistic ideology to an ideology of participation which means health care professionals need to engage in more dialogue, share power, knowledge and intellectual endeavours (p.67)
2	Baillie (2014) Patient and family perspectives on peritoneal dialysis at home: findings from an ethnographic study, *Journal Clinical Nursing*, 24(1/2), pp. 222-234.	UK	16 patients receiving home dialysis treatment and nine relatives (n=25)	To explore patient and family perspectives on peritoneal dialysis (PD) at home.	Qualitative – interviews and observations.	Four themes identified: initiating PD; the constraints of PD due to the medicalization of the home and imposition of rigid timetables; the uncertainly of managing crises and inevitable deterioration; and seeking freedom through creativity and hope of a kidney transplant. The study highlights the culture of patients and their families living with PD.	High	Need for ongoing education from health care professionals' about how to prevent and identify infections. Equally important for further research on peritonitis in patients receiving peritoneal dialysis in the home (p.231).

No	Study (first author, year. title, publication)	Country of origin	Sample/ participants/ setting	Aim/purpose of Study	Method(s)	Key findings	Quality	Implications for practice/research
3	Bayhakki (2012) Lived experiences of patients on hemodialysis: a meta-synthesis, *Nephrology Journal*,39(4), pp. 295-303.	International	224 participants receiving dialysis treatment across ten studies.	To provide an overview of research analysing the qualitative aspects of the lived experiences of patients on haemodialysis and the implications of these for nursing practice.	Qualitative – meta-synthesis.	Four themes emerged; having a physical shackle in life, feeling mental and emotional distress, relying on a haemodialysis machine, and dealing with problems.	High	Nurses can enhance the roles of patients' significant others in supporting patients through making regular visits to the patients homes, making spiritual activities available and involving patients in appropriate social activities. Nurses should help patients develop their internal strategies and enhance their coping capacity. Nurses have a responsibility to improve their own knowledge and that of their patients' through providing adequate time, materials and health education programs. The individual and social aspects of patients" lives should be considered and understood by nurses and significant others (p.303).
4	Bjuresater (2011) Struggling in an inescapable life situation: being a close relative of a person dependent on home enteral feeding, *Journal Clinical Nursing*, 21(7-8), pp. 1051-59.	Sweden	12 close relatives of patients being treated with home enteral tube feeding (HETF).	To examine family carers' experiences of caring for a close relative at home requiring HETF.	Qualitative – interviews.	One core category emerged; struggling in an inescapable life situation and eight categories were identified. The situation led to involuntary changes in the lives of the close relatives, something they could do little about. Their lives had become completely upturned and restricted by the HETF. Togetherness and pleasure was lost and they felt lonely. Relatives faced a new role of being informal caregivers and they had to adjust their daily life accordingly. They felt forced to take on a heavy responsibility for which they lacked support. The close relatives struggled to manage and make the best of their new situation.	High	Nurses at all levels should collaborate with patients and relatives to enable appropriate support. One way to improve care further could be to extend nurse-led clinics to include close relatives (p.1057).

No	Study (first author, year. title, publication)	Country of origin	Sample/ participants/ setting	Aim/purpose of Study	Method(s)	Key findings	Quality	Implications for practice/research
5	Combes (2015) Taking hospital treatments home: a mixed methods case study looking at the barriers and success factors for home dialysis treatment and the influence of a target on uptake rates, *Implementation Science*, 10 (148): DOI 10.1186/s13012	UK	93 patients receiving dialysis across four hospitals.	Identifying barriers and success factors for home dialysis treatment and influence of a target on uptake rates.	Mixed methods.	Four main facilitators identified as: commissioners' target, liked to financial penalties; additional funding for specialist staff and equipment; committed, visible clinical champions and good systems for patient training and ongoing health care support at home. Three main barriers identified as lack of training for non-specialist staff, poorly development patient education and considerable unrecognised and unmet emotional and psychological patient needs.	High	More research needed to identify and evaluate ways of meeting patients' emotional and psychological needs. Research should focus on how these needs can be discussed during routine appointments with doctors and how specialist nurses can incorporate emotional support into discussions about treatment options (p.12-13).
6	Fex (2011) Health-illness transition among persons using advanced medical technology at home, *Scandinavian Journal Caring Sciences*, 25(2), pp. 253-261.	Norway	Ten chronically ill patients with respiratory or kidney disorders.	To elucidate meanings of health-illness transition experiences among adult patients using advanced medical technology at home.	Qualitative – interviews.	The health-illness transition was found to mean a learning process of accepting, managing, adjusting and improving daily life with technology, facilitated by realising the gain from technology at home. The healthy transition experience was characterised by human growth and becoming.	Medium	Further research needed on the meaning of the health-illness transition experience in relation to the use of advanced medical technology in the home (p.260).
7	Hayes (2011) A hermeneutic phenomenological study of why patients with type 1 diabetes mellitus choose to discontinue CSII, *Diabetes Nursing*, 8(1), pp. 12-16.	UK	Five adults with type 1 diabetes who chose to discontinue continuous subcutaneous insulin infusion (CSII).	To examine why people whose to discontinue CSII.	Qualitative – interviews.	Challenges of wearing the pump; lack of control over the pump, body and health; comparing expectations versus reality.	Low	More research needed to explore how patients can adjust to insulin pump therapy (p.15).

No	Study (first author, year. title, publication)	Country of origin	Sample/ participants/ setting	Aim/purpose of Study	Method(s)	Key findings	Quality	Implications for practice/research
8	Hope (2013) A patient perspective on the barriers to home dialysis, *Journal Renal Care*, 39 Suppl 308.	UK	One patient receiving dialysis treatment.	To explore one patient's perceptions of the barriers to home dialysis.	Longitudinal patient narrative approach.	There are significant barriers to all aspects of informed decision making around home therapies, but many are based on perception. Creating decision aids and education programmes may tackle such barriers.	Low	None reported.
9	Jansen (2010) Perceived autonomy and self-esteem in Dutch dialysis patients: the importance of illness and treatment perceptions, *Psychology & Health*, 25(6), pp.733-749.	Netherlands	166 patients with end stage renal disease (ESRD) receiving dialysis.	To explore the perceived autonomy, state self-esteem and labour participation in ESRD patients on dialysis.	Quantitative – survey.	Labour participation among dialysis patients was low, the average autonomy levels were only moderate, and the average self-esteem level was rather high. On the whole, positive illness and treatment perceptions were associated with high autonomy and self-esteem, but no with labour participation. Perceptions of personal control, less impact of the illness and treatment, and less concern were important predictors. Results indicate that dialysis patients' beliefs about their illness and treatment play an important role in their perceived autonomy and self-esteem. Stimulating positive (realistic) beliefs and alternative maladaptive beliefs might contribute to a treater sense of autonomy and self-esteem and to social participation in general. Interventions focusing on these beliefs may assist patients to adjust to ESRD.	High	Research on younger patients' is recommended to investigate the relationship between illness and treatment perceptions and labour participation. Longitudinal studies are needed to determine whether the positive representations of the illness and treatment are a cause or a result of greater feelings of patient autonomy and control (p. 745).

No	Study (first author, year. title, publication)	Country of origin	Sample/ participants/ setting	Aim/purpose of Study	Method(s)	Key findings	Quality	Implications for practice/research
10	Lindberg (2013) Dry weight from the haemodialysis patient perspective, *Renal Society Australasia Journal*, 9(2), pp.68-73.	Sweden	Ten haemodialysis (HD) patients.	To explore how patients on HD perceive the concept of dry weight and how they act in relation to it.	Qualitative – interviews.	Patients either regarded the concept as either an aid to securing treatment-related health, or as a reminder of the daily fluid allotment. Some did not report any specific perception. Many used self-care strategies to control fluid balance, transferring responsibility to the HD team, and managing the physical consequences or social and psychological concerns.	High	Patient misunderstandings regarding the significance of the dry weight concept have to be addressed by the dialysis team in order to successfully develop self-care strategies for dealing with the consequences of end stage kidney disease. Prospective trials need to be developed to evaluate the education effects of tailoring fluid management education to patients' perceptions of the dry weight concept (p.72)
11	Monaro (2014) A 'lost life': coming to terms with haemodialysis, *Journal Clinical Nursing*, 23(21/22), pp.3262-3273.	Australia	11 patients with end stage kidney disease (ESKD) receiving dialysis and 5 family carers (n=16).	To describe the essence of the lived experience of patients and families in early phase of long-term dialysis therapy.	Qualitative – interviews.	Essence of early diagnosis experience was a 'lost life', participants overwhelmed by shock and grief. Reported a loss of self, loss of spontaneity and personal freedom, loss of social connectedness.	High	A greater focus on preparation for the possibility of dialysis and frameworks of care that support patient adjustment to their new way of life are of vital importance. Family presence during haemodialysis and support groups for patients' and their families should be actively facilitated (p.3270).
12	Nagel (2011) Satisfaction and quality of life; a survey-based assessment of patients with a totally implantable venous port system, *European Journal Cancer Care*, 21(2), pp.197-204.	Germany	42 chemotherapy patients with a totally implantable central venous port system.	To evaluate cancer patients' satisfaction with 1 type of totally implantable central venous port system and its impact on day-to-day life.	Quantitative – survey.	The impact of the system on daily life was widely perceived not to be negative. The physical component and the mental component scores were 35.5 and 42.53 respectively. Multiple stepwise regression showed that the cosmetic result was a predictor of overall satisfaction. Overall it was found that the cosmetic result of the implantation procedure was a predictor of satisfaction and quality of life and should thus not be underestimated.	Low	None reported.

No	Study (first author, year. title, publication)	Country of origin	Sample/ participants/ setting	Aim/purpose of Study	Method(s)	Key findings	Quality	Implications for practice/research
13	Nicholson (2013) Patients' experiences of the PICC insertion procedure, *British Journal Nursing*, 22(14), pp.S16-23.	UK	15 patients electing to have peripherally inserted central catheter (PICC) insertion for their chemotherapy treatment. Chemotherapy day unit.	To interview patients who had undergone recent PICC insertion to identify their experiences.	Qualitative – interviews.	Five themes emerged: the context of cancer; expectations; levels of pain and anxiety; coping strategies; and providing explanation. Need for further research.	High	It is recommended that the same study is performed with a group of non-oncology patients, which would focus on the PICC insertion experience outside the context of cancer. Additional research could also examine whether it is possible to further reduce patient anxiety associated with fear of the unknown (p.S22).
14	Orme (2013) The experiences of patients undergoing blood transfusion in a day hospice, *International Journal Palliative Nursing*, 19(4), pp.171-176.	UK	Ten patients receiving blood transfusions. Hospice.	To explore patients' views on living with anaemia and under-going blood transfusions in a day hospice.	Qualitative – interviews.	Tiredness was the most common symptom of anaemia. Participants liked attending the day hospice instead of hospital for their transfusions owing to differences in transport, parking, waiting time, and space to ask questions. The majority had no concerns about hospice transfusion and would be happy to return for further treatment.	Low	Larger prospective study is needed to elucidate whether the disease journey for haematology patients would be altered if there were to have more contact with hospice through repeated blood transfusions (p.176).
15	Quinan (2011) A three-step approach to conversion of prevalent catheter-dependent hemodialysis patients to arteriovenous access, *CANNT Journal*, 21(1), pp.22-33.	Canada	53 patients receiving haemodialysis suitable for conversion from a Central Venous Catheter (CVC) to arteriovenous fistulas (AVF) or arteriovenous grants (AVG). Canadian hospital setting.	To convert 50% of suitable patients to AVFs or AVGs.	A case-crossover evaluation of the efficacy of a three-step conversion strategy.	Long-term CVC use and the unwillingness of medically suitable patients to convert to more optimal forms of vascular access are linked problems with potentially grave consequences. Need to develop a better understanding of the patients' perspective and possible psychological factors affecting patients' decisions in order reduce CVC usage.	Medium	Recommendations for further research examining psychological factors affecting patients' resistance to conversion and whether nurses could play a more active role; implementing strategies aimed at reducing cannulation-related complications' changing the Canadian CVC culture to promote AV access for all suitable patients; RCT studies to assess effectiveness of written materials and teaching methods (p.30).

No	Study (first author, year. title, publication)	Country of origin	Sample/ participants/ setting	Aim/purpose of Study	Method(s)	Key findings	Quality	Implications for practice/research
16	Ream (2013) Informal carers' experiences and needs when supporting patients through chemotherapy: a mixed methods study, *European Journal Cancer Care*, 22(6), pp.797-806.	UK	59 carers supporting patients having chemotherapy (48 returned questionnaire). 13 carers interviewed.	To explore carers' needs when supporting patients through chemotherapy.	Mixed methods approach.	Two-thirds of carers felt their information needs were meet, whilst a third of carers felt unprepared to deal with particular symptoms. Many carers had unmet needs regarding financial support and their own needs as carers. Many carers felt unable to assertive when they were unsupported, and they felt their roles went unrecognised by health care professionals.	High	There is a need for interventions to prepare and support carers and legitimise their informal care –giver role. Longitudinal studies are needed to explore the dynamics of the informal carer experience and determine factors that promote and inhibit confidence and competence to support someone through chemotherapy. Need for surveys to identify predictors and unmet needs (p.805).
17	Rosenkoetter (2013) CSII and MDII for intensive diabetes management: Impact perceptions of older adult patients and their significant others, *Geriatric Nursing*, 34(6), pp.469-476.	USA	20 diabetic patients receiving multiple daily insulin injections (MDII); 20 diabetic patients receiving continuous subcutaneous insulin injection (CSII) (n-40).	To investigate impacts of MDII and CSII on disease management and patient lifestyle by patients and significant others (SOs).	Quantitative – survey.	Whites reported greater satisfaction with CSII and non-Whites with MDII; both reported increased independence. CSII scored significantly higher than MDII. Age did not reduce positive impacts. CSII enhanced independence of SOs but 38.6% of SOs did not know how to suspend CSII for hypoglycaemia; 47.3% of patients believed SOs would not know.	Medium	Significant others should be involved in diabetic teaching to learn about basic pump controls and the risks of insulin use (p.475).
18	Shih (2011) The impact of dialysis on rurally based Maori and their Whanau families, *Nursing Praxis in New Zealand*, 27(2), pp. 4-15.	New Zealand	Seven Maori patients receiving dialysis as outpatients.	To explore the impact that dialysis has on Maori and their families.	Qualitative – interviews.	Four themes were identified: facing their fear; stress from having haemodialysis; learning, adjusting and changing their attitude; and individual needs. Highlights requirement for early referral and effective education to promote self-management,	Medium	Recommendations include the need for early referral and effective education to promote self-management for patients receiving dialysis (p.4).

No	Study (first author, year. title, publication)	Country of origin	Sample/ participants/ setting	Aim/purpose of Study	Method(s)	Key findings	Quality	Implications for practice/research
19	Stephens (2013) Patients' experiences of community IV therapy, *British Journal Nursing*, 22(19), S24-29.	UK	Eight patients receiving intravenous (IV) therapy in the community	To explore patients' experiences of receiving community intravenous therapy compared with traditional inpatient hospital care.	Qualitative – interviews.	Five themes identified: finances, travelling, hospital admission, being at home and safety	Low	None reported.
20	Visaya (2010) Haemodialysis patients' perspectives of home haemodialysis and self-care, *CANNT Journal*, 2010 Apr-Jun; 20 (2), pp.23-28.	Canada	49 patients with end stage kidney disease (ESKD) attending outpatient haemodialysis unit.	To assess in-centre haemodialysis patients' perceptions of home dialysis and their self-care ability.	Quantitative – cross sectional descriptive study.	26 patients reported positive perceptions, but only eight of these would be considered suitable for home dialysis. Only the domains of communication and social support were found to be significantly related to patients; perceptions of home dialysis.	Low	Research needed to identify why patients may refuse to take part in self-care in relation to home dialysis treatment (p.27).
21	Weiss (2011) Blood transfusion: the patient's experience, *American Journal of Nursing*, 111(9), pp.24-30	USA	21 patients receiving blood transfusion in a clinic.	To identify how well patients understand the role of blood transfusion in their treatment and whether it causes them discomfort.	Qualitative – interviews.	Four themes emerged: paternalism and decision-making'; patients' knowledge; blood safety and administration' and the nurse's role.	High	Surveying nurses to identify their needs for further education about blood transfusion. Research exploring the patient's awareness of being typed for blood transfusion and the impact of the reason for a blood transfusion on the patient's experience. More research exploring shared decision-making and cultural attitudes. Duplication of this study with other routine practices would provide a cross section of how clinicians assess patients' knowledge of and comfort with a procedure and the nurse's contribution to the patient experience (p.30).

No	Study (first author, year. title, publication)	Country of origin	Sample/ participants/ setting	Aim/purpose of Study	Method(s)	Key findings	Quality	Implications for practice/research
22	Winterbottom (2012) Choosing dialysis modality: decision making in a chronic illness context, *Health Expectations*, 17(5), pp.710-723.	UK	20 patients with chronic kidney disease (CKD) attending a low clearance outpatient clinic.	To describe patients' decision-making about dialysis and how their experience of CKD is associated with treatment choice.	Qualitative – interviews.	Patients described the challenges of living with CKD, and described being given lots of information about treatment options in different formats. They did not distinguish between different types of dialysis or have in-depth knowledge about options. They did not talk of dialysis options as a choice, but rather as a treatment they were going to have.	High	A more proactive approach is required to enable patients' to engage fully with the dialysis treatment options (p.710).

Findings

The full study characteristics are reported in Table 6 which includes research aims, design, sample, key findings and implications for practice and/or research, as well as the quality rating given to each individual paper.

This review is described as a hybrid of a narrative-thematic analysis: a narrative analysis selects, records and organises the evidence to produce an account, whereas a thematic analysis attempts to identify recurrent or common themes found in the literature and to summarise the findings across all the studies reviewed under thematic headings (Dixon-Woods et al., 2005).

While both narrative analysis and thematic analysis involve an interpretation, the authors applied the thematic headings to the findings using an a priori framework, the *Warwick Patient Experiences Framework WaPEF* (Staniszewska et al., 2014) (see Table 7). The themes are: patient-as-active participant; responsiveness of services (individualised approach); lived experience; continuity of care and relationships; communication; information; and support (see Appendix 4).

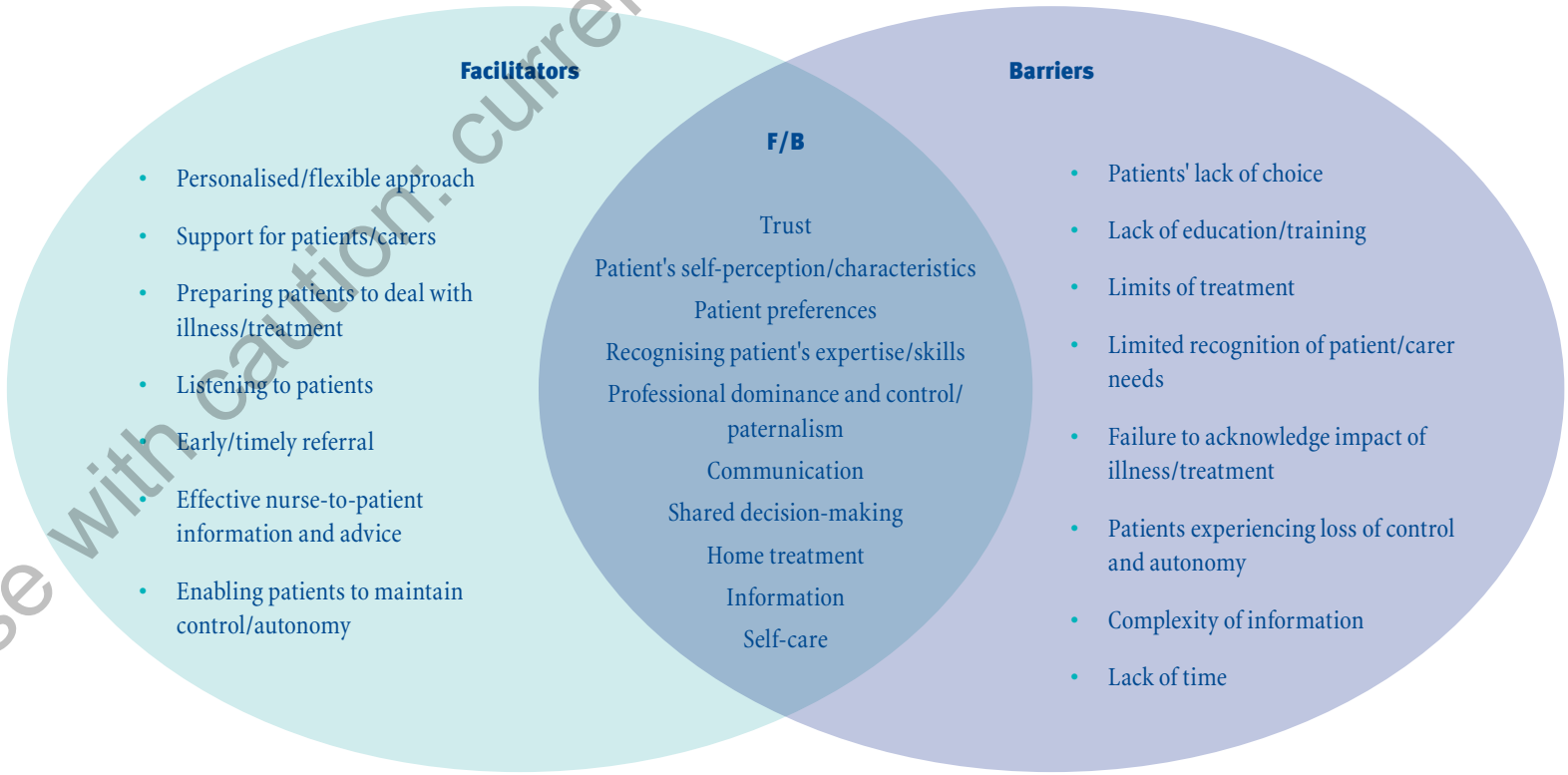
Facilitators and barriers

The research question underpinning the review was to identify facilitators and barriers in the delivery of infusion therapy interventions. Figure 1 presents the results of an analysis looking across all included studies, irrespective of quality or setting, that attempted to identify reported behaviours, situations, perceptions and other constructs that could be conceptualised as barriers or facilitators to the delivery of therapies. These constructs were reported by the participants, identified by the original studies' authors or extrapolated by this review's authors. Findings appearing in the centre oval in Figure 1 have been identified as both facilitator and barrier; how they were perceived depended on individual patients and situations.

Whether patients themselves identify something as a facilitator or a barrier (not necessarily using those words) may depend of their values and their individual characteristics. As such, what may be seen as a facilitator by one patient may be viewed as a barrier by another (Harvey et al., 2015). For patients undergoing a particular type of infusion therapy the concept of self-management may be important for them and as a result they may actively seek additional knowledge and information about their condition and its treatment through communication and shared decision-making with health care professionals. For such patients any perceived shortcomings in the provision of effective communication and information may be viewed as problematic or a barrier. However, for those patients who prefer to have their care and treatment managed by health care professionals the absence of information and communication may be viewed as less problematic.

The identification of facilitators and barriers can be viewed as being pluralistic or having opposing

Figure 1: Facilitators and barriers



meanings, and may also be influenced by context (Harvey et al., 2015). A patient who identifies family support as a facilitator may do so because they want to remain close to the people they care about. However, for another patient family support may be viewed as a barrier because it makes them feel dependant on, or controlled by other people.

In a systematic review of shared decision-making (Joseph-Williams et al., 2013) the authors argue that patient-reported facilitators and barriers relate to the way the health care system is organised and to what happens during the patient-professional consultation process. Patient-reported facilitators and barriers can be seen at the patient, professional and organisational level, and the authors suggest that they can be addressed by attitudinal changes at the patient and the professional level and through organisation change.

Thematic analysis

The process of thematic analysis involved going through the studies' text and identifying statements and passages that could be classified under any of the seven WaPEF themes. The greatest number of findings were mapped against lived experience (20/22 studies: 12 of high quality; three of medium quality; and five of low quality), followed by responsiveness of service (14/22 studies; six of high quality; four of medium quality; and four of low quality), support (14/22 studies: 11 of high quality; and three of low quality), communication (12/22 studies; eight of high quality; one of medium quality; and three of low quality), information (10/22; studies; six of high quality; one of medium quality; and three of low quality) and patient participation (2/22 studies; two of high quality).

Appendix 5 presents the mapping of the evidence against the WaPEF themes, along with study reference number, number of studies per theme and quality ratings.

No findings were mapped against the theme continuity of care and relationships. However, there is overlap between the themes and some of the findings mapped against responsiveness of services and patient participation could equally be interpreted as being linked to continuity of care and relationships.

While the thematic findings are summarised in the following section, please note that the full exploration of each theme and sub-theme together with information on volume, quality, direct references to the source studies and direct quotes from study participants, can be found in Appendix 6.

Theme 1: Lived experience

Key elements under this theme include experiences, preferences, living a restricted life, dependency and loss of control and freedom, and self-perceptions and characteristics. There are overlaps between these elements of the patients' lived experiences with the WaPEF themes responsiveness of services, patient participation and communication.

Experiences

A large number of studies report patients' experience in terms of how they felt about their need for infusion therapy, and in particular dialysis treatment. Patients expressed a range of feelings that can be viewed along a continuum ranging from a complete loss of control to taking control. The words used by patients include fear, anger, depression, anxiety, trauma, hopelessness, incapacitation, isolation, guilt, denial, powerlessness, shock, grief, and loss of control. However, they also spoke of acceptance, hope, adjustment, staying positive, reaching an understanding about their altered life, and taking control of their situation.

Feelings of shock and grief were primarily experienced by patients requiring dialysis treatment. These were expressed in terms of treatment and in relation to coming to terms with knowing you have a life-limiting disease, where any hope of living a normal life would only be realised through a kidney transplant.

Preferences

Patients' reported preferences are identified as both facilitator and barrier as they do sometimes appear to conflict with professionals' preferences. While patients' reported a preference for a catheter over the fistula, they reported not being given a choice because professionals favoured the fistula, which was associated with fewer infections and better dialysis. Patients, however, preferred the catheter because it offered a better quality of life.

Differences in preferences were evidenced in a study reporting patient's unwillingness to convert to arteriovenous grafts (AVG) or arteriovenous fistulas (AVF), even after being informed that the former type of treatment is more effective than the central venous catheter (CVC) route. Patients' refusal to convert from CVC to AVF/AVG could be viewed as a barrier from a professional point of view because it impacts on the delivery of what is described by the researchers as a more optimal form of vascular access. However, from the patient's viewpoint the decision to remain with a CVC arose primarily from concerns about needles, pain and the appearance of a fistula. Other studies exploring patients' decision-making about whether to have haemodialysis in hospital or peritoneal dialysis in the home cited similar concerns with needles and fistulas.

The reasons why some patients prefer home treatment and some do not appears multi-factorial, and home treatment is identified as both a facilitator and a barrier. It is a facilitator because it means patients do not have to have a fistula; it allows the opportunity to carry on working, it means no admission to hospital, no travelling for treatment, and it offers patients greater control over their lives. It was seen as a barrier because patients' described their anxieties around the threat of peritonitis[2], and the medicalisation of the home. The threat of peritonitis was described as the major cause of home dialysis failure, whilst the medicalisation of the home was described altering the patients' living space.

Home-based care often results in increased responsibilities for patients, carers and families and clinicians need to make this known to patients when discussing treatment options. Patients

reported a preference for home care because it offered them a greater sense of control and autonomy; however, it also involves substantial daily work for patients, even though they were often modest about their abilities to manage self-care in the home. Barriers to home dialysis were identified as requiring a significant amount of varied medical paraphernalia, space in the home, ordering, installation of dialysis machines, lack of training of non-specialist staff, and limited professional recognition of patients' emotional and psychological needs.

Studies exploring patient experiences of other infusion therapies in the home or near to home reveal how patients expressed preferences for blood transfusion therapy, and community intravenous therapy. Patients receiving blood transfusion in a hospice setting identified advantages as less travelling and waiting time, better parking, more time to talk, and not having to rely on public transport. Patients prefer receiving intravenous therapy in the community cite similar benefits as well as not having to be admitted to hospital, not at risk of hospital acquired infection, needing less time off work, being able to sleep in their own bed, and eat their own food.

Differences in preferences reveal how professionals appear to emphasise a need to meet patients' clinical needs, whereas patients appear to prefer treatment options that are a better fit with their personal needs and lifestyle, and which allow them greater autonomy and control. In an expert patient narrative, Hope argues a need for decisions about different treatment options that focus more on patient's lifestyle and quality of life, and not just clinical need.

Living a restricted life

Patients receiving dialysis treatment reported perceptions of how their illness and treatment resulted in restrictions in both their personal and social life. Requiring dialysis, whether in hospital, or at home, meant patients were often not able to travel to go on holiday and were unable to participate in paid employment.

Patients spoke of how a diagnosis of kidney disease requiring dialysis treatment resulted in losing their home, leading them to experience further loss of freedom and further limitations placed on their income. Patients also worried about the impact their illness and treatment had on families and friends, with both patients and their carers reporting how illness and treatment can have a negative impact on their relationships, not least a loss of hope.

Dependency, loss of freedom and control

Patients experienced a loss of freedom primarily because they felt more dependent on health professionals, close family members and, for those requiring dialysis, on the dialysis machine. This has been described as experiencing a lost life. Some researchers argue that the dialysis machine cannot be separated from the patient's life and patients' reported both positive and negative associations with the dialysis machine.

Patients' self-perceptions and characteristics

Some patient reports indicate the potential way in which their self-perceptions and characteristics may impact on their experiences. In sharing their experiences of dialysis elderly patients often referred to themselves in disparaging terms, reporting how they felt imprisoned, and speaking of how they both trusted and feared professionals. This combination of trust and fear can create passiveness and become an obstacle to dialogue and shared decision-making, leading to feelings of powerlessness and objectification, which may be further exacerbated by the paternalistic culture of the dialysis unit.

Theme 2: Support

The key elements under this theme include support and networking provision for patients and carers, the role of nursing, and support for shared decision-making. There are overlaps with this theme and the themes of lived experience, responsiveness of services, communication and information.

Support and networking provision for patients, carers and staff

Patients choosing home dialysis require support on several levels: help making the decision about whether or not to choose home dialysis; should they opt for home dialysis they will then require further support and training to use the dialysis machine and ensure they are competent to self-care at home. In addition, patients require on-going technical support once on home dialysis as well as emotional and psychological support to help them adjust to end stage kidney failure. While patients reported the availability of technical support and training on the machine, they did report shortcomings in the provision of emotional and psychological support, which was identified as critical.

The importance of practical, emotional and psychological support was highlighted in a study of carers who looked after patients receiving home enteral tube feeding. Carers reporting struggling with loneliness, a loss of togetherness and closeness, and having to endure a new life situation without any support for, or recognition of, their caring role.

Carers identified a considerable need for support from the health care system, reporting how they would benefit from a range of psychological, emotional and instructional support and counselling. This research highlights how informal caregivers need targeted interventions to prepare and support them and legitimise their caring role, and also reveals that all such interventions should be co-designed with informal carers.

The losses expressed by patients coming to terms with haemodialysis signal a need for increased psychological support during the early stages of dialysis because it can help patients develop coping strategies. However, patient and carer support networks were not visible to many patients even though such networks would be beneficial both before and after dialysis. In addition, many patients reported a desire to have their relatives present in the early stages of haemodialysis since this would create a perception of immediate support.

A study exploring the patient perspective on community intravenous therapy (CIVT) suggests

that CIVT provides a potentially unique opportunity for district nurses to increase their skills in an area that has long been the domain of the acute sector. The study also identified a need for the provision of support and training for district nurses focusing on the theoretical and the practical aspects of intravenous drug administration.

The role of nursing

Research has identified the key importance of ensuring that patients receiving dialysis live as full a life as possible, and has identified nurses as playing a role in supporting patients through exhibiting a clear understanding of their emotional, psychological and social needs. In order to do this, nurses have a responsibility to improve their own knowledge, and that of their patients, through the provision of adequate time, materials and health education programmes. In addition, nurses need to understand patient's limitations and problems and should consider these when planning and providing nursing care for haemodialysis patients.

A further role for nursing has been identified as the development or extension of nurse-led clinics. A nurse-led clinic can be defined as any clinic that is run or managed by registered nurses. Nurse-led clinics are identified as being useful for groups of patients in identifying problems early and finding interventions that prevent problems from becoming too big. Nurse-led clinics could also facilitate greater involvement of close relatives and the provision of support and counselling.

Research has identified the role of nursing in supporting patients on dialysis in particular as multi-faceted. In addition to the provision of education and health promotion, nurses also need to recognise the ethnicity of patients, their life and the social context when considering both the short and long term management of dialysis.

In a study exploring patient experiences of blood transfusion, nurses were viewed as supportive, knowledgeable, attentive and reassuring. Patients reported that nurses were helpful and they felt reassured by the way the nurse adhered to procedures whilst also providing them with support, education and information about safety monitoring

Support for shared decision-making

Some patient commentators argued that genuine shared decision-making is only possible when patients' needs and quality of life are at the heart of discussions with professionals about self-care. The support needed to move from clinical decision-making to shared decision-making includes a requirement for peer support, web-based personal digital assistants (PDA) and 15-minute clinical consultations.

Theme 3: Responsiveness of services

Key elements under this theme include education and training for patients, carers and staff, unmet patient needs and the role of nursing. There are some overlaps between this theme and communication, information and support.

Education, training, and preparing patients, carers and staff

Training and support systems for patients in receipt of home dialysis treatment was identified as a facilitator, while a key barrier was identified as a lack of training for non-specialist staff. Patients were identified as being fulsome in their praise for the training and preparation they received prior to home dialysis. They were positive about the support they received via telephone or through home visits and outpatient

A study exploring the patients' perceptions of dry weight identified a need for the provision of patient education on fluid management. This was seen as important because some patients did not appear to pay attention to dry weight, or they misunderstood its significance in terms of fluid control and self-care strategies.

A study exploring patients with end stage kidney disease reported how they and their families required significant preparation in order to understand the considerable emotional and physical challenges associated with a treatment regime that is invasive, restrictive and painful. A survey exploring chemotherapy patients' satisfaction with a totally implantable venous port system reported that most patients were satisfied with all aspects of the port system other than the cosmetic result. This may point to a similarity in views already reported in terms of patient preference and the impact that treatment has on a patient's quality of life.

A cross-over study exploring the reasons why patients fail to covert from catheter-dependent dialysis to arteriovenous access highlights patient concerns about the impact of treatment and how it influences their choices. Even though arteriovenous access is identified as the most optimal form of vascular access, patients were unenthusiastic about switching from the catheter.

A survey investigating carers' needs and experiences when caring for patients receiving chemotherapy at home reported that one-third of carers felt unprepared for dealing with their carer role. Carers reported a lack of information, or being given inadequate or inappropriate information, together with limited opportunities to speak to health care professionals. There appears to be a need for a range of interventions to prepare and support carers and to recognise and legitimise their caring role. Such interventions could include nurse-led tailored support programmes to address informal carers' information, emotional, social and practical needs.

A study investigating the impact of dialysis on rural Maori patients in New Zealand recommends the need for early referral and effective education provision in order to promote self-management, which in turn will influence quality of life and lead to more cost effective health care.

Unmet patient needs

In addition to the potential conflict existing between patient preferences, which were focused on issues surrounding personal needs and quality of life, and those of professionals, which were focused primarily on meeting patient clinical

needs, a study exploring home dialysis identified a key barrier as the considerable unmet emotional and psychological patient needs, which were described as significant and striking. Over one-third of patients needing dialysis found it scary and traumatic, which made it very difficult for them to adjust emotionally and psychologically. This same study also reports how there was almost a complete absence of service responses to this kind of patient distress, where none of the hospitals participating in the study had adapted their pre-dialysis pathways or their training processes to deal with it. Neither had the hospitals put any support mechanisms in place other than a referral to a psychiatrist or a psychologist for depression. This was in direct contrast to what patients wanted, which was less focus on the medical aspects of their illness, and the provision of more time to talk and be listened to.

The role of nursing

A study exploring patient and family perspectives on home dialysis reported that patients had to learn a range of skills for managing their dialysis, and how specialist nursing services provided a structured education programme, either in the home or the hospital. Patients credited the nursing staff for their teaching expertise.

Patients receiving intravenous therapy at home reported appreciating and valuing the work of the district nursing team in delivering treatments they found to be cathartic rather than just perfunctory. However, patients also flagged up some issues they had in relation to safety, not least the lack of explanations about their care and treatment at home, which made them feel apprehensive and frustrated. They reported some anxiety about the district nurses' ability to administer the IV treatment safely, expressing concerns over hand hygiene and aseptic technique. They also reported inconsistencies about the way the treatment was administered in the hospital and in the home, specifically in the way IV antibiotic was administered as a bolus in hospital and an infusion in the community. Some patients expressed an opinion there were inconsistencies in the training of district nurses in the community, which made district nurses feel less confident.

Theme 4: Communication

Key elements include one-way communication, lack of choice regarding treatment options, time, the role of the nurse, and patient's decision-making processes. There is overlap between this theme and the themes of responsiveness of services, support, information and patient participation.

One-way communication

In a study by Aasen et al. (2012) the authors argue that patients' use of metaphors like "jail" to describe the unit, "guardian" to describe the nurse, and "furniture" to describe themselves depicts a context in which professional dominance and control makes one-way communication common practice. The way the patient used the word "we" instead of "I" demonstrates how patients distance themselves from professional dominance and control. They also suggest that a patient's struggle to be included in shared decision-making was challenging because they had to argue against the professionals view of what was the best treatment.

The study by Shih et al. (2011) reports on how patients, on hearing they needed dialysis, talked of facing their fear whilst also intimating that the way the news was delivered did not provide them with much opportunity to ask questions. However, research exploring patients' experiences of peripheral intravenous central catheter therapy highlighted how one-way communication can be seen as a facilitator because it allows patients to withdraw from the decision-making process as a coping strategy for dealing with their treatment.

Lack of patient choice regarding treatment options

Patients undergoing treatment for end stage kidney disease need considerable preparation for haemodialysis and Monaro et al. (2014) argue that decisions about dialysis treatment options must be a collaborative process between patients, relatives and clinicians. However, many patients reported a lack of treatment options which has been linked to contraindications, physicians' preferences and resource constraint. These all serve to create additional barriers to treatment choice and issues related to home versus hospital treatments.

Weiss and Tolich (2011) argued that whilst alternatives are addressed on the blood transfusion form, when patients were asked about what alternatives they had been offered most reported none were offered. Baillie and Lankshear (2015) report that patients rejecting hospital dialysis treatment did so because they felt home dialysis treatment offered them greater control and autonomy. However, there are significant challenges in delivering home treatments, as discussed above, and it is important that the implications of all the different treatment options available are discussed with patients, carers and relatives.

Patients participating in a study exploring choice of treatment perceived decisions about options as easy; the difficult choice lay in deciding whether or not to have dialysis treatment. This contrasts with the view of professionals, who see the decision as making a choice between different types of dialysis; where information is the key in helping patients understand their kidney disease and treatment options.

Time

The majority of patients reporting their experiences of receiving blood transfusion in a hospice setting spoke of how there was more time for them at the hospice. While they believed the staff working in a hospital setting were very caring, they reported that these professionals had less time to talk than those nurses working in a hospice setting. Conversely, patients participating in a study exploring blood transfusion in a hospital setting reported how discussions were constrained because doctors were too busy to talk to them about the risks and benefits of blood transfusion. Patients undergoing home dialysis reported a lack of time as a barrier in having their needs met and they wanted staff to talk to them about the wider impact of dialysis on their lives, and they wanted to staff to listen to what they had to say.

The role of nursing

There was a recognition by patients that a positive style of communication from the nurse made them

feel more comfortable and calm. When nurses provided clear, concise explanations patients reported feeling reduced levels of anxiety about the procedures they were undergoing. Effective nurse communicators were able to reassure patients throughout the process whilst explaining the risks and benefits, and simultaneously settling the patient down.

Patients undergoing blood transfusion said that nurses, more than other clinicians, advised them about the benefits of transfusion, and they felt nurses were attentive and supportive during the procedure. Nurses also provided patients with options regarding treatments, and while it was reported that it was unclear whether this was used as a technique by the nurse to get the patient to have the transfusion, nonetheless, the nurse did act as both educator and adviser and patients did appreciate being invited into the decision-making process.

Patient decision-making processes

Research has also shown how patients and professionals appear to hold alternative views on how patients make treatment decisions. Staff appear to describe a rational weighting of available options that is based on available information, whereas patients described a more personalised approach in terms of how they thought about their own lives and how different options might work for them. Some patients described a gradual process of decision-making and spoke of only becoming interested in home dialysis later on in the trajectory of their illness.

Theme 5: Information

Key elements include the provision of timely and relevant information, complexity of information, seeing other patients as a source of information, and the nurse's role. There is overlap with this theme and the themes of communication, responsiveness of services, support and patient participation.

Timely and relevant information

While some patients reported satisfaction with the information they received, some described information overload, some wanted relevant, timely, practical information, and some reported a lack of information. Carers looking after patients receiving home enteral tube feeding reported a lack of information from the health care system about what was expected of them in their role as informal caregivers.

Weiss and Tolich (2011) argue that it is common practice for patients receiving blood transfusion to get written information about the risks and the benefits. One patient said they got the information but were too ill to read it, whilst others said they were shocked to hear they needed a transfusion, and only realised when the nurse came in holding a bag of blood in one hand and a consent form in the other.

In terms of the information needs of patients making a choice between treatment options, which often happened over a protracted period of time, Winterbottom et al. (2012) argue that patients are often exposed to biased information and they suggest this can be overcome through the provision of decision aids.

Complexity of information

According to Combes et al. (2015) patients found choice difficult given the range of treatment options and the complexity of information. Some patients reported information overload, and others acknowledged that whilst information was important its application to their lives was more important.

Other patients as a source of information

Patients talked of other patients as a source of information about the specifics of dialysis. They were particularly interested in their skills in carrying out the dialysis, how they were able to integrate the treatment into their daily lives and hearing about what they could tell them about travelling, hygiene, dietary restrictions, timing of treatment and pain.

In a study exploring home dialysis, none of the patients said they had been offered peer support yet one of the most common suggestions they offered about improving the service was the opportunity to get information from other patients about their experiences of home dialysis.

The nurse's role

Research exploring patient perceptions of blood transfusion identified nurses as the primary source of information. Nurses also were the ones who told patients that they would feel better after the transfusion, and were identified as providing accurate information. Whilst patients may need further information before, during, and after the procedure, handing out brochures in not sufficient and a key role of the nurse was to reassure and educate patients.

Theme 6: Patient participation

The key elements include the struggle for shared decision-making and professional dominance and control, which includes the concepts of trust and paternalism. There are overlaps with this theme and the themes of responsiveness of services, support, communication and information.

Struggle for shared decision-making

Aasen et al. (2012) report that long term patients with higher levels of education and those from a higher social class appeared to struggle to be heard in the patient-professional encounter. In particular they felt it was a constant effort to be heard during their discussions with the health professionals about blood access, dry weight, diet and time of treatment.

Patients did not always agree and while they attempted to argue their case they reported difficulties getting their opinions across. In terms of diet for example the key concern of the health professionals was in ensuring patients had a longer life so they would stress the importance of compliance, whereas the key concern for the patient was maintaining the quality of whatever life they had left. Given their struggle to be heard some patients reported resignation and simply did as they were told.

Professional dominance and control/paternalism

Professional dominance is described by Aasen et al. (2012) as the power in the interaction between the health care team and the patients which was

apparent in the experiences of patients and in the words they used when telling their stories. Patients spoke of how "professionals decide" and "always" when speaking about the health care team. When patients talked of themselves they used words like "must", "should", "accept", "trust", which speaks to the potential powerlessness of patients. Patients also used metaphors to describe how they felt referring to the dialysis unit as "jail", "prison", through identifying the nurse as "guardian", and referring to themselves as "furniture", or "package".

Whilst all patients reported trusting health professionals, longer term patients who had become accustomed to living with their disease reported feeling more fearful about what would happen if they did not do as they were told. Patients who had experienced less than two years living with their disease reported feeling more trustful and accepted the idea that the health care had to dominate. However, when talking about participation, patients tended to shift from using "I" to using "we", suggesting that this combination of trust and fear has the potential to create passiveness and become an obstacle to dialogue and shared decision-making. Professional dominance and control exercised through the ideology of paternalism was also highlighted in a study exploring patients' perceptions of blood transfusion. In this study, paternalism is defined as the practices by which the physician makes a decision on what they think is best for the patient. Throughout the study patients reported how the doctor made the decision to transfuse and, because they trusted the doctor, they did not question medical decisions.

Theme 7: Continuity of care and relationships

No findings were mapped against the theme of continuity of care and relationships in this review. However there are overlaps between patient participation, responsiveness of services and support and continuity of care and relationships in the definitions of themes and some of the findings.

Discussion

This review has appraised and considered current available evidence, as identified through a systematic search process, on the patient perspectives of a range of infusion therapies delivered across hospital, community and home settings. The findings from the 22 studies that were included after a process of sifting were examined to identify facilitators and barriers to the delivery of infusion therapy and were mapped across the seven themes identified in the Warwick Patient Experience Framework (WaPEF) (Staniszewska et al., 2014).

As discussed in the introduction section above the review utilised the WaPEF, which in turn was also used to inform the development of the NICE Patient Experiences Guidelines (NICE, 2012). It is reasonable to suggest that the findings from this rapid evidence review reinforce the importance in particular of treating the patient as an individual, understanding the essential requirements of care and tailoring care to meet the patients' needs, and empowering patients so they can actively participate in their care and treatment. However, the findings from this review do reinforce shortcomings in relation to continuity of care and relationships, and these discussions are outlined in the section below.

The unique contribution of this patient experience review, which justifies inclusion in the revised RCN *Standards for Infusion Therapy* is linked to the specific focus on the patient perspective of different types of infusion therapy, including the nursing contribution, coverage of both acute and non-acute settings, the international perspective, identification of obstacles to good infusion therapy practice, and current gaps in the evidence base.

Gaps in the evidence

Overall the size of the evidence identified and retrieved was small, but the majority of the studies reviewed have been rated as high or medium quality. The coverage of infusion therapy range was limited, with the majority of the papers (12 out of 22) focusing on dialysis treatment with only one, for example, looking at peripherally inserted catheters. Only nine of the 22 studies were undertaken in the UK, which limits the applicability of the findings to a UK context.

There was no equal distribution of the studies across the seven WaPEF themes, with the majority of the findings (20/22 studies) mapped against the theme of lived experience. No findings were mapped against the theme of continuity of care and relationships, and only two were mapped against patient participation. It was felt that the description for continuity of care in the WaPEF framework was not specific enough and it was further refined by reference to the NICE Clinical guideline [CG 138]: Patient Experience in Adult NHS Services (NICE, 2012), which was informed by the WaPEF. This theme was described as continuity of care within a health care team or coordination and prioritisation of care for patients who use a number of difference services and the timely exchange of information.

While patients are the bearers of the implications of continuity of care, they may experience it as either good information provision or breakdown in communication, rather than having knowledge of how services are designed. There are overlaps between patient participation, responsiveness of services and support and continuity of care and relationships in the definitions of themes and across some of the findings. Yet as this review did not find any study that covered directly the domain of continuity of care, it may be that a discrepancy between what matters to patients and what gets researched and/or published exists. With the current focus of health policy on integrated care and approaches to address fragmentations in the system, the patient perspective can be used to design services and evaluate their impact. Further research is required to guide this activity and examine how system designs can best address the patient and carer needs.

It is not clear from the studies reviewed what the impact of the patient experience is on adherence to the quality, effectiveness and safety of the infusion therapy. The focus of the studies was on patient and carer perceptions with limited exploration of

possible ways to improve the delivery of a range of infusion therapies across a variety of settings. There appear to be links between the experience of the treatment (clinical and as a service) and psychological state and mental health, but the presence of an effect and its direction remain unclear.

Limitations and strengths

This review has a number of limitations and strengths. The quality appraisal of individual papers was conducted primarily by the first author with a sample of decisions cross-checked by a second reviewer, which may have affected the reliability of the decisions to include or exclude papers. However, to maximise the veracity of the review both the methodology and findings were submitted at various points in the review process to the expert group supporting and guiding the development of the revised RCN *Standards for Infusion Therapy* for close scrutiny. A further limitation was project budgetary and time constraints, which meant we were unable to locate the full range of full text articles for review. Although the number of relevant papers selected to be included on the basis of abstract was not particularly high, further attrition took place when it was not possible to obtain about one-third of the papers as full texts for further assessment. This limitation may have impacted on the validity of the findings.

In terms of the project's strengths, we have strived to ensure full transparency in the review process and in the provision of a clear audit trail of decisions taken as the review progressed. An additional strength of the project lies in the aforementioned expert group acting as an additional source of advice and scrutiny regarding the credibility of findings and the identification of any obvious omissions. With regard to decisions on what to include and what to exclude following the quality appraisal of each individual paper, we erred on the side of caution and included all articles rated as low quality. The key exclusion criteria was to leave out papers that fell out of scope, and full details of all excluded papers are provided in the appendices to this report section.

Implications for practice and research

Table 7: Implications for practice and research identified in 22 review papers

Implications for practice (n=11/22)	Implications for research (n=10/22)
Improvements in professional engaging in dialogue with patients, sharing their power and their knowledge (Papers 1, 22). Provision of more patient and carer education (Papers 2, 10, 11, 17, 18). Provisions of formal/informal networks of support for patient, carers, and family members (Paper 11). Making regular visits to patients homes (Paper 3). Extending nurse-led clinics (Paper 4). Improving early referral (Paper 18).	Research on meeting patients psychological and emotional needs through routine appointments with doctors and specialist nurses (Paper 5). Research on use of medical technology in the home (Paper 6) Research on how patient might adjust to insulin pump therapy (Paper 7). Longitudinal research to explore whether positive representations of illness and treatment are the cause or the result of improved feelings of autonomy and control (Paper 9). Prospective research to evaluate patient education programs (Paper 10). Research on peripherally inserted central catheters (PICC) (Paper 13). Research on reducing patient anxiety/fear of the unknown (Paper 13). Prospective research on provision of repeated blood transfusion in hospice setting (Paper 14). Research exploring patients' resistance to more optimal forms of vascular access (Paper 15). RCT studies to measure effectiveness of written patient information and teaching methods (Paper 15). Research exploring the reasons patients refuse to take part in self-care for home dialysis (Paper 20). Survey nurses to identify their education needs relating to blood transfusion (Paper 21). Research on patient experience of blood transfusion (Paper 21). Research on shared decision making and cultural attitudes (Paper 21). Research exploring how professionals assess patient knowledge and experience of the procedure, including the nurses' contribution to their experience (Paper 21).

Implications identified by review authors

Clinical practice

In functional or operational terms any move towards delivering infusion therapy services closer to home has implications for resource planning and management and nursing workload management. While treatments delivered closer to home (general practice units, community hospitals, nurse-led clinics, hospices) will result in reduced travelling time for patients, they may conversely lead to greater travelling time for community, district, practice and specialist and advanced nurse practitioners given the associated need for increased regular home visits to support patients and their families.

The provision of a range of infusion therapies delivered to patients closer to home will require adequate numbers of community, district, primary care and specialist and advanced nurse practitioners. However, in order to increase the uptake rates of patients choosing home treatments like dialysis, continued investment in hospital-based staff will not diminish. The need for clinical leadership and wider staff support has been described by Combes et al. (2015)[5] who identify the need for strong clinical leaders including renal clinical leads, highly visible and effective individual champions for home dialysis and home therapy nursing teams.

Extending the role and scope of community, district, general practice and specialist and advanced nurse practitioners to meet increased demand for more services closer to home may also require greater investment in continual professional development and support for these nurses to improve their skills and knowledge in order to ensure they are practising competently and safely.

Meeting increased demand from patients requiring a range of infusion therapy treatments closer to home may also require an extension to currently available nurse-led clinics or an increase in their numbers. Extended nurse-led clinics could become hubs for patients, carers and relatives in providing them with education and training support, as well as formal and informal information support and networking opportunities. Nurse-led clinics could also be the 'go to' place where patients, carers and relatives can access a range of tailored, format-friendly, relevant and timely information.

In addition, training programmes may be required for non-specialist staff working in hospitals since Combes et al. (2015)5 report that many staff reported a lack of confidence in talking to patients about home treatment and reported receiving no recent training about home dialysis. The lack of training was reflected in patient statements about how they felt their questions about treatment options were not addressed satisfactorily, and how hospital staff failed to portray the benefits of home dialysis, thus missing an opportunity to encourage patients to consider home dialysis.

Meeting the communication needs of patients, carers and families to improve dialogue and shared decision-making as a result of the increased demand for the provision of infusion therapy treatments closer to home will require improved channels of communication. In addition to face-to-face and telephonic communication, examples of new or improved communication channels could include greater utilisation of video-link consultations and social media interactions.

Delivering infusion therapy closer to home may also need multi-professional interventions as the evidence reports on the multi-faceted impact of disease, treatment and associated coping mechanisms across the various life domains appear to interact. However, it worth noting that only nine of the studies were from the UK, five of which were high quality, and this may affect the applicability of the findings in a UK context, suggesting the need for further research.

Research

There does appear to be a need for more robust research exploring the links between patients' experiences, and the quality, safety and effectiveness of infusion therapy treatments wherever these are delivered. While the majority of the studies included in this review were qualitative, which is the approach most suitable for exploring experiences, they were of varying degrees of quality with low participant numbers. There are understandable practical and ethical barriers in conducting research involving patients and sample size does not have the same implications as in quantitative studies. However, the diversity of infusion therapy options and patient circumstances would require larger studies to ensure the capture of all relevant aspects. In addition, to explore questions about the direction of the relationship between the patient experience and the quality, safety and effectiveness of infusion therapy treatments, study designs that would allow causality to be examined (experimental, longitudinal designs and mixed methods), should be considered, within the aforementioned practical and ethical considerations. Longitudinal studies would be particularly appropriate, given the dynamic nature of the patient experience from diagnosis to treatment decisions and living with the implications of these decisions.

This review did not identify any interventions designed to address the perceived issues as identified and expressed by the patients and subsequent evaluations. Since the search strategy did not target this type of research, we are unable to report a whether this is a gap in the literature. Since the searches focused on the patient perspective as expressed in patients' own words, it would be useful for this body of research aimed at exploring what matters to patients to lead to more applications of implementation and evaluation in practice.

Summary

This review has appraised and considered the currently available evidence on the patient perspectives of a range of infusion therapies delivered across hospital, community and home settings. The majority of the papers reviewed reported on dialysis treatment. The findings have been mapped across the seven themes identified in the *Warwick Patient Experience Framework* (WaPEF) (Staniszewska et al., 2014). The review has revealed gaps in the evidence base, and the review authors have identified a range of implications, both for clinical practice and research. The findings from this review will be used to inform the revision of the RCN *Standards of Infusion Therapy*.

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Appendix 1: Details of out-of-scope papers (at 2nd sift)

First author; year of pub; reference; country of origin	Sample; participants; settings	Aim of study	Method(s)	Key findings	Reasons why out-of-scope
Cohen et al, (2012) *Journal of Pain & Symptom Management*, 43(4), pp.855-865. (USA).	85 patients; 85 caregivers; home hospice care.	To describe the meaning of hydration for terminally ill cancer patients in home hospice care and for their primary caregivers.	RCT.	Patients and family caregivers saw hydration as meaning hope and comfort. Hope was the view that hydration might prolong a life of dignity and enhance quality of life by reducing symptoms such as fatigue and increasing patients' alertness. Hydration also described as improving patients' comfort by reducing pain; enhancing the effectiveness of pain medication; and nourishing body, mind and spirit.	Not patient perceptions of IF therapy.
Ekwall et al. (2010) European *Journal Oncology Nursing*, 15, pp.53-58. (Sweden)	12 women receiving chemotherapy in a hospital setting.	To explore what women with recurrent ovarian cancer perceived as important in their communication with the health care team.	Interviews.	Key theme identified as becoming familiar with the disease, underpinned by four sub-themes; being acknowledged as a unique person' getting help to make sense of information; having the opportunity to be involved and to share responsibility; and feeling confident that medical expertise was adequate.	Not patient perceptions of IF therapy.
Fallowfield et al. (2010) *Psycho-Oncolog*, 20, pp.755-761. (UK)	79 patients (35 receiving bisphosphonate medication; 44 receiving IV treatments) Eight hospitals.	To examine women's experiences with oral and IV bisphosphonate therapy, the impact that treatment had on bone pain and quality of life, and their preferences if choice were available between oral and iv administration.	Prospective study.	Self-reported adherence to oral therapy was good although 21% had chosen not to take their drugs at some time. Most had adapted their lifestyle to accommodate oral therapy with 74% completely satisfied; 24% expressed dissatisfaction with constrains, especially the time required to stand upright after taking their tables. By six months 91% of patients receiving IV therapies were generally more satisfied with the frequency and 88% with the convenience. Overall, 46% of patients reported improved bone pain scores on the validated FACT-BP scale from baseline to six months.	Not patient perceptions of IF therapy.

First author; year of pub; reference; country of origin	Sample; participants; settings	Aim of study	Method(s)	Key findings	Reasons why out-of-scope
Griva et al. (2013) *Psychology & Health*, 28(1), pp 13-29. (Singapore)	37 patients (17 interviews; three focus groups).	To explore the cultural perspectives on facilitators and barriers to treatment adherence in haemodialysis patients.	Exploratory study.	Facilitators identified include: support from family members and social obligation towards others, risk perception, establishment of routines and peer support. Barriers identified include: time consumption, forgetfulness, concerns about safety, poor knowledge/ understanding poor communication and lack of control/social pressure.	Not patient perceptions of IF therapy.
Da Silva-Gane (2014) *Journal Renal Care*, 40 (Supple1), pp.30-35. (UK)	320 patients undergoing haemodialysis. Setting not reported.	To explore the attitudes and perceptions of future end-of-life care planning for patients receiving haemodialysis.	Mixed methods.	Main focus for patients appeared to be holding on to what they had, adapting by living 'from day to day' in the present, and continuing to hope for the best. Advanced planning seem as potentially useful, once clarity surroundings its purpose been established.	Not patient perceptions of IF therapy.
Johnson and Noble (2012) *Journal Clinical Nursing*, 21, pp.1215-1222. (UK)	Nine patients attending clinical nurse specialist (CNS) clinic.	To explore decision-making experiences of patients with stage 5 chronic kidney disease when opting for conservative treatment of their renal failure.	Interviews.	Patients reported age and having to travel three times a week to hospital for dialysis as reason not to opt for treatment, Others felt well with dialysis not wanting to upset the 'status quo' or upset loved ones. Most felt equipped to make the decision following explanation and discussion with the CNS	Not patient perceptions of IF therapy.
Kazemi et al. (2011) *Nursing & Health Sciences*, 13, pp.88-93 (Iran)	21 patients undergoing haemodialysis in hospital setting.	To explore the experiences of social interactions in the daily life of Iranian person who were receiving dialysis.	Exploratory study.	Findings show that patients experienced altered social interactions with others, which led to social avoidance.	Not OECD country.
Lau et al. (2014) *Journal Oncology Practice*, 10(6), pp.380-384. (Australia)	198 patients from two tertiary centres.	To assess patient preferences for scheduling medical oncology outpatients appointments and chemotherapy delivery on the same day (TDS).	Survey.	Majority of patients preferred TSD. Convenience and distance of difficulty in transportation were the most common reasons.	Not patient perceptions of IF therapy.
Levitt and Ziemba-Davis (2013), *Journal PeriAnesthesia Nursing*, 28(4), pp.223-232. (USA)	30 patients; hospital setting.	To add to the body of knowledge about patient preferences for pain management during IV insertion.	Exploratory study	Only four patients chose no pain management strategy. Patients have preferences for pain control and believe they should be involved in decisions about pain management.	Not patient perceptions of IF therapy.

First author; year of pub; reference; country of origin	Sample; participants; settings	Aim of study	Method(s)	Key findings	Reasons why out-of-scope
Lin et al (2011) *Journal Clinical Nursing*, 20, pp.802-810. (Taiwan)	607 patients; home care and hospital setting.	To investigate why patients do not choose percutaneous endoscopic gastrostomy or percutaneous endoscopic jejunoscopy as a route for long-term feeding.	Mixed methods	Prevalence of home enteral tube feeding was 70.3& (n=427). Of the 427 tube fed subjects 93.4% were fed with nasogastric tube. Most common reason for refusing to percutaneous endoscopic gastrostomy of percutaneous endoscopic jejunostomy were 'too old to suffer form an operation' 'worried about wound infection' or leakage' and 'to keep body integrity'.	Not OECD country.
Menakaya et al. (2015) *Journal Perioperative Practice*, 25(4), pp.72-77. (UK)	100 patients; trauma clinic.	To explore patient's perception of a new service and protocol for managing outpatient venous thromboembolism (VTE) prophylaxis using either subcutaneous Dalterparin or oral off-license Dabigatran in patients with lower limb injury requiring mobilisation.	Mixed methods.	Overall rating score was 4.26 (range 105), with 90%^ of patients recommending the service. Overall patient satisfaction for a VTE prophylaxis is high, although there is room for improvement.	Not patient perceptions of IF therapy.
Merrick and Farrell (2012) *European Journal Cancer Care*, 21, pp.493-504. (UK)	15 patients; hospital setting.	To explore patients' experiences of PEG feeding while undergoing cancer treatment.	Survey.	Three perspectives emerged: factor 1 'constructive cognitive appraisal' – positive adaptation and acceptance of PEG feeding' factor 2 'cognitive-affective-dissonance – ambivalence between cognitive acceptance and affective rejection of the PEG tube; and factor 3 'emotion-focused appraisal' – characterised by rube-focused anxiety and fear.	Not patient perceptions of IF therapy.
Mueller et al. (2010) *Health & Quality of Life Outcomes*, 8, p41. (Germany)	16 patients.	To investigate patients' perspectives on their experience of functioning and health in relation to home parenteral nutrition.	Interviews.	Extracted 94 different International Classification of Functioning, Disability & Health (ICF) categories' 32 from ICF component 'body functions'; 32 from 'activities 7 participation'; 18 from 'environmental factors'. 8% of concepts derived from patient interviews could not be linked to specific ICF functions because there were too general, disease-specific, or pertained to 'personal factors'.	Not patient perceptions of IF therapy.
Nizamli et al. (2011) *Nursing & Health Sciences*, 13, pp.481-487. (Syria)	17 women undergoing chemotherapy in hospital setting.	To explore the experiences of Syrian women with breast cancer regarding chemotherapy.	Interviews.	Four main themes identified; psychological discomfort; physical problems, social dysfunction, and failure in the family role.	Not OECD country.

First author; year of pub; reference; country of origin	Sample; participants; settings	Aim of study	Method(s)	Key findings	Reasons why out-of-scope
Palmer et al (2014) *BMJ Open*, 4:e005020, Doi:10.1136/bmjopen-2014-005020. (UK)	2,748 adults treated in haemodialysis clinics	To evaluate patient experiences of specific aspects of haemodialysis across several countries.	Survey.	Fewer than half 46.5% rated their overall care as excellent. Older adults were less critical of their care and those with depressive symptoms were less satisfied.	Customer satisfaction.
Sadala et al. (2010) *Journal Renal Care*, 36(1), pp.34-40. (Brazil)	14 patients receiving continuous ambulatory peritoneal dialysis (CAPD).	To investigate how patients perceive the communication between them and the nurses during routine home visits.	Interviews.	Findings suggest that effective communicator and the development of the relationship for a working partnership with patients is crucial. Improvements in the nurses' communications is significant for achieving better outcomes.	Not OECD country.
Schwappach and Wernli (2010) *Quality Safety Health Care*, 19:e9. (Switzerland)	30 chemotherapy patients.	To assess chemotherapy patients' perceptions of safety and their attitudes towards participating in error prevention strategies.	Interviews.	Patients only moderately worried about safety, risk of errors and the potential for ham. At follow up interview worries about safety had increased and patients reported a higher degree of vigilance. Patients agreed that they can make contributions to their safety. No indication that patients perceive participation in safety actions as eroding trust in their providers.	Not patient perceptions of IF therapy.
See et al. (2014) *Nephrology Nursing Journal*, 41(1), pp.37-40: 51. (USA)	12 patient ambassadors (11 receiving dialysis).	To explore attitudes and preferences of patients on haemodialysis regarding education and engage such patients in bloodstream infections (BSI).	Focus groups.	Patients reported that education on infection prevention should begin early in the process of dialysis, and patients should be actively engaged as partners in infection control.	Not patient perceptions of IF therapy.
Yu and Tsai (2012) *Journal Advanced Nursing*, 69(9), pp.1942-1952. (Taiwan)	25 patients undergoing haemodialysis in hospital.	To explore the perceptions of patients experiences of their illness trajectory and decision to undergo dialysis.	Interviews.	Core theme identified was 'from silence to storm'; with five phases of patient experiences emerging: diabetes onset stage; stable stage; burden stage; shock stage; and coping stage.	Not OECD country.
Yamada et al (2010) *Journal Pain & Symptom Management*, 40(1), pp. 60-66. (Japan)	219 patients; palliative care unit.	To clarify the levels of patient perceived comfort and convenience in addition to procedure-related distress, in using PICCs.	Clinical audit.	68% reported the procedure was not distressing; 8% reported in as slightly distressing' and 24% reported it as distressing. 94% patients reported becoming more comfortable; 6% reported no change. 94% of patients reported levels of parenteral access as becoming more convenient' 6% reported no change.	Clinical audit.

Appendix 2: Systematic review of qualitative papers (n=15) using CASP appraisal tool

Study (first author, year)	Was there a clear statement of the aims of the research?	Is the qualitative methodology appropriate?	Was the research design appropriate to address aim(s) of the research?	Was the recruitment strategy appropriate to aims of the research?	Were the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been considered?	Was the data analysis sufficiently rigorous?	Is there a statement of findings?	Is the research valuable?	Overall quality rating
Aasen (2014)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Baillie (2014)	Yes	Yes	Yes	Yes	Not reported	Yes	Yes	Yes	Yes	Yes	HIGH
Bayhakki (2012)	Yes	Yes	Yes	Yes	Yes	Not reported	Yes	Yes	Yes	Yes	HIGH
Bjuresater (2011)	Yes	Yes	Yes	Yes	Yes	Not reported	Yes	Yes	Yes	Yes	HIGH
Fex (2011)	Yes	Yes	Not reported	Yes	Yes	Not reported	Yes	Not reported	Not reported	Not reported	MED
Hayes (2011)	Yes	Yes	Not reported	Not reported	Yes	Not reported	Yes	Not reported	Not reported	Not reported	LOW
Hope (2013)	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	LOW
Lindberg (2013)	Yes	Yes	Not reported	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Monaro (2014)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Orme (2013)	Yes	Yes	Not reported	Not reported	Yes	Not reported	Yes	Not reported	Not reported	Not reported	LOW
Shih (2011)	Yes	Yes	Not reported	Yes	Yes	Not reported	Yes	Yes	No	Not reported	HIGH
Stephens (2013)	Not reported	Yes	Not reported	Not reported	Not reported	Yes	Not reported	Not reported	Not reported	Not reported	LOW
Winterbottom (2012)	Yes	Yes	Not reported	Yes	Yes	Not reported	Yes	Yes	Yes	Yes	HIGH
Weiss (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH

Appendix 3: Systematic review of mixed methods papers (n=7) using in-house appraisal tool

Study	Is there a convincing rationale for overall research strategy and how it was designed to meet research aims/questions, including a comprehensive review of previous research and justification for collecting new primary data?	Is there good discussion of the research design, strengths and weaknesses of data sources? Are any implications or limitations taken into consideration in the analysis and findings? Ethics?	Does the study describe locations and population(s) of interest and how and why chosen to allow comparisons to be made? Was the sampling strategy appropriate to the research question(s)?	Is there detailed description of data collection methods used, explaining any limitations and methods to maximise inclusion or limit bias?	Is there an explicit and analytic procedure for processing raw data into results or themes that could be repeated with a similar methodology? Was there triangulation of data analysis (multiple scorers or coders)?	Did the study report findings on all variables or concepts investigated and does it include discussion/ mention of any negative cases and outliers and confounding variables? Are limitations reported? Is there any discussion of study context and biases/ flaws in design?	Are conclusions presented supporte4d by study findings and previous research and theory where appropriate? Is there evidence of new of openness to new or alternative ways of viewing subject, theories or assumptions? Is any attempt made to quantify or explain the strength or value of findings if appropriate?	Overall quality rating
Coombes et al. (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Jansen et al. (2010)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Nagel et al. (2011)	Yes	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	LOW
Quinan et al. (2011)	Yes	Not reported	Yes	Not reported	Not reported	Yes	Yes	MED
Ream (2013)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	HIGH
Rosenkoetter et al. (2013)	Yes	Not reported	Yes	Yes	Not reported	Not reported	Yes	MED
Visaya et al. (2010)	Yes	Yes	Yes	Not reported	Not reported	Not reported	Not reported	LOW

Appendix 4: Warwick Patient Experiences Framework (WaPEF)

Generic theme	Narrative description
Patient as active participant.	Reflects the role of patients as potential active participants in their health care, co-creators and co-managers of their health and use of services; responsible for self-care, participators in health care, shared decision-makers, self-managers, risk managers and life-style managers. Confidence in self-management is crucial. Associated with issues of power and control.
Responsiveness of services – an individualised approach.	Needing to be seen as a person within the health care system. The responsiveness of health services in recognising the individual and tailoring services to respond to the needs, preferences and values of patients, taking into account both shared requirements and individual characteristics (such as individuals expectations of service cultural background, gender, subtle issues such as preferences for humour). Includes how well clinical needs are met (for example, pain management) and evaluation of how well services perform from a patient perspective.
Lived experience	The recognition that individuals are living with their condition and experiencing it in a unique way, that family and broader life need to be taken into account and that all of these aspects of lived experience can affect self-care. Taking into account individual physical needs and cognitive needs because of condition. Everyday experiences, hopes, expectations, future uncertainty, feelings of loss, feelings of being morally judged and feeling of blame. Some of these experiences originate 'outside' of the health care system but are brought with the patient into the health system; other experiences may be affected by attitudes and expectations of health professionals.
Continuity of care and relationships.	Initiating contact with services, interpretation of symptoms, coordination, access (barriers to), and availability of services, responsiveness of services and feelings of abandonment (when treatment ends or support is not made available). Being known as a person rather than a 'number'. Trust in health care professionals built up over time. Recognition/questioning of expertise of health care professional. Respect, including respect for patient's expertise. Partnership in decision-making. Issues of power and control.
Communication.	Needing to be seen as an individual; communication style and format (for example, over telephone or in person); skills and characteristics of health care professional; body language (which can convey different information from that spoken); two-way communication and shared decision-making, compassion, empathy; the importance of the set-up of consultation (for example, appropriate time for questions, appropriate physical environment and number of people present). Listening and paying attention to the patient. Enabling questions and providing answers.
Information.	Information to enable self-care and active participation in health care, importance of information in shared decision-making, tailored information to suit the individual, patient wanting/not wanting information and timely information. Sources of information, including outside the health service (for example, peer support, Internet). Quality of information. Sources of further information and support. Developing knowledge and understanding, and making sense of one's health.
Support.	Different preferences for support: support for self-care and individual coping strategies. Education. Need for emotional support, and need for hope. Responsiveness of health care professionals to individual support needs (may vary according to gender, age and ethnicity). Importance of peer support, groups and voluntary organisations. Practical support. Family and friends support, role of advocacy. Feeling over-protected, not wanting to be a burden.

Source: Staniszewska et al., 2014

Appendix 5: Patient reported perspectives of infusion therapy treatments mapped against WaPEF themes

Patient participation [1,21) (2/22) (High=2)	**Responsiveness** (1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	**Lived experience** (1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	**Continuity of care and relationships** (0/22)	**Communication** (1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	**Information** (1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	**Support** (2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
Professional power and dominance [1]. Patients struggle for shared decision-making [1]. Patients' report "professionals decide" [1]. Patient's become passive and/or resigned [1]. Patients reported "they had to satisfy the nurses" [1]. The haemodialysis unit did "not promote participation in a satisfying manner" [1]. Combination of "trust" and "fear" may create passiveness, becoming an obstacle to dialogue and shared decision-making" [1]. Patients reported that dry weight is determined by professionals and patients found it difficult to get their opinions across [1]. Patients used "we" as opposed to "I" when distancing themselves "Even if we wanted to decide what should happen it doesn't mean that we could" [1]	Patients describe professionals as "guardians" [1]. Patients say "nurses do not give them priority" [1]. Patients' identify nurses as "nice" and "good" [1]. In terms of blood access (mainly catheters and fistulas), patients reported a preference for catheter rather than fistula [1]. Patients preferred catheter but felt they had no real choice because professionals preferred the fistula [1]. Patients' questions about the fistula were not addressed [1]. In terms of time of treatment some patients said they had opportunities to discuss treatment, others did not [1]. Patients recognised the control offered by home dialysis was "limited" and that it may prove unsustainable [2].	Patients used words like "must", "should", "accept", "trust" when talking about themselves [1]. Patients use "jail" to describe haemodialysis (HD) units, and "animal" to describe the HD machine [1]. Patients describe themselves as "furniture" or "package" [1]. Patients report being in "prison", feeling "bound", having "no freedom" [1,3,11,18,22]. Patients spoke of "mental strain", being "controlled", feeling "incapacitated" [1,3,5]. Patients felt "pity" for nurses because they're so "busy" [1]. All patients "trusted the health care team" [1,21]. Some patients reported feeling "afraid of what might happen if they refused to do as they were told" [1].		Professional dominance seen through "one-way communication" [1]. Patients report how nurses "do not have time" to talk [1]. Some patients felt able to ask questions, some felt "more passive" and "did not know what to ask" [1]. Interpersonal relationships expressed by patients as "I can ask", " I want", "they could" [1]. Some patients "told" they required renal replacement therapy [2]. Some patients presenting with end stage kidney disease (ESKD) were advised of their options by the clinical nurse specialist and then made the decision [2]. One patient reported "no choice other than peritoneal dialysis" [2]	Patients report they miss engaging in dialogue and sharing knowledge [1]. Some patients satisfied with information, other not; it depended on how sick they were [1]. Patients felt information giving could be "accidental" [1]. Some patients wanted more information but said "nurses do not tell me anything" [1]. Long term patients felt it "got more difficult to obtain information" [1]. Patients talk as if professionals "owned they knowledge", and "they decided what patients needed to know" [1]. Carers lack information from professionals [4]. Carers felt they lacked information about how long home enteral tube feeding (HETF) would last [4].	Once decision was made to have peritoneal dialysis (PD) patients had to "learn the skills for managing PD" [2]. Anxious patients learned skills with ease and credited nurses for their teaching expertise [2] Patients also supported by relatives [2,6]. Dialysis patients require social support [3]. Professionals do need to make regular visits to patient's homes [3]. Nurses have a responsibility to improve their own and their patients' knowledge; provide time, materials and education [3,18]. Carers lack support from professionals [4]. Lack of support for carers/ relatives meant they had to assume a great level of responsibility [4].

Patient participation [1,21) (2/22) (High=2)	Responsiveness (1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	Lived experience (1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	Continuity of care and relationships (0/22)	Communication (1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	Information (1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	Support (2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
Patients with higher level of education or higher social class and patients on restricted diet and dialysis reported how "they struggled to be listened to" [1]. Patients said doctors made the decision to transfuse [21]. Patients said they rarely questioned the doctor's decision [21]. Patients felt overwhelmed in discussing the risks and benefits of blood transfusion with doctors [21].	Boundaries between relatives' responsibilities and home care services responsibilities were vague [4]. Barriers to home dialysis treatment identified as housing, space at home, ordering and installation of haemodialysis machines [5]. Lack of training for non-specialist staff, pre-dialysis education, lack of recognition by professionals of patients' emotional and psychological needs [5]. Patients reinforced need for training for ALL staff [5]. Patients wanted a more personalised approach but staff saw it only in terms of information provision [5]. Most patients found it hard to adjust psychologically and emotionally to need for dialysis, and felt this was not recognised or responded to by staff [5]. Patients reported there were no service responses to their distress [5].	Patients felt "ignored" "forgotten about", "powerless", and found it difficult to be "active" [1,3]. Patients felt "isolated" [1,3,5,11] and shattered [18]. Some patients chose home dialysis so they might "remain at home"; this offered some "autonomy" and "control" [2]. Fear of the fistula was why some patients chose peritoneal (home) dialysis [2]. Medicalisation of the home and following a rigid timetable seen as barrier to home dialysis treatment [2,18]. Medicalisation of the home affected all patients and was an important consideration in the decision to have home dialysis [2]. Home dialysis requires substantial daily work for patients [2].		Patients recognised peritoneal dialysis (PD) as "life-sustaining treatment", and they identified ESKD as a "palliative condition" [2]. Patients felt their questions were often not dealt with well by staff [5]. Patients felt staff failed to fully portray the benefits of home dialysis [5]. Patients wanted opportunities to talk and be listened to [5] Patient reported no choice, no discussion, no joint discussion, no other options were discussed, and no chance to say no to home dialysis [8]. Development of decision aids that fully incorporate patient experience [8]. Treatment choice discussions need to focus more on lifestyle and quality of life, not just clinical needs [8]. Shared decision-making should involve patients, relatives, peers and clinicians [8].	Relatives' participation in care required relevant information, which was often lacking [4]. With regard to pre-dialysis education patient felt treatment choice was very difficult due to number of treatments available and complexity of information [5]. Patients described "information overload" [5]. Patients wanted a wider range of teaching methods to be used [5]. For patient it was the "application of information" to their own lives that was more significant [5]. Patients only became interested in home dialysis once they started dialysis [5]. Current focus on providing detailed, complex information and leaving patients to make the decision needs to change [5]. At pre-dialysis stage patients would like information on symptoms and symptom management [8].	Relatives/carers of patients on HETF need comprehensive support from professionals, including psychological, emotional and instructional support [4]. Nurses should collaborate on such support and nurse-led clinics should include close relatives [4]. No patients were offered peer contact or support [5]. Patients reported there were no support arrangements in place other than referral to psychologist or psychiatrist for depression [5]. There is a need to support decision-making in a more 'non-directive' way [5]. Patients required professional support tailored to their needs [6]. If support was not tailored it was seen as having "no value" [6]. Knowing help was always available was a "source of security" [6]. Patients would like better emotional and mental support [8].

Patient participation [1,21) (2/22) (High=2)	Responsiveness (1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	Lived experience (1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	Continuity of care and relationships (0/22)	Communication (1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	Information (1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	Support (2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
	Shifting health care from hospital to home is unlikely to increase without the routine provision of psychological and emotional support to patients and the upskilling of professionals to recognise and respond to patients' needs [5]. Patients required manual skills and knowledge of technology for managing daily life with technology at home [6]. Patients and their homes need to be prepared prior to taking delivery of medical technology at home [6]. Patients preferred insulin injections to wearing a pump to deliver insulin [7]. Haemodialysis teams need to help patients successfully develop self-care strategies for dealing with the consequences of end stage kidney disease [10]. Prospective trials needed to evaluate the educational effects of tailoring fluid management education to patients' perceptions of dry weight [10].	Home dialysis treatment increases the patients workload and their skills in managing the treatment [2,6]. Patients reported anxieties related to "contracting peritonitis and the threats associated with this" [2]. Threat of peritonitis caused patients "pain" and "uncertainty", and made them "feel guilty" if they got an infection [2]. Patients were committed to an "onerous treatment regime", and worked "hard to ensure complications were not missed" [2]. Patients managed their home dialysis treatment by being creative regarding equipment, training and location; they adapted their lifestyle to accommodate treatment [2,6,18,22]. Patients alter their behaviour to optimise their chance of transplantation; but some felt they had no control over transplantation; others resented the wait for a transplant [2,11,18].		Need to move away from modality neutral discussions to actively encouraging self-care modalities [8]. Need to explore patient beliefs about personal control, the impact illness and treatment has on their lives, and any concerns they have [9]. Few patients could recall engaging in any discussions about dialysis as a likely treatment option [11]. Some patients had limited perception of the need for lifestyle management prior to need for dialysis [11]. Some patients could not recall any discussions about renal replacement therapy [11]. Decisions regarding dialysis need consideration and collaboration between patients, relatives and clinicians [11]. High level of trust identified between the patient and the nurse performing the PICC is the result of the good communication and explanation skills of the nurse [13].	Patients would like more information on prevention [8]. Patient would have like more information on home dialysis following failed transplantation [8]. Need for honest patient-centred information to meet personal, not just clinical needs [8]. Important that patients understand concept of dry weight for their wellbeing and treatment adequacy [10]. Lack of discussion about timing of dialysis led to patients experiencing limited opportunities for timely information of pre-dialysis education or the establishment of permanent dialysis access [11]. Crucial that staff meet the pre-procedural and peri-procedure needs of patients undergoing PICC [13]. Patients requiring PICC struggled with the amount of information given, identifying it as unhelpful, excessive and frightening [13].	More support needed about symptoms during dialysis especially severe anaemia and sleep disruption [8]. Provision of small group patient-centred education emphasising self-care [8]. Need for active support for employed patients well before end stage renal disease diagnosis [8]. Need to support self-care across the system; at home and in satellite and hospital dialysis units [8]. Encourage and support wider range of treatment choice including partial or full self-care in dialysis units and extending dialysis at home [8]. Psychological interventions to support renal patients is required and such interventions need to be developed and tested [9]. Patients reported that support networks would be beneficial before and after treatment initiation [11,18]. Important that staff ascertain if patients want family members present during PICC procedure [13].

Patient participation [1,21) (2/22) (High=2)	Responsiveness (1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	Lived experience (1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	Continuity of care and relationships (0/22)	Communication (1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	Information (1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	Support (2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
	People with end stage kidney disease (ESKD) and their families need considerable preparation for haemodialysis [11]. The design and culture of dialysis units should enable family members to be present to support patients [11]. Chronic kidney disease (CKD) management requires a focus on comprehensive and patient-centred model of care [11]. Focus during implantation procedure should be placed on low visibility of the port system (catheter and capsule/) and minimal scar [12]. The cosmetic result of implantation procedure should not be underestimated as it is a significant predictor of patient satisfaction and quality of life [12].	Haemodialysis seen as a physical shackle in life reflecting the physical limitations resulting from lack of energy and weakness associated with limited food/ fluid intake [3]. Dialysis patients experience reduced functional capacity [3]. Dialysis patients experience limited income [3]. Dialysis patients experience restricted social life [3,6,11,18,22]. Dialysis affects patients' relationships [3,11,]. Dialysis patients experience depression, uncertainty, changes in personality, anger, denial, worthlessness, hopelessness, fear and anxiety [3,5,11,18]. Patients report the dialysis machine cannot be separated from their lives [3]. Patients view the dialysis machine positively as it removes metabolic waste and makes them feel "more fresh" [3].		Patient fear related to late referral [18]. Patients expressed frustration regarding the methods of communication between primary, secondary and community intravenous therapy (CIVT) services [19]. Patients' ability to communicate effectively impacts on their decision to engage in home haemodialysis (HHD) [20]. Patients asked nurses for clarification, opinion, information and advice on blood transfusion [21]. Patients felt doctors were too busy to answer questions [21]. Patients said they were offered no alternatives to blood transfusion [21]. Patients said they were told they needed blood transfusion when the nurse walked into the room with blood in one hand and a consent form in the other [21].	Staff need to be aware that some patients need time to assimilate written and verbal information [13]. Patient fear related to lack of information [18]. Patients said no information on blood transfusion was provided [21]. Some patients said they received information on blood transfusion but were too sick to read it [21]. Patients viewed the nurse as the primary source of information regarding treatment and the transfusion process [21]. Patients said the nurses provided accurate information about the blood transfusion procedure [21]. Patients identify information as a tool for helping them understand their illness and prepare them for dialysis [22]. Some patients did not identify information as a tool for their decision-making [22].	Many carers feel unsupported and their role went unrecognised by professionals [16]. Nurses need to be instrumental in health promotion through partnership with patients [18]. Nurses need to recognise the social, cultural context of patients' with chronic kidney disease (CKD) when planning short and long term management [18]. Education of CKD requires simplification [18]. Development of community intravenous therapy (CIVT) services provides opportunities for district nurses to increase their skills [19]. District nurses need support and training which focus on the theoretical and practice aspects of intravenous drug administration [19]. Social support was significantly related to patients' perceptions of home haemodialysis (HDD) [20].

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
	Strategies aimed at improving patient, family and staff education about the risk of long term catheter use together with implementing measures to reduce cannulation complications may improve patient satisfaction with vascular access, increase fistula rates, help improve fistula development and improve patient compliance [15]. Interventions to prepare carers for their caring role need to be developed to improve carer involvement and patient outcomes [16]. Patients' significant others (SO) should be included in diabetic training [17]. Implications of lack of referral left patients with less opportunities for preserving kidney function and prevent chronic end stage renal disease (ESRD), reducing patient's capacity to maintain quality of life [18]. An individualised and flexible approach may be the most beneficial for ESRD patients [18].	Patients view the dialysis machine negatively because they become tied to the machine", they can't travel [3,11,18,]. Patients apply internal (psychological) and external (physical) coping strategies for dealing with dialysis; internally they "accept it", and "hope for a transplant"; externally they get "support from family and friends" and try to manage a restricted life [3,11,18,]. Informal carers of patients receiving home enteral tube feeding (HETF) experience loss of togetherness and pleasure [4]. Carers feel guilty about eating [4]. Daily life becomes tied to tube feeding and social activities are hindered [4]. Carers experience loneliness [4]. Carers unable to share feelings with patients because they had to protect them [4]. Carers worried about the future [4].		All communication seen as inadequate [21]. Patients viewed the difficult decision as a choice between dialysis or no dialysis [22].	For some patients the source of information was other patients they had heard in workshops, and they asked them about benefits, advice, timing of treatment, pain, diet and hygiene [22]. Information is key but patients held a simplified view of the options as they made no distinction between the different types of HD and PD that were available [22]. Patients appeared to receive more information HD than PD and this was often presented in more accessible forms; this is likely to bias information seeking and patients' assimilation of the information [22].	Community nurses identified as encouraging patients about the need for a blood transfusion [21]. Patients felt nurses were more supportive and attentive during the blood transfusion procedure [21].

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
	Early referral following diagnosis with chronic kidney disease (CKD) may reduce patient stress [18]. Home treatment meant patients avoided admission to hospital, thus avoiding sharing space with others, being bored, and avoiding hospital acquired infections [19]. Patients made some criticism of professionals' time-keeping when delivering treatment in the patient's home [19]. Patients expressed concerns over district nurse's aseptic, non-touch techniques suggesting these could be improved [19]. Patients expressed some concerns about district nurse training, believing that some nurses required refresher courses (for example, lack of technique, lack of confidence) [19]. Patients did appreciate the work of the district nurses – seen as cathartic [19].	Heavy responsibilities placed on carers seen as a burden [4,11,18]. Carers "forced to adjust" their lives to tube feeding [4]. Carers experienced a distance in their relationship with the patient [4]. Carers strived for closeness, and spouses "longed for physical closeness" [4]. High demand and vulnerability placed on those caring for a patient on HETF [4]. While some patients felt they had benefited from being able to make their treatment choice, other felt unable to do so [5]. Patients reported strong emotional reactions to reaching end stage renal failure, leaving them unable to make decisions [5,16]. Patients too scared to consider home dialysis [5]. Patients saw dialysis as scary, traumatic, feelings of shock and trauma [5,11,18].				

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
	Health care professionals need to implement interventions incorporating an assessment of communication and social support when addressing home haemodialysis (HHD) with patients with ESRD) [20]. Clinicians may be missing opportunities to improve patients' knowledge of and comfort with blood transfusion, and improvement is required in meeting patients' needs before, during and after the transfusion [21].	Accepting patients trusted their capacity to manage medical technology in the home [6]. Accepting patients trusted medical technology [6]. Some patients felt they had no choice but to accept medical technology in the home [6]. Accepting patients displayed positive attitude and a goal of still having an active life, despite the inconvenience of medical technology in the home [6]. Patients reported wearing an insulin pump was inconvenient [7]. Wearing an insulin pump was time consuming, patient preferred to control the decision making process [7]. Not able to hide the pump [7]. Difficult managing the pump on the beach [7]. Wearing the pump was uncomfortable and caused skin irritation [7]. Patients doubted the pump; they did not trust it [7].				

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
		The pump fell off and disconnected [7]. Patients said wearing the pump left them feeling not in control of their body of their health [7]. Wearing the pump prevented intimacy with partners [7]. Dialysis patients view illness as chronic with serious consequences [9,11,16,]. Dialysis patients experience quite a few symptoms and are fairly concerned about their illness [9]. Dialysis patients experience little emotional impact [9]. Dialysis patients report high degree of understanding and consider their illness controllable with medical treatment, but not with self-care [9]. Dialysis patients experience moderate disruption from treatment [9]. Personal control and treatment control correlated with understanding [9]. Patients identify dry weight as an aid, an indicator, and a reminder [10].				

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
		Some patients have no specific perception of dry weight [10]. Patients actions with regard to dry weight include; self-care as a means of control, transferring responsibility for dry weight to the haemodialysis team, managing physical, emotional and psychological consequences [10]. Physical consequences of fluid removal had negative impact on patient's daily life [10]. Dialysis results in patients feeling loss of personal autonomy, ability work or to travel, self-sufficiency, independence, wages [11,22]. Caring role identified as unremitting and requiring intense vigilance [11]. Spousal carers buffered against patients being seen as a burden [11]. Non-spousal carers identified care as a burden and some expressed feeling of anger and resentment [11].				

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
		Dialysis patients worry their relatives will not withstand the illness and its consequences [11]. Dialysis patients worry about loss of intimacy [11]. 36/42 patients very/quite satisfied with port system [12]. 38/42 patients very/quite likely to choose port again [12]. 28/42 patients reported the port system very/quite simplified their course of treatment [12]. 30/42 patients said they enjoyed their spare time very much/quite a lot [12]. 34/42 patients reported the port obstructed their life a little/or not at all [12]. 21/42 patients were very/quite satisfied with the cosmetic result [12]. Patients receiving a peripherally inserted central catheter (PICC) reported the procedure as expected, or better than expected [13]. Patients had misconceptions and felt anxious about the PICC line [13].				

Patient participation [1,21) (2/22) (High=2)	**Responsiveness** (1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	**Lived experience** (1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	**Continuity of care and relationships** (0/22)	**Communication** (1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	**Information** (1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	**Support** (2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
		Patients experienced minor pain during the PICC procedure [13]. Patients having a PICC used a process known as blunting to avoid thinking about it [13]. Patients having a PICC displayed information seeking through a process identified as monitoring [13]. Patients presenting for blood transfusion experience fatigue, shortness of breath and dizziness [14]. Some patients saw the benefits of blood transfusion, others did not [14]. Patients prefer to have a blood transfusion in a hospice setting [14]. Patients believe having blood transfusion in hospice is less time consuming, it involves less travelling, parking is better, and staff have more time to talk to [14].				

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
		Patients who converted to fistulas or grafts tended to be younger, had higher rates of diabetes and hypertension, had a catheter in place for a shorter time, had less cerebrovascular and heart disease [15]. Patients refusing conversion to fistula or graft were less likely to have been on peritoneal dialysis, had a catheter in place longer, they experienced fewer arteriovenous attempts and higher rates of heart disease [15]. Patients unsuitable for fistula or graft tended to be female with higher rates of cerebrovascular and peripheral vascular disease [15]. Patients reasons for remaining with a catheter including ease in getting on and off the dialysis machine quicker, no pain, no needles, no large bump on their arm, and no waiting around after dialysis to hold needle sites [15].				

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=5)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
		Patients who converted from catheter to fistula reported being able to swim and shower better, not worried about infection, and not having a tube coming out their chest [14]. 33% of carers felt unprepared to deal with symptoms experienced by patients having chemotherapy at home [16]. Many carers had unmet needs regarding financial support [16]. Diabetic patients of white origin reported greater satisfaction with continuous subcutaneous insulin infusion (SCII) [17]. Diabetic patients of black and ethnic background reported greater satisfaction with multiple daily insulin injections (MDII) [17]. Both groups of diabetic patients reported increased dependence [17]. SCII scored significantly higher that MDII and age does not reduce possible impacts [17].				

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=5)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
		CSII enhanced the independence of significant others (SO) [17]. Around one-third of SOs did not know how to suspend CSII if the patient became hypoglycaemic [17]. Patients preferred home treatment because they did not have to travel to hospital, take time off work, or lose money, and it meant their sleep was not interrupted [19]. Patients preferred home treatment as it meant their relatives did not have to spend their time visiting hospital [19]. 26/49 patients held positive perceptions of home haemodialysis (HHD) [20]. Patients expressed shock on hearing they needed a blood transfusion [21]. Patients viewed blood transfusion as slow, tedious, lengthy [21]. Most patients unaware their kidneys were failing, and referred to their illness as kidney trouble [22].				

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=5)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
		Most patients said their kidney disease was identified through a series of routine tests by GP [22]. Patients experienced a lack of specific symptoms to indicate kidneys were failing [22]. Some patients believed their kidney disease was hereditary, others said it was the result of alcohol or medication [22]. Some patients said they did not know why they had CKD [22]. Patients recognised the decision about dialysis was theirs and they took responsibility for it [22]. Patients saw their choice as being between haemodialysis (HD) and peritoneal dialysis (home dialysis) (PD), but they made no distinction between the different types of HD and PD Patients evaluated both HD and PD positively and negatively but were more negative about PD [22].				

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=5)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
		Patients saw the advantage of HD as having days when no dialysis would be required, they would be supported by hospital staff, and they would not need a general anaesthetic to create a fistula [22]. Patients saw the advantage of PD as flexibility of treatment, fitting their treatment into their work commitment, lack of dietary restrictions, and having treatment at home [22]. Disadvantages of HD identified as inflexibility, side-effects, dislike of needed, needing a minor operation to create a fistula [22]. Disadvantages of PD identified as having a catheter in the stomach, needing anaesthetic, having to store boxes of fluid, having to be responsible for treatment, potential for infection, and concerns related to work, going on holiday, coping with treatment [22].				

Patient participation	Responsiveness	Lived experience	Continuity of care and relationships	Communication	Information	Support
[1,21) (2/22) (High=2)	(1,2,5-7,10,12,15-21) (14/22) (High=6; Med=4, Low=4)	(1-5,7,9,10-22) (20/22) (High=12; Med=3, Low=5)	(0/22)	(1,2,5,8,9,11,13,18-22) (12/22) (High=8, Med=1, Low=3)	(1,2,4,5,8,11,13,18,21,22) (10/22) (High=6, Med=1, Low=3)	(2-6,8-9,11,13,16,18-21) (14/22) (High=11, Low=3)
		Patients were unable to say explicitly how they were able to make a trade-off between the pros and cons of HD and PD in order to make a choice [22].				

Appendix 6: Exploration of each theme/sub-theme

Theme 1: Lived experience (20/22 studies)

Lived experience is defined as reflecting a view that those living with a particular condition will experience it in a unique way, and that a patient's family and broader life must be taken into account since lived experience can affect self-care. In addition, there also needs to be an acknowledgement that while patients' lived experiences originate outside of health care they are brought into the health care system and can be affected by other experiences and the attitudes and expectations of health care professionals (Staniszewska et al., 2014).

Patient encounters with a range of infusion therapy treatments include their experiences, preferences, living a restricted or lost life, dealing with dependency and loss of freedom, and how their self-perception may impact on their experiences. There are overlaps between these elements of the patients' lived experiences with the WaPEF themes responsiveness of services, patient participation and communication.

Experiences

A large number of studies report patients' experience in terms of how they felt about their need for infusion therapy[1-3,5-7,9-22]. Patients expressed a range of feelings that can be viewed along a continuum ranging from a complete loss of control to taking control. Some of the terms used by patients include fear, anger, depression, anxiety, trauma, hopelessness, incapacitation, isolation, guilt, denial, powerlessness, shock, grief, and loss of control.

> "…Feeling useless, that you're no good for anybody…I've always been independent…Ever since I've been sick I've been relying on my family to keep me going….f***ing useless. I should have died and it would have been better for everybody…"[11]

Patients also talked of acceptance, hope, adjustment, staying positive, reaching an understanding about their altered life, and taking control of their situation.

> "At the beginning I thought this can't be happening to me. But now it's just something that happened. I actually feel like I've gained rather than lost something with dialysis. As I lost my kidneys I found my family and things I'd forgotten to cherish in my life. This change in attitude is like seeing every cloud has a silver lining."[18]

Feelings of shock and grief appear to be experienced primarily by patients requiring dialysis treatment[11,18,22]. These were expressed not only in terms of the treatment, but also in relation to coming to terms with knowing you have a life-limiting disease, one that not only required a life-saving therapy, but one where any hope of living a normal life may only be realised through a kidney transplant[2,18].

> "Sylvia was shocked by what she perceived as unexpected invasive medical management…. Carer Janelle related a lack of understanding of her husband's kidney disorder…Sarah…was forced to confront the immediacy of dialysis… and was overwhelmed and fearful of lifelong incapacity or early death……the shock resulting from the sudden need for dialysis, and confronting the possibility of death, turned people's world upside down."[11]

Preferences

Patients' reported preferences are identified as both facilitator and barrier, as they do sometimes appear to conflict with professionals' preferences[1,2,15,22].

> "They [the health care team] want a fistula…I think it is much better with a catheter; it is much faster to attach and remove, and there is no bleeding."[1]

Aasen et al. (2012)[1] suggest that even though patients prefer the catheter over the fistula they were not given a choice; professionals favoured the fistula as it was associated with fewer infections and better dialysis. However, from the patient perspective the catheter was the preferred option because it offered a better quality of life.

Differences in preferences are also evidenced in a study reporting patients' unwillingness to convert to arteriovenous grafts (AVG) or arteriovenous fistulas (AVF), even after being informed that the former type of treatment is more effective than the central venous catheter (CVC) route[15]. Patients' refusal to convert from CVC to AVF/AVG could be viewed as a barrier from a professional point of view because it impacts on the delivery of what is described by the researchers as a more optimal form of vascular access. However, from the patient's viewpoint, the decision to remain with a CVC arose primarily from concerns about needles, pain and the appearance of a fistula. Other studies exploring patients' decision-making about whether to have haemodialysis in hospital or peritoneal dialysis in the home cited similar concerns with needles and fistulas[2,22].

> "The main thing about haemo is sticking those needles in. I don't like needles."[22]

The reasons why some patients prefer home treatment and some do not appears multi-factorial[2,5,22]. For patients requiring dialysis home treatment has been identified as both a facilitator and a barrier. It is a facilitator because it means patients do not have to have a fistula, it allows the opportunity to carry on working, it means no admission to hospital, no travelling for treatment, and it offers patients greater control over their lives.

> "I thought…I'll have the HD because its less hassle for me, somebody else can do it and then I thought about it…I'll have to rely on other people to do it…the other one (PD) is better for me in the long run because I'm in control of it."[2].

The identification of home dialysis treatment as a barrier is linked to patients' described anxieties around the threat of peritonitis[2], and the

medicalisation of the home[2]. The threat of peritonitis was identified as a concern for some patients and has been identified as "the major cause of home dialysis failure"[2].

Baillie and Lankshear (2015)[2] describe the medicalisation of the home as something that impacts on the homes of all patients because it alters their living space

> "Signs of Laila's dialysis were evident throughout the living room…a metal drip-stand with hanging weighing scales, a grey plastic organiser…for the dialysis system…a small box of caps to cover the end of the Tenckhoff catheter."[2]

In addition, preference for home-based care often results in increased responsibilities for patients, carers and families and clinicians need to make this known to patients when discussing treatment options. Patients reported a preference for home care primarily because it offered them a greater sense of control and autonomy, even though it does involve substantial daily work, even though patients were often modest about their abilities to manage self-care in the home[2].

> "…it only takes 10 minutes…do your blood pressure…take your blood…and I mean jump on the scales is nothing at all."[2]

Barriers to home dialysis have also been identified as requiring a significant amount of "varied medical paraphernalia"[2] a finding supported by Combes et al. (2015)[5] who also identified housing, space at home, ordering, installation of dialysis machines, lack of training of non-specialist staff, and limited professional recognition of patients' emotional and psychological needs.

Studies exploring patient experiences of other infusion therapies in the home or near to home reveal how patients expressed preferences for blood transfusion therapy[14], and community intravenous therapy[16]. Patients receiving blood transfusion in a hospice setting identified advantages as less travelling and waiting time, better parking, more time to talk, and not having to rely on public transport.

> "Well it's calmer in the atmosphere….You [at the hospice] answer a lot more problems….The staff at the [hospital] were rushed off their feet."[14]

Patients prefer receiving intravenous therapy in the community and cite similar benefits to those reported by Orme (2013)[14]. Additional benefits include not having to be admitted to hospital, not at risk of hospital acquired infection, needing less time off work, being able to sleep in their own bed, and eat their own food.

> "I am much better off being at home, as opposed to being in hospital and maybe picking something up…it's nice to have my own food…being able to sleep, [hospital] is boring and frustrating."[16]

Differences in preferences also shine a light on the way professionals appear to emphasise a need to meet patients' clinical needs[1,2,15,22], whereas patients appear to prefer treatment options that are a better fit with their personal needs and lifestyle, and which allow them greater autonomy and control. In an expert patient narrative Hope (2013)[8] argues there is a need for decisions about different treatment options that focus more on patient's lifestyle and quality of life, and not just clinical need.

Living a restricted life

Patients receiving dialysis treatment reported perceptions of how their illness and treatment led them to experience restrictions in both their personal and social life. Requiring dialysis, whether in hospital, or at home, meant patients not being able to travel to go on holiday, and not being able to participate in paid employment.

> "I'm not working…I get part superannuation and part disability…I have assets which bring me over the threshold, I have liabilities like mortgages, investments so I'm going to have to re-look at my finances…I don't have anybody else to rely on."[11]

Patients also spoke of how a diagnosis of kidney disease requiring dialysis treatment resulted in losing their home, leading them to experience further loss of freedom and further limitations placed on their income.

> "I've had to put my house up for sale because otherwise I'm not going to be able to afford to pay the mortgage or anything, so I've had to make that decision."[22]

Patients also worried about the impact their illness and treatment had on families and friends, with both patients and their carers reporting how illness and treatment can have a negative impact on their relationships.

> "I feel guilty 'cos I was Dad's girl…I would have walked over hot coals for my father…he expected nothing…but Mum expects everything.., she's good at emotional blackmail…she's just transferred her dependency on Dad to me, she said if you put me in a home I'll starve myself."[11]

Carers also spoke of the futility of treatment and loss of hope.

> "I don't think I saw any improvement…I hope of course. I usually say I'm glad I don't know anything about tomorrow, because I don't want to. And at the same time you have to take each day at a time and live it. And then…then we hope it will get better…I can't do anything more…."[4]

This sense of a restricted life is reported in 8/10 of the papers reviewed in a meta-synthesis of the lived experiences of dialysis patients undertaken by Bayhakki and Hatthakit (2012)[3].

> "[A physical shackle] was reflected as physical limitation…lack of energy...weakness…[feeling] tied down….left out…shackled…physical fatigue…reduced functional capacity…limits on travel, restricted diet, limited income…inability to perform

activities, roles or responsibilities…[also linked to social aspects]…restrictions on social life, dependency upon others…..limited social contact."[3]

Dependency, loss of freedom and control

Patients experienced a loss of freedom primarily because they felt they became much more dependent, not only on health professionals and close family members but also, for those requiring dialysis, on the dialysis machine. This increase in dependency also led to a loss of sense and a loss of self. This is described by Monaro et al (2014)[11] as patients' experiencing 'a lost life'.

> "The essence of the experiences of this lost life…..were well developed and richly described by participants…confirming end stage kidney disease as a family experience…a lost life sits in contrast to what some might expect as a relief associated with like-saving treatment…the losses are multifactorial: physical, emotional and social."[11]

Dependency and reliance on the dialysis machine is a key theme identified by Bayhakki and Hathakitt (2012)[3] and was identified in 4/10 papers they reviewed. They argue that the machine cannot be separated from the patient's life and patients reported both positive and negative associations with the dialysis machine.

> "The haemodialysis machine was created to give advantages to patients…but the patient's point of view and their level of knowledge about the machine influence how they view, perceive and respond to their need for the machine…a positive view may be create a positive impact….a negative view may create a negative impact…physically and mentally."[3]

Patients' self-perceptions and characteristics

In one small high quality study[1] patient reports indicate the potential way in which their self-perceptions and characteristics may impact on their experiences. In sharing their experiences of dialysis elderly patients often referred to themselves in disparaging terms, reporting how they felt imprisoned and speaking of how they both trusted and feared professionals. According to the authors this combination of trust and fear can create passiveness and become an obstacle to dialogue and shared decision-making. The authors argue that this happens because long term dialysis patients reported powerlessness and objectification. The authors go further and suggest that patient's identities are influenced by the paternalistic culture of the dialysis unit.

> "They have probably got tired of me after all these years. Probably they are aren't interested anymore. It's like I've become a piece of furniture….I feel like I have really become isolated…I lay like a package."[1]

Theme 2: Support (14/22 studies)

This theme has been defined as support for self-care and individual coping strategies, emotional, practical and peer support, education and the need for hope, and inclusive of support from carers, friends and families who may act as advocates for the patient (Staniszewska et al., 2014). The key elements in this theme include support and networking provision for patients and carers, the role of nursing, and support for shared decision-making[2-6,8-9,11,13,16,18-19,20-21]. There are overlaps with this theme and the themes of lived experience, responsiveness of services, communication and information.

Support and networking provision for patients, carers and staff

For patients who choose home dialysis Combes et al. (2015)[5] argue the need for support on several levels. Firstly patients need support to help them make decisions about whether or not to choose home dialysis, and if they do choose home dialysis then they require further support and training to use the dialysis machine and ensure they are competent to self-care at home. Thirdly, patients will require on-going technical support once on home dialysis, and lastly they will need emotional and psychological support to help them adjust to end stage kidney failure. Although patients reported the availability of technical support and training on the machine, they did report shortcomings in the provision of emotional and psychological support.

> "I have to admit for the first 12 months or so I found it very, very depressing. I couldn't get my head around it with these big bloody needles going up in my arm, maybe for 10 years or so."[5]

The authors conclude that supportive emotional and psychological care is critical.

> "…it helps patients during a difficult transition in treatment, potentially reducing depression and improving a sense of well-being [and to ensure patients are] supported emotionally if they are to think through a difficult treatment choice….and taking on the undoubted challenges of home-based self-care."[5]

The importance of practical, emotional and psychological support is also highlighted in a study of carers looking after patients receiving home enteral tube feeding[4]. Carers struggled with loneliness and a loss of togetherness and closeness.

> "He sits by himself upstairs…I sit down here…it gets very lonely…I have tried to talk to him about it….but he only said I must think about him…since he is ill."[4]

In addition carers spoke about how they had to endure this new life situation without any support for, or recognition of, their caring role[4,16].

> "I don't want to live life like this because this is not a normal life…I become very listless…I feel a little depressed…will this never end?."[4]

Bjuresater et al (2012)[4] report that carers have identified a considerable need for support from the health care system, and they would benefit from a range of psychological, emotional and instructional support and counselling in order to function in their role as informal caregivers. Ream et al (2013)[16] conclude that there is a need for interventions to prepare and support informal cancer carers and legitimise their caring role. They further suggests that such interventions should be

co-designed with informal carers in order to determine feasible, acceptable and effective packages of care for delivery in a chemotherapy day care setting. However, the authors report that no such interventions have been trialled in a chemotherapy day unit.

The losses expressed by patients coming to terms with haemodialysis[11] signal a need for increased psychological support during the early stages of dialysis because it can help patients develop coping strategies. However, Monaro et al. (2014)[11] report how patient and carer support networks were not visible to many patients but which many felt would be beneficial both before and after dialysis. In addition many patients reported a desire to have their relatives present in the early stages of haemodialysis and the authors conclude this creates a perception of immediate support, and has:

> "…important implications for dialysis unit design and culture, including issues of available space and staff receptiveness."[11]

A study exploring the patient's perspective on community intravenous therapy (CIVT)[19] suggests that CIVT provides a potentially unique opportunity for district nurses to increase their skills in an area that has long been the domain of the acute sector. The study also identified a need for the provision of support and training for district nurses focusing on the theoretical and the practical aspects of intravenous drug administration.

The role of nursing

Research by Bayhakki & Hathakit (2012)[3] and Shih et al. (2011)[18] identified the key importance of ensuring that patients receiving dialysis live as full a life as possible, and they identify nurses as playing a key role in supporting patients through exhibiting a clear understanding of the emotional, psychological and social needs of patients and their families. To do this, nurses have a responsibility to improve their own knowledge and that of their patients through the provision of adequate time, materials and health education programmes. They conclude by suggesting that nurses should understand patient's limitations and problems and should consider these when planning and providing nursing care for patients receiving haemodialysis.

Bjuresater et al (2012)[4] identify a role for nurses in meeting the support needs of informal carers and patients through an extension of nurse-led clinics. Nurse-led clinics are identified as being useful for groups of patients in identifying problems early and finding interventions that prevent problems from becoming too big. They argue for an extension of the nurse-led clinic to include close relatives and the provision of support and counselling.

Research undertaken in New Zealand[18] identifies the role of nursing in supporting patients on dialysis as multi-faceted. In addition to the provision of education and health promotion, nurses also need to:

> "…recognise a person's ethnicity, life and social context when considering goals for short term care and long term management."[18]

The study by Weiss & Tolich (2011)[21] on patient experiences of blood transfusion describes how patients identified nurses as supportive, knowledgeable, attentive and reassuring.

> "I remember the nurse telling me about the itchiness….the [nurse] just hooked it up and it went so smooth…I had never had a blood transfusion before and all the things you hear made me panic…but she was so good it was no big deal…she asked me if it was as bad as I thought it would be, and it wasn't…"[21]

The authors suggest that patients were helpful and they were reassured by the nurse's adherence to procedures, and it was nurses who provided patients with support, education, and safety monitoring.

Support for shared decision-making

According to Hope (2013)[8] genuine shared decision-making is only possible when patient's needs and quality of life are at the heart of discussions with professionals about self-care. The support needed to move from clinical decision-making to shared decision-making in that study included a requirement for peer support, web-based personal digital assistants (PDA) and 15-minute clinical consultations.

Theme 3: Responsiveness of services (14/22 studies)

This theme has been defined as recognizing the patient as an individual and tailoring services to respond to patients' needs, preferences and values. It also includes how well clinical needs are met and postulates that evaluations of how well services perform should be undertaken from a patient perspective (Staniszewska et al., 2014).

Key elements under this theme include education and training for patients, carers and staff, unmet patient needs and the role of nursing[1,5-7,10-12,15-20]. There are some overlaps between this theme and communication, information and support.

Education, training, and preparing patients, carers and staff

Training and support systems for patients in receipt of home dialysis treatment was identified as a facilitator by Combes et al. (2015)[5], while a key barrier was identified as a lack of training for non-specialist staff.

> "…it was actually one of the health care assistants, I was asking her about something and she said "Oh, I don't know why you're bothered about asking for, you're not going home…" and I was completely…shot down in flames…I'm asking because I'm interested in it…I mean for some people they just go "Ok, well I won't bother asking then."[5]

Patients were identified as being fulsome in their praise in terms of the training and preparation they received prior to home dialysis. They were also

offered support via telephone or through home visits and outpatient appointments.

> "…they'll say some patients need three days [training], some need seven and some people need two weeks……So it's quite good really."[5]

A study exploring the patients' perceptions of the dry weight concept identified a need for the provision of patient education on fluid management. This is seen as important because some patients did not appear to pay attention to dry weight, or they misunderstood its significance in terms of fluid control and self-care strategies for patients in receipt of dialysis.

> "I don't think about dry weight…..I guess it's some weight you should be at that they [the staff] are interested in…..it means the combination of blood pressure and weight it's just a target and really it's only your blood pressure that matters."[10]

A phenomenological study[11] reports that patients with end stage kidney disease and their families require significant preparation in order to understand the considerable emotional and physical challenges associated with a treatment regime that is invasive, restrictive and painful.

> "Often the diverse needs of people and families experiencing haemodialysis exceed the capacity and scope of practice of the haemodialysis team, particularly the … nurses…this underlies the benefits of interdisciplinary and social input."[11].

In one survey[12] exploring chemotherapy patients' satisfaction with a totally implantable venous port system, the authors report how most patients were satisfied with all aspects of the port system other than the cosmetic result. This may point to a similarity in views already reported in terms of patient preference and the impact that treatment has on a patient's quality of life.

> "Overall it was found that the cosmetic result of the implantation procedure was a predictor of satisfaction and ...quality of life and should not be underestimated."[12]

A cross-over study exploring the reasons why patients fail to covert from catheter-dependent dialysis to arteriovenous access[15] highlights patients' concerns about the impact of treatment and how it influences their choices. Even though arteriovenous access is identified as the most optimal form of vascular access patients were unenthusiastic about switching from the catheter.

> "…there is a need to develop a better understanding of the patient's perspective and possible psychological factors affecting patients' decisions if we are to have an impact on the high central venous catheter use prevalent in Canadian patients."[15]

A survey investigating carers' needs and experiences when caring for patients receiving chemotherapy at home[16] reported that one-third of carers felt unprepared for dealing with the role. Carers reported a lack of information, or being given inadequate or inappropriate information, together with limited opportunities to speak to health care professionals.

> "The patient receives a package of information….the carer…never receives a package that caters to the needs of the carer, what to expect and how to deal with symptoms…"[16]

The author suggests there is a need for a range of interventions to prepare and support carers and to recognise and legitimise their caring role. Such interventions could include nurse led tailored support programmes to address informal carers' information, emotional, social and practical needs[16].

> "When you're within these four walls, there's no escaping…I felt like I wanted to run away…I found it all a bit too much."[16]

A study investigating the impact of dialysis on rural Maori patients in New Zealand recommends the need for early referral and effective education provision in order to promote self-management, which in turn will influence quality of life and lead to more cost effective health care[18].

Unmet patient needs

In addition to the potential conflict existing between patient preferences, which were focused on issues surrounding personal needs and quality of life, and those of professionals, which were focused primarily on meeting patient clinical needs1, a high quality mixed methods paper by Combes et al. (2015)[5] identified a key barrier to home dialysis treatment as considerable unmet emotional and psychological patient needs, which they described as significant and striking. Over one third of patients needing dialysis found it scary and traumatic, which made it very difficult for them to adjust emotionally and psychologically.

> "I went through a period towards the end of my preparations for dialysis where I had to go to the doctor with depression because I was just so unhappy because I felt sick every day and my whole life just kind of crumbled around me really."[5]

However, Combes et al. (2015)[5] report that there was almost a complete absence of service responses to this kind of patient distress, and none of the hospitals had adapted their pre-dialysis pathways or their training processes to deal with it, nor had they put any support mechanisms in place other than a referral to a psychiatrist or a psychologist for depression. This was in direct contrast to what patients wanted, which was less focus on the medical aspects of their illness, and the provision of more time to talk and be listened to.

> "…they focus totally on the practical…Have they done it? Why haven't they done it? You're going to die if you don't do it…No disrespect but sometimes you don't want to tell them you've got a problem…[There's] a huge mental side to it…a psychological element that they probably don't press."[5]

The role of nursing

A study exploring patient and family perspectives on home dialysis[2] reports on how patients had to learn a range of skills for managing their dialysis,

and how specialist nursing services provided a structured education programme, either in the home or the hospital. Patients credited the nursing staff for their teaching expertise.

> "They make you very aware of how serious it is….it was quite a big thing to learn how to do dialysis."[2]

Patients receiving intravenous therapy in the home[19] reported how they appreciated and valued the work of the district nursing team in delivering their treatment, and the author reports that patients found this cathartic and not just perfunctory.

> "They came and they did it and we had a laugh while they were there, between us."[19]

Patients also flagged up some issues they had in relation to safety, not least the lack of explanations about their care and treatment at home, which made them feel apprehensive and frustrated.

> "…she didn't explain it all…it is as if she thought I knew and I had never heard of this before…so it was a bit confusing…it was a bit strange."[19]

Patients reported their perceptions about the district nurses' ability to administer the IV treatment safely, expressing concerns over hand hygiene and aseptic technique. They also reported inconsistencies about the way the treatment was administered in the hospital and in the home, specifically in the way IV antibiotic was administered as a bolus in hospital and an infusion in the community. Some patients expressed an opinion there was some inconsistencies in the training of district nurses in the community that perhaps district nurses' training was inconsistent, and as a result they felt less confident.

> "[nurses fresh from secondary care]…were on track. They knew exactly the latest thinking, how it should be done. Whereas perhaps the nurses from the community were lacking in that knowledge…" [19]

Theme 4: Communication (11/22 studies)

Communication has been defined in terms of style, format, skills, characteristics, and use of body language that enhances communication and shared decision-making, compassion, empathy. It also includes the development of consultations that optimise time for questions to be asked and answers to be given, listening and paying attention to the patient (Staniszewska et al., 2014)

Key elements under this theme include one-way communication, lack of choice regarding treatment options, time, the role of the nurse, and patients' decision-making processes[1-2,5,8-9,11,13,18-22]. There is overlap between this theme and the themes of responsiveness of services, support, information and patient participation.

One-way communication

In the Aasen study (2012)[1] the authors argue that patient's use of metaphors like "jail", to describe the unit, "guardian" to describe the nurse and "furniture" to describe themselves depicts a context in which professional dominance and control makes one-way communication common practice.

> "One would think that it would be in their interest to know what we think [but] it is much one-way communication…I haven't experienced being asked about how we feel about different things."[1]

According to the authors the way the patient use the word "he" instead of "I" demonstrates how the patient wants to distance themselves from professional dominance and control. They also suggest that patients' struggle to be included in shared decision-making was challenging because they had to argue against the professionals view of what was the best treatment. One-way communication can also be discerned in the study by Weiss and Tolich[21], in the way that patients reported decisions were communicated to them.

> "They just came up to me and said you're getting a blood transfusion…it was kinda fast."[21]

In a study undertaken by Shih et al. (2011)[18] the ways patients describe hearing they needed dialysis talked of facing their fear, whilst also intimating that the way the news was delivered did not provide much opportunity to ask questions.

> "When the doctor told me…I didn't know what it meant. I didn't want to go to hospital but he said if I didn't I would die…that's what frightened me to go…A doctor had warned me earlier…that my kidneys were only functioning at 70%...I wasn't sure if my kidneys were failing. I never questioned him."[18]

Research exploring patients' experiences of peripheral intravenous central catheter therapy[13] highlights how one-way communication can be facilitative because it allows patients to withdraw from the decision-making process as a coping strategy for dealing with their treatment.

> "I think I handle things better when I don't know too much detail."[13]

Lack of patient choice regarding treatment options

Patients undergoing treatment for end stage kidney disease need considerable preparation for haemodialysis and Monaro et al. (2014)[11] argue that decisions about dialysis treatment options must be a collaboration between patients, relatives and clinicians. However, many patients report a lack of treatment options which has been linked to contraindications, physicians' preferences and resource constraint. These all serve to create additional barriers to treatment choice and issues related to home versus hospital treatments. Furthermore, the authors argue:

> "…the rapidity of the pre-dialysis decline was also a major factor."[11]

Weiss and Tolich (2011)[21] argue that whilst alternatives are addressed on blood transfusion form, when patients' were asked about what alternatives they had been offered most of them reported none were offered.

> "They just told me that was what I was gonna get...[when a patient asked about alternatives they were told] that medications, unlike transfusions, would take, like, three months."[21]

Baillie and Lankshear[2] report that patients rejecting hospital dialysis treatment did so because they felt peritoneal dialysis treatment at home offered them greater control and autonomy. This finding was also reported by Fex[6]. However, there are significant challenges in delivering home treatments, as discussed above under medicalisation of the home, and it is important that the implications of all the different treatment options available are discussed with patients, carers and relatives[2,6].

Patients participating in a study exploring patient choice of treatment perceived decisions about options as easy; for patients, the difficult choice was in deciding whether or not to have dialysis teatment[22]. The authors argue that this contrasts with the view of professionals who see the decision as making a choice between different types of dialysis, and they go on to suggest that information is the key in helping patients understand their kidney disease and treatment options, and is discussed further in the section below on information.

Time

The majority of patients reporting their experiences of receiving blood transfusion in a hospice setting spoke of how there was more time for them at the hospice. While they believed staff working in the hospital were very caring, they had less time to talk than the nurses working in the hospice[14]. Conversely patients participating in a study exploring blood transfusion in a hospital setting[21] reported how discussions were constrained because doctors were too busy to talk to them about the risks and benefits of blood transfusion.

Patients undergoing home dialysis reported lack of time as a barrier in having their needs met[5]. They wanted staff to talk to them about the wider impact of dialysis on their lives and they wanted to talk and be listened to.

> "Some patients need listening to…they just need 5 minutes to explain how they're feeling about their illness."[5]

The role of nursing

There was a recognition by patients that a positive style of communication from the nurse made them feel more comfortable and calm. When nurses provided clear, concise explanations this resulted in patients experiencing reduced levels of anxiety about the procedures they were undergoing. Effective nurse communicators were able to reassure patients throughout the process whilst explaining the risks and benefits and simultaneously settling the patient down[13].

> "She was sort of nice…just more relaxed…she explained everything…she took away some of the anxiety…she asked me if I had any pain…. she told me what it was all about...the nurse calms you anyway…once I was on the bed I settled down."[13]

Patients undergoing blood transfusion said that nurses, more than other clinicians advised them about the benefits of transfusion, and they felt nurses were attentive and supportive during the procedure[21]. Nurses also provided patients with options regarding treatments, and while the authors argue that it is unclear whether this was used as a technique by the nurse to get the patient to have the transfusion nevertheless the nurse did act as both educator and adviser and patients did appreciate being invited into the decision-making process.

> "I asked the nurse why I was getting blood and if I really needed it. She said my blood counts were very low and that was why I was tired. So this would make me feel better."[21]

Patients' decision-making processes

Two qualitative studies rated high quality[1,5] reveal how patients and professional appear to hold alternative views on how patients make decisions about treatment. Staff appear to describe a rational weighting of available options that is based on available information, whereas patients described a more personalised approach in terms of how they thought about their own lives and how different options might work for them. Some patients described a gradual process of decision-making and spoke of only becoming interested in home dialysis, and yet none of the hospitals participating in the Combes et al. (2015)[5] study had built routine reviews of treatment choice into their dialysis pathways.

Theme 5: Information (10/22 studies)

Information is defined as that which enables self-care and active participation in health care; it should provide opportunities for shared decision-making, and it should be tailored to suit individual patients, taking account of both patients that want information and those that do not want information. It should also be timely, relevant and offered in different formats (Staniszewska et al., 2014).

Key elements of this theme include the provision of timely and relevant information, complexity of information, seeing other patients as a source of information, and the nurse's role1,[4-5,8,10-11,13,18,21-22]. There is overlap with this theme and the themes of communication, responsiveness of services, support and patient participation.

Timely and relevant information

While some patients reported satisfaction with the information they received, some described information overload[5], some wanted relevant, timely, practical information[1,8,11,13,21], and some reported a lack of information[4,18,21].

Carers looking after patients received home enteral tube feeding[4] reported a lack of information from the health care system about what was expected of them in their role as informal caregivers.

> "…So, no written information, no information at discharge, there was nothing! So we did not know what we should do, and when the feeding formula began to run low, we did not even know where to get it."[4]

Weiss and Tolich[21] argue that it is common practice for patients receiving blood transfusion to get written information about the risks and the benefits. One patient said they got the information but were too ill to read it, whilst others said they were shocked to hear they needed a transfusion, and only realised when the nurse:

> "…walked into the room with a bag of blood in one hand and a consent form in the other."[21]

In terms of the information needs of patients making a choice between dialysis treatment options, and because patients often make their decision over a protracted period of time, Winterbottom et al. (2012)[22] argue that patients are exposed to biased information and this can be countered by the use of decision aids.

> "Techniques exist to help people engage actively with information about treatment options which enables them to evaluate the advantages and the disadvantages of options in accordance with their lifestyle and values. These…can help de-bias the information patients encounter and help them to make informed decisions."[22]

Complexity of information

According to Combes et al. (2015)[5] patients found choice difficult given the range of treatment options and the complexity of information. Some reported information overload, and others acknowledged that whilst information was important its application to their lives was more important.

Other patients as a source of information

Patients talked of other patients as a source of information about the specifics of dialysis and they were particularly interested in their skills in carrying out the dialysis, how they were able to integrate the treatment into their daily lives and hearing what they could tell them about travelling, hygiene, dietary restrictions, timing of treatment and pain[22].

> "…being taken through each stage and then actually talking to people that actually had the treatment …that was absolutely marvellous."[22]

In a study exploring home dialysis[5] none of the patients said they had been offered peer support, yet one of the most common suggestions they offered about improving the service was the opportunity to get information from other patients about their experiences of home dialysis.

> "Speaking directly to someone who has had it [dialysis] so you're getting all the unfiltered information…it was useful to be able to speak to a person who had gone through that to give us, you know, warts and all."[5]

The nurse's role

Nurses were identified as the person who told patients they would be receiving a transfusion most of the time and they were seen as the primary source of information. Nurses also were the ones who told patients that they would feel better after the transfusion, and were identified as providing accurate information[21]. The authors conclude that patients may need further information before, during, and after the procedure.

> "Handing out a brochure is insufficient…the interaction with practitioners, especially nurses, was most helpful in reassuring and educating patients."[21].

Theme 6: Patient participation (3/22 studies)

Patient participation is described as reflecting the role of patients as active participants, co-creators and co-managers of their health care and their use of services. It is associated with issues of power and control (Staniszewska et al., 2014). The key elements of this theme are the struggle for shared decision making, and professional dominance and control which includes the concepts of trust and paternalism[1,4,21]. There are overlaps with this theme and the themes of responsiveness of services, support, communication and information.

Struggle for shared decision-making

Aasen et al (2012)[1] report that long term patients with higher levels of education and those from a higher social class appeared to struggle to be heard in the patient-professional encounter. In particular, they felt it was a constant effort to be heard during their discussions with the health professionals about blood access, dry weight, diet and time of treatment.

> "…you are supposed to really follow [the diet] regime [but] I would rather cut a couple of years off my lifespan…There is almost nothing you could eat…I certainly don't want to become worse/more ill because of that……you can't even take a slice of bread with cheese….I don't say that I just don't care…but they observe…test reports…phosphate…calcium…then I get scolded a bit…they say…pull yourself together; this doesn't go well. Now you destroy your years…but this is my choice……We don't do it…I am not able to do this."[1]

Patients did not always agree and while they attempted to argue their case they reported difficulties getting their opinions across. In terms of diet for example the key concern of the health professionals was in ensuring patients had a longer life so they would stress the importance of compliance, whereas the key concern for the patient was maintaining the quality of whatever life they had left. Given their struggle to be heard some patients reported resignation and simply did as they were told.

> "When I had a lot of water removed I feel awful afterwards…[but] it's decided for us…I think…my dry weight should be increased…but it's not easy to get approval for that…I just do what they say."[1]

Professional dominance and control/ paternalism [1,21]

Professional dominance, described by Aasen et al. (2012)[1] as "the power in the interaction between the health care team and the patients" was apparent in the experiences of patients and in the words they used when telling their stories. Patients spoke of how "professionals decide" and "always" when speaking about the health care team. When

patients talked of themselves they used words like "must", "should", "accept", "trust", which the authors argue might say something about the powerlessness of patients. Patients also used metaphors to describe how they felt referring to the dialysis unit as "jail", "prison", identifying the nurse as "guardian", and referring to themselves as "furniture", "package".

Whilst all patients reported trusting health professionals, longer term patients who had become accustomed to living with their disease reported feeling more fearful about what would happen if they did not do as they were told. Patients who had experienced less than two years living with their disease reported feeling more trustful and accepted the idea that the health care had to dominate. However, when talking about participation, patients tended to shift from using "I" to using "we", and the authors argue this combination of trust and fear has the potential to create passiveness and become an obstacle to dialogue and shared decision-making.

> "I have to say that when you start dialysis you must accept what they think……The people who treat you are professionals. These doctors always think they ought to decide and that I should listen to them……you should listen to them because they know what they're doing. Even if we want to decide what should happen it doesn't mean that we could…"[1]

Professional dominance and control exercised through the ideology of paternalism was also highlighted in a study exploring patients' perceptions of blood transfusion[21]. The authors define paternalism as the practices by which the physician makes a decision on what they think is best for the patient. Throughout the study patients reported how the doctor made the decision to transfuse and because they trusted the doctor they did not question medical decisions.

"There's no question…the doctor says you need it…you need it….I trusted the doctors were doing what they were supposed to do…I didn't question the fact……or the whole process in general."[21]

Theme 7: Continuity of care and relationships (0/22 studies)

Continuity of care has been defined as initiating contact with services, interpretation of symptoms, coordination, access, availability of services, and responsiveness of services. It is associated with treating the patient as a person not a number, maximising trust in health care professionals over time, facilitating the recognition and the questioning of professional expertise, and recognising the patient's knowledge, skills and expertise (Staniszewska et al., 2014).

No findings were mapped against the theme of continuity of care and relationships in this review. However there are overlaps between patient participation, responsiveness of services and support and continuity of care and relationships in the definitions of themes and some of the findings.

Section 5 : Summary of evidence and implications

Contents

Section 5 authors – Toni McIntosh and Anda Bayliss

Introduction

The scope of this review was to update the standards for infusion therapy, last published by the Royal College of Nursing (RCN) in 2010. The specific aims were to identify areas of infusion therapy practice with robust, promising, or no evidence, and evidence identifying harmful practice. A further objective was to identify gaps in the literature and agree on where professional consensus is required.

The decision to conduct a rapid evidence assessment (REA) was made in order to ensure a rigorous and systematic search aimed at identifying all relevant evidence, under the constraints imposed by the time and resources available.

The resulting evidence review comprises three strands:

- evidence obtained from randomised controlled trials (RCTs) and systematic reviews (SRs) (Phase 1)
- evidence obtained from the consideration of the body of evidence from other quantitative study designs (Phase 2)
- evidence relating to the patient perspective of infusion therapy.

RCTs are widely accepted to provide the gold standard of evidence to inform practice[33], however in nursing it is not always practical or ethical to conduct this type of study. The inclusion of non-RCT evidence, therefore, ensures all relevant studies are included in order to provide a broad evidence base to inform the revision of the standards.

There is a clear shift towards increased patient involvement in their care[36,84] and this should extend to decisions about infusion therapy. For this reason the review of evidence relating to the patient perspective is included to increase understanding of the implications of taking into account the barriers and facilitators, identified from examining the patient perspective, in the delivery of a range of infusion therapies.

A key indication for the revision of the existing standards was the changing landscape of how care is delivered. Traditionally associated with the acute hospital setting, infusion therapy is now increasingly delivered in community and rural settings, as well as self-administration in the home by patients and carers. Consequently, this review aimed to include evidence from a variety of settings in order to develop standards which can be applied by nurses in all areas where infusion therapy is delivered; the revised standards must acknowledge the impact of moving delivery of infusion therapy into the community on service provision, the nursing workload and the patient experience.

The research questions for the current review of evidence were as follows:

> What is the latest evidence that can be used to update the previous iteration of the infusion therapy standards?
>
> What are the facilitators and barriers perceived by patients receiving a range of infusion therapies?

The RCN *Standards for Infusion Therapy* cover a wide cross-speciality area, however the focus of this review was to provide evidence on practice that is relevant to the management of infusion therapy by nurses in a variety of settings, and is linked with clinical effectiveness and patient safety outcomes.

Methods

The aim of the literature search was to identify the research evidence, appropriate standards and guidelines on infusion therapy from the UK and other OECD countries, in order to update the RCN IV Therapy Forum (2010) *Standards for Infusion Therapy*. Full details of the search strategy are provided in previous sections of this document.

A total of 12 areas of clinical practice were identified as relevant to infusion nursing practice and in need of updated evidence. These areas informed the search process and included add-on devices; arterial catheters; blood sampling; central venous access devices; flow control devices; infusion-related bloodstream infection; infusion therapy phlebitis; intraosseous access; midline catheters; parenteral nutrition; peripheral access devices and flushing; and subcutaneous infusions.

The review of clinical evidence comprised two phases; the first reviewed RCTs and SRs only, while the second phase reviewed other quantitative designs and reviews of literature. A separate search identified literature relating to patient perspectives and experiences of receiving infusion therapy in various settings. Quality appraisal of the papers retrieved was conducted using a variety of tools suitable for the type of the considered evidence.

Key findings and gaps in the literature

In addition to the main research question of identifying evidence about infusion therapy that relates to nursing practice and is linked with clinical effectiveness and patient safety outcomes, a number of specific points of research interest were identified as important to the revision of the infusion therapy standards. These questions relate to various aspects of infusion therapy (for example, the impact of various procedures like flushing and replacement of equipment), however, not all of the areas had specific research questions.

Key findings and gaps in the literature identified during each of the three reviews are presented in the corresponding sections of this report. A synthesis is presented below which aims to bring together the findings of each of the strands of the review to provide an overall appraisal of the evidence relating to infusion therapy.

Evidence levels relate to those produced by the US Infusion Nurses Society[46], with Level I representing the highest level of evidence (see Section 3 for full

description of the approach). However, it should be noted that a high quality systematic review may uncover only low quality evidence or provide inconclusive results. As a consequence, when producing the standards the quality of the findings of studies must be considered alongside the robustness of the study design, when making decisions about the appropriateness of incorporating such findings in the revised RCN standards.

Add-on devices

Table 1: Summary of evidence relating to add-on devices

Two SRs of low and medium quality[81,109] did not find conclusive evidence on how to reduce contamination and infection rates when using different needle-less connectors (LEVEL I).
One SR of high quality[83] identified very low quality evidence that closed connector devices for central venous catheters reduced risk of infections and improved safety (LEVEL I).
One high quality clinical survey/lab study[102] found scrubbing the hub with a 70% isopropyl alcohol pledget significantly decreased contamination (LEVEL IV).
One low quality prospective cohort study[68] found that changing to an intraluminal protection device can reduce infection rates (LEVEL V).
No evidence was found on patient safety and outcomes of: • changing add-on devices with each cannula or administration set replacement • changing add-on devices when integrity of either product is compromised.

While several SRs were identified which looked at the effects of various connector devices and methods of reducing contamination, they either produced inconclusive results or identified only low quality evidence[81,83,109]. The limited evidence available suggests that closed connector devices for central venous catheters (CVCs) may reduce the risk of infection as may changing to an intraluminal protection device[68].

A high quality clinical and laboratory study[102] found that scrubbing the connector hub with a 70% isopropyl alcohol pledget is an effective measure for decreasing bacterial contamination in both contexts. Gaps remain in the evidence base with regards to patient safety and outcomes of changing add-on devices with each cannula or administration set replacement, or when the integrity of either product is compromised.

Arterial catheters

Table 2: Summary of evidence relating to arterial catheters

One RCT of low quality[93] did not find that use of radial arterial catheters caused finger or hand ischaemia nor did hourly blood glucose monitoring using the catheter increase the rate of infection (LEVEL IV).
One RCT of high quality[32] compared different dressings; bordered polyurethane (BPU) with standard polyurethane (SPU) dressing was associated with the least arterial catheter failure (LEVEL III).
One SR of high quality[23] found inconclusive results about the optimum timing of administration set replacement (LEVEL I).
One high quality SR[83] found that arteriovenous fistula cannulation was comparable to central venous catheters for intensive haemodialysis in terms of access loss, failure or complications (LEVEL I).
Patient preferences may differ from those of professionals. For example, while professionals favour a fistula over a CVC due to its association with improved clinical outcome, patients may prefer a catheter due to the perceived impact on quality of life[1].
No evidence was found on patient safety and outcomes of: • different line flushing frequencies for arterial catheters • flushing arterial catheters with saline vs heparinised solutions • using different arteries for cannulation.

There is evidence to suggest that the use of radial arterial catheters does not lead to finger or hand ischaemia, however this is the finding of only one low quality RCT[93]. The same RCT found hourly blood glucose monitoring from the catheter did not result in increased infection rates. Further research is required to confirm these findings. The research is inconclusive with regard to the optimum timing of administration set replacement[23].

There is limited but high quality evidence to suggest that dressing type can influence the success of the arterial catheter; with a bordered polyurethane with standard polyurethane dressing resulting in lower failure rates than standard polyurethane dressing[32].

High quality evidence demonstrates that arterio-venous fistula cannulation is comparable to CVC for intensive haemodialysis in terms of access loss, failure or complications[83]. However, patient preference data suggests that while professionals tend to favour a fistula over a CVC due to the association with improved clinical outcome, patients may prefer the catheter as they perceive it will offer them a better quality of life[1,15].

There was no evidence found relating to the impact of different line flushing frequencies for arterial catheters, or the effect of flushing with saline versus heparinised solutions.

Blood sampling

Table 3: Summary of evidence relating to blood sampling

Three RCTs of low quality looked at the impact of different methods for obtaining blood samples (LEVEL IV): • sampling speed for taking venous blood from pulmonary artery catheters did not change the level of oxygen (five seconds compared to one to two minutes)[50] • repeat blood glucose levels could be effectively measured using samples from the arterial catheter compared to standard fingertip blood glucose monitoring[93] • blood samples taken by nurses from the IV catheter hub immediately after insertion had similarly high rates of haemolysis as samples taken from the IV catheter hub via an extension tube immediately after insertion[107].
One high quality prospective cohort study[25] demonstrated acceptable rates of rejection due to haemolysis can be achieved using blood samples collected from IV starts in the ED setting (LEVEL IV).
One high quality prospective cohort study[42] demonstrated similar haematology, biochemistry and coagulation parameter results between blood samples obtained from a PVC compared with venepuncture. Significant differences were only found in venous blood gas results (LEVEL IV).
One high quality quasi experimental study[51] compared lab values of blood samples obtained via CVC with those obtained by venepuncture and found that while some results produced significant differences, these differences were not clinically significant (LEVEL IV).
One high quality quasi experimental study[45] found that drawing blood samples from heparinised PICCs produced similar coagulation test results, except for INR (LEVEL IV).
One medium quality quasi experimental study[22] found that there was no significant difference in activated partial thromboplastin time (aPTT; a coagulation parameter) results when specimens are collected from a CVC compared with venepuncture in patients receiving continuous heparin infusions. However, values were significantly prolonged if samples were taken from a port used to deliver heparin (LEVEL IV).
One high quality quasi experimental study[7] found that 1ml was the minimum waste volume required to produce an undiluted blood sample (LEVEL IV).
One high quality prospective cohort study[60] found that taking samples from the wire hub of a CVC produced significantly higher contamination rates than the non-wire hub (LEVEL IV).
One high quality quasi experimental study[63] demonstrated the 'Holdex' tube holder to be more effective in preventing erythrocyte injury compared with a standard BD Vacutainer One Use holder (LEVEL IV).
No evidence was found for: • venepuncture interventions to reduce fear, pain and anxiety • the effect of site selection for an infusion cannula on patient safety and outcome • the impact of different infusion device flushing before blood sampling • best practice for different devices.

There is evidence to suggest that routine blood sampling from IV catheters may be justified as similar results are reported in a range of parameters[22,42,45,51]. This is the conclusion from several high quality quasi experimental studies; however, as each study addresses a different aspect of blood sampling, the level of evidence does not exceed level IV.

Several RCTs looked at the impact of different methods of blood sampling, however all of these studies were rated as low quality. Results, which should be treated with caution, suggest that sampling speed for taking venous blood from pulmonary artery catheters does not change the level of oxygen[50], and the use of an extension tube when sampling from the IV catheter hub does not result in reduced levels of haemolysis[10].

Patient preference literature suggests many patients find needles uncomfortable and distressing[6,92,121] therefore judgement should be made based on the tests required and taking into account the preferences of the patient. Caution should be applied when measuring venous blood gases or INR as discrepancies have been noted when these samples are taken from IV catheters[42,45]. Limited evidence suggests 1ml is a sufficient waste volume to produce an undiluted blood sample from a PVC[7].

In terms of device selection, limited evidence suggests that sampling from a non-wire rather than wire hub results in decreased infection rates[60]. Similarly, there is limited evidence for the 'Holdex' tube holder to reduce risk of erythrocyte injury[63].

While patient preference literature identifies pain and distress as frequently associated with the experience of needles, no evidence was found for venepuncture interventions to reduce fear, pain and anxiety.

There are also gaps in the literature in relation to the effect of site selection for an infusion cannula on patient safety and outcomes. In light of findings from the patient perspective review, it is suggested the patient's lifestyle should be taken into account when selecting the most appropriate site.

If blood sampling from IV catheter hubs is to be encouraged, then gaps in the literature regarding the impact of different flushing practices before blood sampling must be addressed. Furthermore, with the various devices for blood sampling available, further research is required to identify best practice for different devices.

Central venous access devices

Table 4: Summary of evidence relating to central venous access devices

Two SRs of high and medium quality[66,123] and one RCT of low quality[122] did not find any difference between flushing with heparin, sodium chloride or ethanol, and locking with heparin or citrate. The medium quality SR[123] found that locking with citrate plus gentamicin, taurolidine or methylene blue plus methylparaben plus propylparaben reduced the risk of catheter-related blood stream infection (LEVEL I).
Two SRs of medium quality[18,79] examined the effect of site and vein selection, with peripherally inserted central venous catheters (PICCs) having double the risk of deep vein thrombosis over centrally inserted catheters (LEVEL I). One medium quality RCT[47] found no difference in thrombosis or safety between non-tapered or reverse-tapered PICCs.
One high quality prospective cohort study[71] examined risk factors for upper extremity deep vein thrombosis (UEDVT) in patients with PICCs and found a statistically significant association between UEDVT and hypertension, obesity, an increase in PICC arm circumference and oedema (LEVEL IV).
One SR[114] and 1 RCT[112], both high quality, found that chlorhexidine dressings and silver dressings reduce major catheter-related infections, catheter-related blood stream infections and catheter colonisation (LEVEL I).
Three SRs[56,79,117] and 5 RCTs[5,47,87,89,91,104] of varying quality considered different types of central venous catheter devices for durability, infection risk and complications, further details can be found in the main body of the report (LEVEL I).
Four RCTs[17,35,37,62] compared insertion techniques but no firm conclusions can be drawn as the studies were either of low quality or were conducted on a manikin. Having the bevel facing down and using ultrasound appeared to be beneficial (LEVEL III).
One high quality retrospective cohort study[8] found no significant differences in infection rates between self-administered outpatient parenteral antimicrobial therapy, compared with administration in a hospital or clinic setting (LEVEL IV).
One medium quality quasi experimental study[75] found implementing an evidence-based practice intervention related to CVAD flushing, resulted in significant improvement in nurses' knowledge and flushing technique (LEVEL IV).
No evidence was found on the effect on patient safety and outcomes of different line flushing frequencies.

There is strong evidence to demonstrate that there is no difference in infection rates when devices are flushed with heparin, sodium chloride or ethanol, or locked with heparin or citrate[66,122,123]. However, locking with citrate plus gentamicin, taurolidine or methylene blue plus methylparaben plus propylparaben may reduce the risk of catheter-related blood stream infection[123].

Implementing an evidence-based practice intervention may result in improvements in nurses' knowledge and flushing technique; however, this is the conclusion of only one medium quality quasi experimental study[75].

There is strong evidence to suggest PICCS are associated with a higher risk of DVT than centrally inserted catheters[18,79]. Further risk factors include hypertension, obesity, an increase in PICC arm circumference and oedema[71].

One high quality prospective cohort study found no significant differences in infection rates between self-administered outpatient parenteral antimicrobial therapy compared with administration in a hospital or clinic setting[8].

The evidence relating to the most effective device in terms of infection and complication risk is inconclusive; however it would appear that coating or impregnating catheters with antimicrobial substances (including silver, CHG and bismuth) results in reduced infection risk[5,104,117]. Chlorhexidine and sliver dressings have a protective effect against catheter-related infection[112,114].

No firm conclusions can be drawn about the most effective insertion technique due to design limitations of the studies identified.

No evidence was found on the effect of different line flushing frequencies on patient safety and outcomes.

Flow control devices

Table 5: Summary of evidence relating to flow control devices

Two RCTs compared different types of central venous catheters for haemodialysis: • a high quality RCT[91] found that the twin permanent central venous haemodialysis catheters LifeCath and TesioCath enabled the same flow rate but there were more complications with LifeCath (LEVEL III) • a low quality RCT[116] found that the Palindrome Symmetric Tip tunnelled catheter gave higher blood flow rate and fewer occlusions than HemoStar but both lasted the same length of time (LEVEL IV).
One RCT of high quality[10] found no benefit in using a local infusion of anaesthetic into the wound following hiatus hernia repair (LEVEL III).
One SR of medium quality[43] found that intrathecal pain relief was moderately effective for pain that had not responded to other methods of pain relief (LEVEL I).
One low quality narrative review[69] described connector design features which facilitate scrubbing and flushing and improve outcomes. These features included a smooth, tight-fitting septum, low intra-luminal fluid pathway volume, a straight fluid pathway, no dead space, no reflux with connection or disconnection, and fail safe back-up systems (LEVEL V).
No evidence was found for: • prognostic factors (for example, age, condition, therapy, care setting) affecting selection of different manual flow control devices on patient outcomes • how different frequencies of flow rate monitoring of different manual flow control devices affect patient outcomes • the effect of electronic devices which generate flow through positive pressure or low pressure devices on patient safety and outcomes.

This search did not produce any studies relating directly to flow control devices. Two RCTs[91,116] compared different types of CVCs with relation to flow rates and complications; however the evidence is insufficient to make recommendations regarding the most effective devices.

Two studies identified in the search were not directly related to flow control devices; however these are mentioned, as the findings may be of use in the revision of the infusion therapy standards. Limited evidence suggests that local infusion of anaesthetic into the wound following hiatus hernia repair provides no benefit[10]. There is, however, evidence to suggest that intrathecal pain relief may be effective in alleviating pain which has not responded to other methods of pain relief[43].

No evidence was found for prognostic factors affecting selection of manual flow control device, different frequencies of flow rate monitoring, or the effect of electronic devices which generate flow through positive pressure or low pressure devices.

Infusion-related bloodstream infections

Table 6: Summary of evidence relating to infusion-related bloodstream infections

Two SRs of medium quality[123,106] found that locking with citrate plus gentamicin, taurolidine or methylene blue plus methylparaben plus propylparaben reduced the risk of catheter-related blood stream infection compared to either heparin or citrate alone, and antibiotic-heparin or antibiotic-citrate were more effective than heparin alone. One RCT of low quality[122] found no difference between heparin and ethanol flushes (LEVEL I).
One SR[114] and one RCT[112] both of high quality found that chlorhexidine dressings and silver dressings reduce catheter-related blood stream infections, and one SR of low quality[86] found they reduced infections in general. One SR of high quality[83] found low quality evidence that topical mupirocin reduces catheter-related blood stream infections for buttonhole arteriovenous cannulation (LEVEL I).
One high quality quasi experimental study[48] found the use of a silver coated needleless connector reduced CLABSI rates by 32% compared with a standard needleless connector (LEVEL IV).
One multicentre medium quality RCT7[4] found that a 5-item blood stream infection bundle and staff engagement protocol reduced catheter-related blood stream infection by 81% (LEVEL III).
One medium quality prospective cohort study[44] found self-reported compliance with five evidence-based CLABSI reduction practices was associated with reduced CLABSI rates. The practices included hand hygiene, chlorhexidine skin preparation, full barrier precautions, avoidance of femoral line placement and removal of unnecessary lines. Avoidance of femoral site and removal of unnecessary lines had the strongest independent effects (LEVEL IV).
Two medium quality quasi experimental studies[30,41] demonstrated a decrease in CLABSI rates as a result of a post-insertion maintenance bundle including hand hygiene, aseptic technique during use of connectors, dressing changes, regular assessment of the need for the catheter, scrubbing the hub for 10-15s before access, daily inspection of insertion site and site care if dressing wet or soiled (LEVEL IV).
One high quality observational cohort study using historical controls[26], one low quality prospective observational study[55], and two low quality quasi experimental studies[65,76] demonstrated significant reductions in CLABSI rates with the introduction of daily chlorhexidine gluconate bathing for patients (LEVEL IV).

One medium and one low quality prospective cohort study[82,30] demonstrated a decrease in CLABSI rates as a result of a step-wise multimodal intervention over a period of time (LEVEL IV).

One medium quality prospective cohort study101 demonstrated the effectiveness of various device-related interventions over a three year period on the reduction of CLABSI. These included a change to positive displacement needleless connectors, enforcement of maximal barrier precautions on insertion, implementation of a CHG-impregnated disk, change to a clear connector, and implementation of a 'scrub the hub' campaign (LEVEL IV).

Three SRs[56,109,117] and four RCTs[5,87,91,116] of varying quality compared infection rates for different types of central venous catheters, further details can be found in the main body of the report (LEVEL I).

One SR of high quality[23] found insufficient evidence on how often the arterial catheter tubing should be changed or flushed. One RCT of low quality[93] found no difference between a non-waste needle-less setup or non-waste syringe setup for radial arterial catheters. One SR of low quality[86] found that femoral arterial catheters had double the risk of catheter-related blood stream infection compared to radial arterial catheters (LEVEL I).

One high quality SR[113] concluded that administration sets that do not contain lipids, blood or blood products may be left in place for up to 96 hours without increasing the risk of infection (LEVEL I).

One high quality RCT[98] was inconclusive regarding the optimal removal time for peripheral catheters on risk of catheter-related blood stream infection (LEVEL III).

One medium quality retrospective cohort study[2] found that the most common organism causing bloodstream infection in patients with PICCs was Candida glabrata, and that a higher BSI rate was observed in the ICU setting. The study hospital also experienced an increase in PICC use with the withdrawal of an IV specialist service for the placement of difficult PVCs (LEVEL IV).

One medium quality prospective cohort study[85] and one medium quality quasi experimental study[111] demonstrated significant decreases in CLABSI rates with the introduction of a lead nurse to standardise and facilitate good practice (LEVEL IV).

One medium quality case-control study[90] explored patient- and device-related risk factors for BSI in patients with PICCs and found the following to be associated with BSI: congestive heart failure, intra-abdominal perforation, history of *C. diff*, recent chemotherapy, presence of tracheostomy tube, and use of a multi lumen catheter. History of COPD and PICC placement in oncology, orthopaedics or surgery proved to be protective factors (LEVEL IV).

One low quality literature review[120] identified a need for research into the effectiveness of interventions to reduce CLABSI rates in the non-ICU setting (LEVEL IV).

No evidence was found on the management of infusion-related blood stream infections.

There is strong evidence to suggest that locking devices with antimicrobial solutions in addition to heparin or citrate, is more effective in reducing catheter-related bloodstream infection than heparin or citrate alone[106,123].

Evidence suggests that chlorhexidine and silver act as effective barriers against bloodstream infection, when used to impregnate catheters, connector devices or dressings[5,48,112,114,117].

Pre- and post-insertion bundles have been shown to be effective in reducing catheter-related infections[30,41,44,74]. Pre-insertion bundles commonly include hand hygiene, chlorhexidine skin preparation, full barrier precautions, aseptic technique and avoidance of femoral line. Post-insertion bundles commonly incorporate hand hygiene, aseptic technique during use of connectors, scrubbing the hub, daily inspection of the insertion site, regular assessment of the need for the catheter and removal of unnecessary lines. Several studies have also shown daily chlorhexidine gluconate bathing to be an effective prevention control measure alongside other infection prevention practices[26,55,65,76].

Evidence suggests that introducing a lead nurse to standardise and facilitate good practice may result in reduced infection rates[85,112].

Evidence is inconclusive with regards to the set-up of arterial catheters or how often the tubing should be changed. There is limited evidence that femoral arterial catheters have an increased infection risk compared with radial catheters[86]. Research also indicates that the femoral area should be avoided where possible when placing CVCs[44].

One high quality SR[113] concluded that administration sets that do not contain lipids, blood or blood products may be left in place for up to 96 hours without increasing the risk of infection. This is in agreement with studies in other areas which found replacement of catheters on clinical indication did not result in increased infection compared with those replaced routinely every two to three days[97,98].

No evidence was found relating to the management of infusion-related bloodstream infections in this review. While the focus must remain on preventing such infections occurring in the first place, it is unlikely they will be eliminated completely; it would therefore be useful to identify the most effective methods of managing infusion-related bloodstream infections to limit the impact on patient morbidity and mortality.

Infusion therapy parenteral nutrition

Table 7: Summary of evidence relating to infusion therapy parenteral nutrition

One SR of low quality[28] highlighted the importance of hand hygiene and training for home parenteral nutrition (PN) as gram positive human skin flora caused the most infections (LEVEL II).
Two high quality RCTs[15,27] did not find any improvement in outcomes by starting PN early on during admission of adults to ICUs (LEVEL II).
One low quality RCT[52] found that total parenteral nutrition (TPN) and enteral nutrition were both effective routes for people with traumatic brain injury (LEVEL IV).
One medium quality SR[88] found that omega-3 fatty acid supplements did not improve mortality, infectious complications or length of ICU stay. Four RCTs of low to high quality[54,103,110,115] found no difference in outcomes between PN supplements if based on soybean, medium-chain triglycerides, olive oil or fish oil (LEVEL I).
One medium quality prospective cohort study[34] found the most frequent cause of spurious bloodwork in PN patients was the failure to clamp the PN infusion prior to blood collection, or too short a time between clamping and drawing (LEVEL IV).
One high quality case control study[67] found the strongest risk factor for candidemia infection in elderly hospitalised adults was duration of PN. Other factors included presence of other invasive devices such as CVC or urinary catheter, and concurrent use of antibiotics (LEVEL IV).
One medium quality prospective cohort study[99] found that previous immunosuppressive therapy and patient age were independent predictors of 30-day mortality in patients with PN-related catheter-related BSI. Catheter removal within 48h and appropriate antibiotic therapy were protective factors (LEVEL IV).
One low quality audit[70] found a 2% chlorhexidine gluconate transparent antimicrobial dressing eliminated infection in PN patients compared with a standard dressing (LEVEL V).
No evidence was found for: • the effect of different frequencies of change of PN administration sets and add- on devices on patient safety and outcomes; • the performance of nutrition screening tools to assess nutritional status; • the effect of different ways of monitoring for metabolic related complications and electrolyte imbalances and catheter-related complications on patient safety and outcomes.

There is low quality evidence to suggest PN is an effective route for patients with traumatic brain injury[52]. However early initiation of PN on admission to ICU does not appear to result in improved outcomes[15,27]. Various composition of supplements have also not been shown to result in different outcomes[54,88,103,110,115].

Failure to clamp the PN infusion prior to blood collection – or too short a time between clamping and drawing – may lead to spurious bloodwork amongst PN patients[34].

One high quality case control study found the strongest risk factor for candidemia infection in elderly hospitalised adults was duration of PN. Other factors included the presence of other invasive devices, such as CVC or urinary catheter, and concurrent use of antibiotics[67]. In terms of home PN patients, gram positive human skin flora appears to be the most common cause of infections[28], highlighting the importance of hand hygiene and training in this patient group.

In patients with PN catheter-related bloodstream infections, previous immunosuppressive therapy and patient age have been shown to be independent predictors of 30-day mortality. Catheter removal within 48 hours and appropriate antibiotic therapy appear to be protective factors[99].

No evidence was found for the effect of different frequencies of change of PN administration sets and add-on devices, the performance of nutritional screening tools, or the effect of different ways of monitoring for metabolic related complications of electrolyte imbalances and catheter-related complications.

Infusion therapy phlebitis

Table 8: Summary of evidence relating to infusion therapy phlebitis

One high quality RCT[98] found that the incidence of phlebitis was 7% whether PVCs were replaced routinely every three days or replaced according to clinical indications (LEVEL I).
One high quality RCT[97] found no significant differences in complication rates, time to first complication, infections or duration of IV therapy when PVCs were replaced routinely compared with replacement on clinical indication (LEVEL I).
One medium quality prospective cohort study[19] found the likelihood of phlebitis increased with duration of catheter, highest after 96h. Phlebitis was more likely when the catheter was placed in the dorsum of the hand compared with the antecubital fossa or forearm (LEVEL IV).
One high quality RCT[87] found that the rate of phlebitis for proximal valve polyurethane (PVP) PICCs was half that for distal vein silicone (DVS) PICCs. One medium quality RCT[39] found that phlebitis was less likely with closed-system peripheral intravenous catheters than open-systems (LEVEL III).
One low quality SR[94] identified that there are 71 different phlebitis scales (LEVEL II).
One high quality RCT[64] found that a "catheter care station" in operating rooms reduced the combined rate of phlebitis and health care associated infection (LEVEL III).
One high quality quasi experimental study[77] demonstrated a 48% reduction in peripheral vein phlebitis as a result of a quality improvement intervention including education and training of health care staff, a catheter maintenance bundle and surveillance of pvc-related adverse events (LEVEL IV).
One medium quality quasi experimental study[100] found patients receiving vancomycin compared with other antibiotics had no significant differences in incidence of phlebitis. They did, however, have increased venepunctures, number of attempts and time spent resiting catheters. Patients receiving vancomycin were also more likely to end the study with a CVC (LEVEL IV).
No evidence was found on the impact of different phlebitis severity/degrees on patient safety and outcomes.

High quality evidence suggests that replacing PVCs on clinical indication, rather than routinely every three days, does not result in increased infection rates[97,98]. However, one medium quality prospective cohort study[19] found the likelihood of phlebitis increased with duration of catheter, and was highest after 96 hours.

PVP PICCS have lower phlebitis rates than DVS PICCS[87]. Closed systems also appear to result in fewer incidences of phlebitis than open systems[39]. Other risk factors for phlebitis include increased duration of catheter and placement in the dorsum of the hand[19]. There is also evidence to suggest that the education and training of staff, as well as a catheter maintenance bundle or 'catheter care station' in the operating theatre, has a beneficial impact on infection rates[64,77].

Vancomycin does not appear to significantly increase the risk of phlebitis; however, this is the conclusion of only one quasi experimental study[100]. The same study found that while phlebitis incidence was similar, receiving vancomycin did result in several other complications.

No evidence was found on the impact of different phlebitis severity/degrees on patient safety and outcomes. One low quality SR[94] identified 71 different phlebitis scales, therefore it may be useful to identify the most effective scale in order to standardise the grading of phlebitis and simplify the assessment of phlebitis severity.

Intraosseous access

Table 9: Summary of evidence relating to intraosseous access

One SR of high quality[53] found intraosseous access much more likely to succeed than intravenous access for infants, though dislodgement was twice as likely in both infants and adults. Intravenous routes were also found to be able to deliver more fluids (LEVEL I).
One low quality RCT[95] found that intraosseous tibial access was faster, more initially successful and less likely to dislodge than humeral intraosseous access (LEVEL IV).
One high quality quasi experimental study[59] and one low quality observational study[13] demonstrated that success rate was significantly higher, and procedure time significantly lower for IO access compared with CVC. A survey included as part of the observational study showed that CVC remains the preferred choice for both second and third attempts at IV access, with IO selected only if a fourth attempt is required (LEVEL IV).
One medium quality literature review[38] found that while IO is a safe and effective method of gaining access when IV access is unobtainable, IO is rarely used and guidance often not followed. The proximal tibia appears to be the favoured access site and the EZ-IO the most popular device (LEVEL IV).
No evidence was found relating to patient safety and outcomes of: • different durations of intraosseous access device • different durations of intraosseous ports • site management after removal.

In adults, intravenous access allows for the delivery of more fluids than intraosseous routes, with a decreased risk of dislodgement[53]. However, when intravenous access is not possible, intraosseous access has been shown to be more successful and quicker than inserting a central venous catheter[13,53,59]. Despite the evidence for intraosseous access, CVC remains the preferred method of access amongst clinicians when IV access is unobtainable[13,38]. There is also evidence to suggest that when IO access is obtained, guidance is often not followed[38].

When IO access is performed, the proximal tibia appears to be the site most favoured by clinicians[38,95], however the evidence regarding the most effective site remains inconclusive. There is evidence to suggest the humeral head is the most effective site for IO access due to its closer proximity to the central circulation and faster infusion rate[38,78]. However, there is also an increased risk of dislodgement if the device is inserted into the humerus during CPR, due to the activity taking place around the torso region[38]. The humeral head can also be more difficult to locate, particularly if the patient is obese, and there are reports of decreased first-time success rates when this site is selected. More studies are required to clarify the most effective site; however, it appears site selection should be based on individual patient and situation characteristics.

There are various IO access devices on the market, and there is no evidence to suggest any one device is more successful in terms of placement. The EZ-IO battery operated power driver, however, has been reported to be easier to use and was the most commonly used device across all studies reviewed by Garside et al.[38].

No evidence was found relating to different durations of IO access devices, different durations of IO ports, or site management after removal of the IO device.

Midline catheters

Table 10: Summary of the evidence relating to midline catheters

One low quality RCT[16] concluded that vancomycin can be safely given through a midline catheter, with similar complication rates to PICCs (LEVEL IV).
One high quality literature review[40] concluded that pH alone is not an evidence-based indication for CVC placement over midline catheter placement (LEVEL IV).
One high quality literature review[4] discusses advantages and disadvantages of midline catheters along with insertion and management issues. Advantages include avoidance of repeated cannulation; increased vessel diameter which reduces the incidence of complications such as chemical phlebitis; toleration of isotonic solutions and high flow rates; reduced infection rate compared with other vascular devices. Disadvantages include high risk of extravasation; not recommended for dextrose solutions >10%; risk of mechanical phlebitis. Insertion and management issues include the requirement for a thorough clinical and vascular assessment prior to insertion (LEVEL IV).
One high quality prospective cohort study[14] found low levels of pain and distress were by palliative care patients during positioning of PICC or midline catheters, with the devices resulting in significant improvement of global quality of life (LEVEL IV).
One low quality descriptive study[29] found no relationships between infusates or dwell time and complications (LEVEL V).
One low quality prospective pilot study[24] reported the success of a novel, resident-driven programme for the placement of ultrasound-guided midline catheters in critically ill patients (LEVEL V).
No evidence was found on patient safety and outcomes of: • different flushing frequencies • flushing lines with saline versus heparinised solutions • use of different veins • effect of site selection.

Evidence suggests that pH alone is not an evidence-based indication for central line over midline catheter placement[40] and that vancomycin can safely be given through midline catheters[16].

Evidence suggests placing PICC or midline catheters does not appear to result in pain or distress in palliative care patients. Furthermore, the devices are associated with an improved quality of life[14].

No evidence was found on the effect of different flushing frequencies, flushing lines with saline versus heparinised solutions, use of different veins, or site selection. There is evidence relating to flushing with different solutions and site selection, for CVCs and PVCs (see Tables 4, 6 and 11). However these factors should be addressed in relation to midline catheters as this method of access becomes more widely used in the delivery of infusion therapy.

Peripheral access devices and flushing

Table 11: Summary of the evidence relating to peripheral access devices and flushing

One high quality RCT[11] found flushing with 3ml 100 IU heparin/ml was better than normal saline (LEVEL III).
One high quality RCT[98] found peripheral venous catheters could be changed according to clinical indication rather than routinely on day 3. A high quality SR[23] was inconclusive about the optimal duration of time for peripheral arterial catheter administration sets (LEVEL III).
One medium quality RCT[39] found that open system peripheral venous catheters were more likely to be inserted first time and less likely to rupture a vein than closed system peripheral venous catheters but closed systems stayed in place longer (LEVEL III).
One small low quality RCT[73] found no difference between four techniques of securing peripheral venous catheters (LEVEL IV).
One low quality SR[108] found ultrasound-guided peripheral venous access for people of any age with difficult venous access had higher success rates compared to traditional techniques (LEVEL IV).
One medium quality quasi experimental study[61] found two 20-g IV catheters are significantly faster than a single 18-g IV catheter. Both were markedly slower than infusion rates observed in in vitro testing and based on manufacturer data (LEVEL IV).
One low quality retrospective case control study[58] identified risk factors associated with the development of infection in patients with PVC. These included >24h continuous infusion, insertion in the lower extremity, use of infusion pumps and hospitalisation for neurological or neurosurgical conditions (LEVEL V).
One low quality audit[31] demonstrated the reduction of HCAI in an underperforming hospital as a result of the implementation of a change initiative relating to the use of peripheral venous catheters (LEVEL V).
No evidence was found relating to patient safety and outcomes of: • different line flushing frequencies for peripheral access devices • use of different veins • effect of site selection.

Low quality evidence suggests risk factors for infection include over 24 hours of continuous infusion, insertion in the lower extremity, use of infusion pumps and hospitalisation for neurological or neurosurgical conditions[58]. Strong but limited evidence suggests flushing with heparin is more effective than normal saline[11].

There is evidence to suggest that replacing PVCs on clinical indication does not result in increased infection rates compared with routine replacement every three days[97,98].

Two 20-g IV catheters have been demonstrated to produce a significantly faster flow rate than one 18-g catheter; however both rates are markedly slower than those observed in in vitro testing and based on manufacturer data[61].

It is widely accepted and practiced that IV lines should be flushed prior to administering medication or blood sampling, however no evidence was found for the effect on patient safety and outcomes of different line flushing frequencies, nor the use of different veins, or site selection.

Subcutaneous infusions

Table 12: Summary of evidence relating to subcutaneous infusions

One RCT of medium quality[21] found that smaller needles caused less pain for subcutaneous injections. 1 low quality RCT[57] found that retractable fixed needles caused less bruising (LEVEL III).
One high quality SR[3] found low quality evidence that subcutaneous injection of heparin over 30 seconds may be less painful than fast injection over 10 seconds (LEVEL I).
One low quality RCT[72] found that subcutaneous morphine infusions were less initially effective than intravenous morphine post-operatively (LEVEL IV).
No evidence was found on patient safety and outcomes of: • electronic devices for this procedure • site selection • site management • solution tonicity • electrolytes used (for example, sodium chloride, dextrose saline, dextrose 5%).

There is evidence that smaller needles may cause less pain for SC injections[21] and weak evidence that retractable fixed needles cause less bruising[57]. Evidence is weak with regards to optimal speed of injection[3].

Low quality evidence suggests that subcutaneous morphine infusions are less initially effective than IV morphine at controlling post-operative pain[72].

The overall volume of evidence was very low in this area, thus no studies were found in relation to

electronic devices for SC infusion, site selection, site management, solution tonicity or electrolytes used.

Patient perspective literature

Table 13: Key findings from the patient perspective literature

Patients experience infusion therapy in a variety of ways (for example, from loss of control to taking control)[80,105].
Patient preferences may differ from those of professionals (for example, focus on quality of life versus focus on clinical outcome)[1,92].
Some factors can act as both facilitators and barriers depending on individual characteristics and context[6,49].
Lack of psychological / emotional support is widely reported (patients and carers)[20,96].
Lack of choice available to patients / predominance of one-way communication[1,119,121].
Struggle for shared decision-making[1,119].
The nurse has a wide ranging role including education, provision of information, emotional support, assistance with self-care, nurse-led clinics[6,9,12,20,119].

The key issues emerging from the patient perspectives literature are that patient experiences and preferences are individual and dependent upon several factors relating to the patient and context[6,49,80,105]. There is evidence that a paternalistic system dominates in the delivery of infusion therapy and that patients are often dissatisfied with the extent to which they are involved in decisions relating to their care[1,119,121].

It is clear the nurse has a wide ranging, holistic role in the delivery of infusion therapy in a range of contexts, including education of patients and carers, provision of information, emotional support, assistance with self-care, and involvement in nurse-led clinics[6,9,12,20,119].

A limitation of this review is that the majority of studies related to the experience of dialysis patients, so there is little evidence relating to other areas of infusion therapy. In addition, the included studies dealt with individual settings of care delivery separately and these did not address continuity of care which was one of the themes identified in the literature relating to the *Warwick Patient Experiences Framework* (WaPEF) [i], which was used to guide the thematic analysis in this review.

Furthermore, it is not clear from the studies reviewed what the impact of patient experience is on adherence, quality, effectiveness and safety of infusion therapy. Specifically, the link between the clinical and patient perspective literature is unclear. In addition, no studies were identified which aimed to improve the patient experience through interventions.

i The *Warwick Patient Experiences Framework* (WaPEF) was the framework chosen to map the findings of the patient perspectives literature review. See Section 4 for more details.

Limitations of the review process

This review is subject to the limitations associated with carrying out REAs. The main difference between a systematic review and REA is the extent of the search strategy. Specifically, by limiting the search to only three databases and omitting the search for grey literature, there is a risk that not all relevant references have been identified in the current study.

However the three databases were selected due to their relevance to nursing research, and Watt and colleagues[118] demonstrated that restricting the search to the most productive databases does not impact adversely upon the REA as the additional number of relevant studies identified is generally very low.

Another limitation is that due to time and resource constraints, the current study included only papers which could be retrieved electronically or from the RCN library; however, the number excluded due to inaccessibility was low, and therefore unlikely to affect the quality of the final review. It is of note that in the patient perspective review, the unobtainable rate of papers was higher; about one-third of papers that were included, on the basis of abstract to be further assessed as full text on their relevance and then quality, could not be obtained within the time and resource available. This needs to be taken into account when considering the findings.

By including only studies which have been published in peer reviewed journals, there is a risk of omitting some potentially relevant studies due to publication bias. In order to address this limitation, any papers submitted by sponsors during the review process were given full consideration based on the scope of the review, inclusion and exclusion criteria.

While the search terms were exhaustive, some terms may have lacked specificity. For example, the search included 'parenteral nutrition' but not 'parenteral antimicrobial', which may account for the low yield of results relating to parenteral antimicrobial therapy.

The scope of the patient perspective search was also limited which meant no studies were retrieved in areas such as intraosseous access. As pain management is an issue amongst conscious patients receiving this type of therapy, including studies which explore patient experiences of this intraosseous access may have provided useful evidence in areas where the clinical literature is equivocal. Furthermore, in the review of patient perspectives literature, expansion of the search terms to include terms such as 'lived experience' may have elicited more results in relation to patient experiences of receiving infusion therapy.

Studies published prior to 2010 were omitted on the basis that these would not provide new evidence, based on the fact the current standards document was published in that year. However, due to the possibility of some studies being missed during the previous review, it may have been useful to include

a wider range of years in the current study. Similarly, studies published after 2015 are not included in this review. Since the literature search and quality assessment process have been completed, several articles have been published which are relevant to the topic of the review. In order to meet study deadlines, however, it would not be possible to obtain and quality assess every potentially relevant paper.

The processes of quality assessment and data extraction were conducted by only one researcher, which introduces the potential for reviewer bias; for this reason, a random sample of papers was checked by a second researcher at each stage of the process and no major discrepancies found. A clear audit trail has been created at all stages to ensure transparency during the entire process.

It should be noted that this review was only part of the evidence considered for the development of the RCN Infusion therapy standards. Existing guidance, good practice and expert consensus also informed the work.

Limitations of the evidence retrieved

Due to the heterogeneity of the studies identified, it was difficult to combine results to produce robust conclusions. In addition, the volume of research in some areas was very low. However, by synthesising the results of all of the reviews, a picture begins to emerge of where there is strong evidence available and where there is a need for further research or professional consensus.

During the sifting process we de-duplicated references across the 12 areas, but it was recognised that some studies related to more than one area. This may have implications for the volume of evidence reported for each area – in other words, it may have resulted in an underestimate for some, but ensured more accurate reporting across the findings of the study, in that evidence was not double-counted and thus not overestimated. In the summary and synthesis of findings, studies were looked across all 12 areas; as a consequence, some duplication may be noted.

While a key aim of the current review was to identify evidence relating to infusion therapy outside of the hospital setting, the majority of the evidence still remains in this area, with few studies conducted in non-acute settings such as the community or patient homes.

By including the patient perspectives part of the review, useful information emerges about patient experiences of infusion therapy. However, a clear path that takes us from understanding the patient experience to understanding how it can influence nursing practice and clinical outcomes is missing. Further research is required in this area; identifying and testing interventions to ensure that patient perspectives are not only acknowledged, but integrated into policy and practice in order to enhance service delivery and improve patients' experience of receiving infusion therapy.

Discussion

The literature search produced a large volume of evidence across a variety of areas relating to infusion therapy; however, some areas are clearly more researched than others.

The area which has received the most research attention is infusion-related bloodstream infections, which is not surprising given the huge impact of these infections on both an individual patient level and on health board resources.

Within several of the other areas, much of the literature is focussed on reducing such infections. Arterial catheters and subcutaneous infusions produced the lowest volume of literature in the review of clinical evidence, with only four studies found in each of these areas.

In the patient perspectives review, the evidence was heavily biased towards experiences of dialysis treatment; with a lack of studies conducted in other settings. In terms of the WaPEF framework, most of the studies were mapped against the theme of lived experience; no literature was identified as relating to the theme of continuity of care and relationships.

After synthesising and analysing the evidence as a whole, several themes emerged relating to various aspects of infusion therapy practice. These themes are discussed below to provide recommendations for practice and for the development of the new standards

Flushing and locking

The largest volume of evidence suggests that there is no difference between flushing CVCs with heparin or normal saline (one high quality and one medium quality SR[66,123] and one low quality RCT[122]). Although one high quality RCT[11] found that flushing PVCs with 3ml 100 IU heparin/ml was better than normal saline.

There is also no evidence that locking CVCs with heparin is any more effective than normal saline or citrate[66,122,123]; however, locking with an antimicrobial solution has been linked with decreased infection rates (two medium quality SRs[106,123]). There is a need for more research into the effect of flushing and locking using various solutions with regards to PVCs, as well as arterial and midline catheters.

One low quality review[69] aimed to identify connector design features that facilitate scrubbing and flushing and improve outcomes. Identified features include a smooth, tight fitting septum; low intraluminal fluid pathway volume; a straight fluid pathway; no dead space; no reflux with connection or disconnection; and fail-safe back-up systems.

There is weak evidence to suggest that implementing an evidence-based practice intervention relating to flushing and locking, may have a positive impact on nurses' knowledge and flushing technique[75].

Infection prevention and control

Several studies have demonstrated chlorhexidine and silver to be effective antimicrobial agents, when impregnated into catheters, connector device or securement dressings[5,48,70,112,114,117]. Chlorhexidine gluconate bathing has also been demonstrated to be effective at reducing infection risk, as part of a quality improvement intervention[26,55,65,76].

Pre- and post-insertion care bundles have been shown to reduce infection rates in a variety of settings[30,41,44,74,76]. A care bundle is a number of interventions that, when performed together, result in improved outcomes. Elements which should be considered for inclusion in a care bundle include hand hygiene, aseptic technique, dressing changes, scrub the hub, daily inspection of insertion site, full barrier precautions on insertion, CHG bathing and removal of unnecessary lines.

Three high quality studies (one SR[113] and two RCTs[97,98]) found that routine replacement of catheters every three days does not result in decreased infection rates, compared with replacement on clinical indication. However one medium quality prospective cohort study did find the risk of phlebitis increased with duration of catheter, highest after 96 hours[19]. There is, therefore, a clear rationale for replacement of catheters on clinical indication; however, it is vital that insertion sites are monitored daily for signs of infection and catheters removed promptly whenever infection is suspected.

Blood sampling

Several studies have demonstrated that blood samples can safely and effectively be obtained from IV access devices without significantly affecting the results obtained[22,42,45,51]. In addition, similar levels of haemolysis have been observed in blood samples taken from IV starts in the emergency department, compared with venepuncture[25]; and also samples taken from the catheter hub during an IV start, and from the catheter hub via an extension tube[107]. However several parameters do appear to be affected by sampling using this method including venous blood gases[42] and INR[45]. As patient perspective literature suggests patients can find repeated venepuncture uncomfortable and distressing[6,92,121], sampling from IV starts or existing IV access devices should be considered for routine blood testing. It should be noted, however, that when measuring coagulation parameters in patients receiving continuous heparin infusion, samples should not be taken from the port used to deliver the heparin as this may affect results[22].

Given the wide reporting of pain and distress in patients undergoing venepuncture and cannulation, there is a need for research into interventions aimed at reducing these outcomes and improving the patient experience.

It is widely accepted that when sampling from IV catheters, a volume of blood must be initially drawn and discarded as waste, in order to produce an undiluted blood sample. The results of one high quality quasi experimental study[7] demonstrate that 1ml is an adequate amount, therefore drawing larger volumes of waste is unnecessary and may lead to insufficient samples being obtained where there is a difficulty obtaining blood, or where multiple samples are required and the total volume exceeds the maximum which may safely be extracted.

Placement of devices

The evidence relating to the best access site in terms of safety and effectiveness is quite sparse. Placement of catheters in the femoral area has been associated with increased risk of infection in studies of both arterial[86] and central venous catheters[44]. In addition, one RCT of low quality did not find that use of radial arterial catheters caused finger or hand ischaemia[93]. Therefore the evidence available would suggest avoiding the femoral site where possible. In terms of peripheral access devices, placement in the dorsum[19] of the hand was shown to increase the risk of phlebitis in one medium quality cohort study.

Further studies are required in order to determine the most appropriate placement sites. In light of the patient perspectives review, however, any decisions made regarding placement of access devices should take into account patients' lifestyles and preferences as well as clinical evidence.

In terms of insertion techniques, the only evidence uncovered was of low quality[17,35,37,62,108]. From the limited evidence available it would appear that using ultrasound guidance is beneficial[37,108]. A low quality pilot study[24] reported the success of a novel, resident driven programme for placement of ultrasound-guided midline catheters in critically ill patients; however, it is unclear whether this could be replicated in the UK.

Effectiveness and safety of PICC and midline catheters compared with central venous catheters

The evidence regarding the safety and effectiveness of PICCs and midline catheters compared with CVC is limited. One high quality literature review[4] discusses advantages and disadvantages of midline catheters. Advantages include avoidance of repeated cannulation; increased vessel diameter which reduces the incidence of complications such as chemical phlebitis; toleration of isotonic solutions and high flow rates; and reduced infection rate compared with other vascular devices. Disadvantages include a high risk of extravasation; not recommended for dextrose solutions >10%; and an increased risk of mechanical phlebitis.

There is limited evidence to suggest midline catheters may be an acceptable route for the administration of vancomycin. While it is not advised to administer this antibiotic through PVCs due to the risk of various complications[100], there is evidence to suggest it may safely be given through midline catheters[16]. Another high quality literature review[40] suggests that pH alone is not an evidence-based indication for the placement of a central line rather than a PICC.

There is evidence to suggest that peripherally inserted central venous catheters (PICCs) have double the risk of deep vein thrombosis (DVT)

compared with CVCs[18,79]. A high quality prospective cohort study[71] found that hypertension, obesity, an increase in PICC arm circumference and oedema are risk factors for upper extremity DVT in patients with PICCs. A high quality RCT[87] demonstrates that PVP PICCs result in half the incidence of phlebitis compared with DVS PICCs.

In addition, one medium quality case-control study[90] explored patient and device-related risk factors for BSI in patients with PICCs and found congestive heart failure, intra-abdominal perforation, history of C. diff, recent chemotherapy, presence of tracheostomy tube, and use of a multi lumen catheter to be associated with increased infection risk in this population. History of COPD and PICC placement in oncology, orthopaedics or surgery appeared to be protective factors although reasons for this are unclear. This highlights the importance of a thorough clinical and vascular assessment of patients prior to insertion of a PICC or midline catheter.

A high quality prospective cohort study[14] carried out amongst palliative care patients showed that the placement of PICCs or midline catheters was associated with very low levels of distress, while their presence resulted in an increased global quality of life for the patients.

Infusion therapy in the non-acute setting

There was little research conducted with regards to infusion therapy in the non-acute setting. The study[14] which explored levels of pain and distress experienced by palliative care patients, during the placement of PICC or midline catheters, was carried out using patients in home and hospice settings. The positive findings of this study, in terms of low levels of distress and the resultant increase in quality of life, provide support for the use of PICCs and midline catheters amongst palliative patients in the community setting.

Evidence for the delivery of antimicrobial therapy in the community is strengthened by a study which found no significant differences in infection rates between self-administered outpatient parenteral antimicrobial therapy, compared with administration in a hospital or clinic setting8.

A systematic review[28] concluded that the most common cause of infections in home parenteral nutrition patients is gram positive human skin flora. While this systematic review was of low quality, it highlights the importance of hand hygiene and training for home parenteral nutrition patients, and indeed any patients in the community with indwelling infusion devices.

The patient perspective review found that treatment at home or in the community could be viewed as both a facilitator and a barrier; depending on the characteristics of the individual and the situation[6,49]. For example in patients undergoing dialysis, home treatment was viewed as a facilitator as it means patients do not have to have a fistula, it allows them to continue working, doesn't require admission to hospital or travelling for treatment, and it was perceived to offer patients greater control over their lives. However it was also viewed as a barrier as patients described their anxieties around the risk of peritonitis and the medicalisation of the home[6].

Studies exploring patient experiences of other infusion therapies in the home or community suggest that in many cases patients prefer to receive treatment in this setting. However the research uncovered an increased need for practical, psychological and emotional support for both patients and carers[12,20,80,96]. Nurses would be in an ideal position to provide this additional support, however it is vital that nurses working in this setting are provided with appropriate education and training; and sufficient time to provide the range of support required by patients receiving infusion therapy in the home of community setting.

Recommendations for further research

The findings of the review of clinical literature add to the evidence base in many areas of infusion therapy; however the volume of evidence is low in some areas (particularly arterial catheters and subcutaneous infusions). Further research should aim to answer the RCN questions which remain unaddressed, with a particular focus on the delivery of therapy out with the acute hospital setting.

The patient perspectives study offers useful information about patients' experiences of receiving infusion therapy both in acute and non-acute settings. The studies reviewed provide evidence that in many situations, patients prefer to receive infusion therapy at home or in the community; however several barriers are identified and it is clear that moving towards increased treatment in the non-acute setting will have considerable implications for the organisation of service delivery and the planning and management of resources, to include nursing workload management. Further research is required in this area to identify patient and carer needs and how systems design can best address them.

In this review no study was found that covered directly the domain of continuity of care, which may demonstrate a discrepancy between what matters to patients and what gets researched and/or published. With the current focus of health policy on integrated care and approaches to address fragmentations in the system, the patient perspective can be used to design services and evaluate their impact.

The overall volume of research identified and accessed in the patient perspectives study was low and mainly confined to patients receiving dialysis treatment. Further research is required to explore patient preferences and experiences in other areas of infusion therapy.

Furthermore, it is not clear from the studies reviewed what the impact of the patient experience is on adherence to, quality, effectiveness and safety of the infusion therapy. More longitudinal, experimental and mixed methods research is required in order to explore this link.

Recommendations for the development of the revised standards

This review identified a number of studies in a variety of areas of infusion therapy. Due to the heterogeneity of the clinical studies, there are few areas which contain strong evidence. Many high quality studies were identified however, and these should be assessed in the context of the existing evidence base in order to add strength to existing standards or challenge areas where new evidence may have emerged. Where ambiguity remains, it is advised that professional consensus be sought.

In light of the increased focus on delivering infusion therapy in settings out with the acute hospital, including references to the patient perspectives literature will allow guidance to be provided which addresses various situations and contexts, and acknowledges the holistic role played by the nurse in the delivery of infusion therapy.

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