NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical Technologies Evaluation Programme

Sponsor submission of evidence: Section C
Evaluation title: Sherlock 3CG®[1] Tip Confirmation System for placement of peripherally inserted central catheters
Sponsor: C.R. Bard Limited
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August 2011 (Version 1.1)

[1] Sherlock 3CG® TCS is a registered trademark of C. R. Bard Inc or an affiliate

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Instructions for sponsors

This is the template for submission of evidence to the National Institute for Health and Care Excellence (NICE) as part of the Medical Technologies Evaluation Programme process for developing NICE medical technologies guidance. Use of the submission template is mandatory.

The purpose of the submission is for the sponsor to collate, analyse and present all relevant evidence that supports the case for adoption of the technology into the NHS in England, within the scope defined by NICE. Failure to comply with the submission template and instructions could mean that the NICE cannot issue recommendations on use of the technology.

The submission should be completed after reading the 'Medical Technologies Evaluation Programme Methods guide' and the 'Medical Technologies Evaluation Programme Process guide' available at www.nice.org.uk/mt. After submission to, and acceptance by, NICE, the submission will be critically appraised by an External Assessment Centre appointed by NICE.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence'). When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly. For further information on disclosure of information, submitting cost models and equality issues, users should see section 11 of this document 'Related procedures for evidence submission'.

The submission should be concise and informative. The main body of the submission should not exceed 100 pages (excluding the pages covered by the template and appendices). The submission should be sent to NICE electronically in Word or a compatible format, not as a PDF file.

The submission must be a stand-alone document. Additional appendices may only be used for supplementary explanatory information that exceeds the level

of detail requested, but that is considered to be relevant to the case for adoption. Appendices will not normally be presented to the Medical Technologies Advisory Committee when developing its recommendations. Any additional appendices should be clearly referenced in the body of the submission. Appendices should not be used for core information that has been requested in the specification. For example, it is not acceptable to attach a key study as an appendix and to complete the economic evidence section with ‘see appendix X’.

All studies and data included in the submission must be referenced. Identify studies by the first author or trial ID, rather than by relying on numerical referencing alone (for example, ‘Trial 123/Jones *et al*.[126], rather than ‘one trial[126]’).Please use a recognised referencing style, such as Harvard or Vancouver.

The sponsor should provide a PDF copy of full journal articles or reports – in electronic or hard copy form – included in the submission, if the sponsor is either the copyright owner or has adequate copyright clearance to permit the intended use by NICE. This clearance must be wide enough to allow NICE to make further copies, store the article electronically for a limited period of time on a shared drive to be accessed by a limited number of staff. Additionally, any full article obtained and submitted in electronic format must be done so in a manner compliant with the relevant contractual terms of use permitting the sponsor electronic access to the article. If the sponsor does not have sufficient copyright clearance, they are asked to submit references or links only, or details of contacts for unpublished research. NICE will then itself obtain full copies of all relevant papers or reports, paying a copyright fee where necessary. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

If a submission is based on preliminary regulatory recommendations, the sponsor must advise NICE immediately of any variation between the preliminary and final approval.

Document key

Boxed text with a grey background provides specific and/or important guidance for that section. This should not be removed.

Information in highlighted black italic is to help the user complete the submission and may be deleted.

The user should enter text at the point marked ‘Response’ or in the tables as appropriate. ‘Response’ text may be deleted.

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Glossary of terms

If a glossary of terms is required to inform the submission of evidence include in the table. Delete if not required.

Term	Definition
ECG	**Echocardiograph**
NHS	**National Health Service**
PICC	**Peripherally Inserted Central Catheter**
TCS	**Tip Confirmation System**
TLS	**Tip Location System**
TPS	**Tip Positioning System**
CAJ	**Cavo-atrial junction**
SVC	**Superior Vena Cava**
UK	United Kingdom

Section A – Decision problem

Section A describes the decision problem, the technology and its clinical context. There is also information about ongoing studies, regulatory information and equality issues.

Sponsors should submit section A before the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

1 Statement of the decision problem

The decision problem is specified in the final scope issued by NICE. The decision problem states the key parameters that should be addressed by the information in the evidence submission. All statements should be evidence based and directly relevant to the decision problem.

Table A1 Statement of the decision problem

	Scope issued by NICE	Variation from scope	Rationale for variation
Population	Any adult patient with an indication where therapy requires venous access through a PICC.	None	N/A
Intervention	Sherlock 3CG Tip Confirmation System.	None	N/A
Comparator(s)	1). PICC insertion followed by chest X-ray to confirm tip placement 2). Fluoroscopy to guide PICC insertion and confirm tip placement.	None	N/A
Outcomes	1). Accuracy of catheter tip placement 2). Incidence of catheter malposition 3). Need for catheter re-positioning 4). Impact of malposition-related complications such as infection/thrombosis 5). Treatment delay following catheter placement 6). Reduced staff time 7). Reduced in-hospital stay 8). Requirement for confirmatory chest X-ray 9). Requirement for fluoroscopy to correctly place the PICC tip 10). Time taken to insert PICC		

	11). PICC failure/re-insertion rates 12). Patient experience measures 13). Quality of life 14). Device-related adverse events.		

Cost analysis	The cost analysis will include both the standard method of PICC placement and fluoroscopic method as comparators. The use in different care settings (e.g. secondary, tertiary care) will be considered. This includes considering the difference between inpatient and outpatient costs. Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios where the use of Sherlock removes the requirement for post-insertion confirmatory chest X-Ray.	None	N/A
Subgroups to be considered	None	None	N/A
Special considerations, including issues related to equality	Many patients requiring a PICC would be classed as disabled under the Equality Act 2010 but there are no equality issues	None	N/A

	with the use of Sherlock 3CG TCS.		

2 Description of technology under assessment

2.1 Give the brand name, approved name and details of any different versions of the same device.

Brand name and approved name is Sherlock 3CG Tip Confirmation System (TCS). The Sherlock 3CG TCS is a fifth generation device and the development timelines and different versions of the device are detailed below:-

1). Sherlock – Rectangular magnetic field sensor. No ECG. Tip location only.

2). Sherlock II – Y Shaped magnetic field sensor. No ECG. (with/without USB for Ultrasound). Tip location only.

3). Sherlock 3CG Tip Positioning System – Single ECG channel. Tip location and tip positioning.

4). Sapiens TCS and Sherlock II TLS – Double ECG channel (with/without USB for Ultrasound). Tip location and confirmation.

5). Sherlock 3CG TCS – Double ECG channel. USB for Ultrasound). Tip location and confirmation. The USB for Ultrasound is available in the US and not in the EU.

2.2 What is the principal mechanism of action of the technology?

Sherlock 3CG TCS is a fully integrated tip location and confirmation system which enables the magnetic and electrocardiographic (ECG) real-time tracking of the PICC tip during insertion, allowing the PICC placer to detect and correct any tip malpositions identified during the PICC placement procedure. Sherlock 3CG TCS is used in conjunction with ultrasound.

Sherlock comprises a system console including a control processor with display interface, a tip location sensor, a PowerPICC SOLO PICC Catheter with Sherlock stylet which displays on the interface when the tip location mode is active) and a remote control which allows the user to change settings through the procedure and maintain the sterile field. To aid documentation, a printer can also be purchased separately.

Sherlock is used with the PowerPICC SOLO Catheters which have the Sherlock 3CG TLS Stylet. The PowerPICC catheter is indicated for short or long-term peripheral access to the central venous system for intravenous therapy, power injection of contrast media, and allows for central venous pressure monitoring. The PowerPICC SOLO Catheter with Sherlock 3CG TLS stylet contains permanent, passive magnets encapsulated within the tip of the Sherlock 3CG TLS stylet. The magnets generate a magnetic field, which can be detected by the Sherlock TLS sensor, enabling magnetically-based tracking of the PICC tip during its advancement providing the placer rapid feedback on catheter tip location during PICC insertion. The mode of action of Sherlock is detailed below.

Sherlock is used in conjunction with the existing ultrasound machine. The Sherlock and ECG electrodes are placed on the patient's torso and remain in situ during the procedure and removed after. The ultrasound is used to introduce the PICC into the patient's vasculature. The Sherlock sensor picks up the magnetic signal at the tip of the PICC and the path it takes through the patient’s vasculature is visualised in real time on the interface. The interface displays the relative position, and orientation, of the magnet-tipped stylet to the sensor by (1) Taking a background measurement of the ambient magnetic field during the calibration cycle and (2) Sensing changes in the magnetic field. If the PICC passes to the contra-lateral side, up the internal jugular or does not drop into the superior vena cava (SVC) the PICC placer will see this and be able to adjust the tip into the correct position at the time of placement.

The Sherlock interface also simultaneously displays real-time ECG waveforms received from the patient’s skin (baseline) and from the tip of the catheter (intravascular). Intravascular ECG is acquired from a column of saline injected

into the PICC by the placer. Through observation of the displayed ECG P-wave, a clinician can determine the PICC tip location as it travels through the SVC, right atrial junction and right atrium – relative to the sino-atrial node from which ECG signals originate. Royal College of Nursing guidelines for infusion therapy (2010) recommend that the distal tip of a PICC should be in the lower third of the SVC. In patients with a distinct P-wave, the P-wave will increase in amplitude as the catheter approaches the top of the cavo-atrial junction (CAJ). A maximum P-wave height is recorded at the entrance of the atrium (close to the crista terminalis, at the CVJ. If the PICC is retracted, a gradual reduction of the P-wave height is obtained until the height is approximately half of the maximum P-wave height. This means that that tip is in the lower third of the SVC, just above the CAJ. If the catheter is retracted further, the P-wave reaches 'normal' dimensions and becomes similar to that shown by the baseline ECG and indicates the PICC is in the upper part of the SVC. However, if the PICC is advanced beyond the maximum P-wave height, the P-wave will decrease in amplitude and may be biphasic or inverted indicating that the PICC has entered the right atrium.

3 Clinical context

3.1 Provide a brief overview of the disease or condition for which the technology is being considered in the scope issued by NICE.

Sherlock 3CG TCS is indicated for use on any adult patient who requires a PICC and is not specific to any disease or condition. Limiting but not contraindicated situations for Sherlock 3CG TCS is in patients where alterations of cardiac rhythm change the presentation of the P-wave, as in atrial fibrillation, atrial flutter, severe tachycardia, and pacemaker driven rhythm. In such patients, who are usually identifiable prior to PICC insertion, the use of the Sherlock tip location sensor will track the PICC into the correct position but an additional method is required to confirm PICC tip placement.

PICCs are used in a variety of clinical scenarios and there is no single source for the average annual number of insertions. A review conducted in 1994, and

quoted by NICE, (NICE technology appraisals 49: The Use of Ultrasound Locating Devices for Placing Central Venous Catheters, September 2002. London, NICE) estimated that there were more than 200,000 central venous catheters (including PICCs) inserted in the UK annually. The figure quoted in this review does not exclusively refer to PICCs and include other types of central venous access devices used for a variety of indications and diseases. A report evaluating the state of the vascular access device market, indicates that in the UK, PICC sales for 2013 were approximately 74, 490 (iData, 2014). The report estimates that by 2020, PICC sales in the UK will have risen by 74% to approximately 129,198.

Indwelling times for PICCs can range from a few days to over a year, but on average PICCs tend to be in situ for periods of one week to three months, with the most frequent indwelling time being three weeks (iData Research Inc, June 2014). PICCs have a wide range of applications and are commonly used for:

1. Intravenous access for drugs and fluids
    - Infusion of irritant drugs—for example, chemotherapy
    - Total parenteral nutrition
    - Long term administration of drugs such as antibiotics
2. Monitoring or interventions
    - Central venous pressure
    - Repeated blood sampling
    - Where there is poor peripheral access.

3.2 Give details of any relevant NICE or other national guidance or expert guidelines for the condition for which the technology is being used. Specify whether the guidance identifies specific subgroups and make any recommendations for their treatment. If available, these should be UK based guidelines.

NICE technology appraisal [TA49], published in September 2002 is relevant for the condition for which Sherlock 3CG TCS is being used. This guidance recommends using two-dimensional imaging ultrasound guidance as the preferred method for insertion of central venous catheters (CVCs) into the internal jugular vein (IJV) in adults and children in elective situations. CVCs include PICCs. NICE recommends using 2-D imaging ultrasound guidance in most clinical circumstances where CVC insertion is necessary either electively or in an emergency situation. The guidance does not identify any specific subgroups. Sherlock 3CG TCS is used in conjunction with 2-D imaging ultrasound. The ultrasound is used to introduce the PICC into the patient's vasculature and then the Sherlock 3CG TCS is used to position the PICC and confirm the tip placement.

3.3 Describe the clinical pathway of care that includes the proposed use of the technology.

In current NHS clinical practice, PICCs are inserted in a wide range of clinical settings by a diverse group of clinicians including interventional radiologists, anaesthetists, general physicians, nurse specialists and intensivists. The range of settings in which PICCs are inserted includes operating theatres, emergency rooms, haematology, oncology, orthopaedic and other wards, radiology departments, Intensive Therapy / High Dependency Units and outpatient clinics. Current local NHS practice guidelines and policies determine that a chest x-ray must be performed before the PICC line can be used. Once the chest X-ray is performed, the guidelines state that no PICC line should be used, unless the X-ray has been checked and documented in the medical notes to confirm that the line is in the correct position for use. In some clinical settings, PICCs are placed in the interventional radiology suite

using fluoroscopy. Also, some patients may be referred to interventional radiology where a PICC cannot be repositioned at the bedside.

3.4 Describe any issues relating to current clinical practice, including any uncertainty about best practice.

3.5 Describe the new pathway of care incorporating the new technology that would exist if the technology was adopted by the NHS in England.

The new pathway of care will involve placing Sherlock 3CG TCS at the bedside in all cases where Sherlock 3CG TCS is indicated. Bedside placement could be in an inpatient, ward setting or in an outpatient setting. Using Sherlock 3CG negates the need for chest X-rays and fluoroscopy for tip confirmation post PICC insertion. Tip location will be confirmed by the PICC placer at the site of insertion and intravenous therapy can begin immediately following PICC insertion without the delays associated with waiting for a confirmatory chest x-ray.

Sherlock 3CG TCS will replace chest x-ray confirmation for the majority of patients (>90%) requiring a PICC for venous access therapy, however, Sherlock 3CG TCS will be used alongside chest X-ray for patients for whom it's use for tip location confirmation is limited (<10%) in patients.

Furthermore, by negating the need for radiological confirmation, PICCs could potentially be placed in community settings, reducing in-patient bed occupancy to start initial treatment through a PICC or used in patients for whom a confirmatory X-ray is contra-indicated e.g. during pregnancy.

3.6 Describe any changes to the way current services are organised or delivered as a result of introducing the technology.

In places where PICCs are placed in costly radiology suites, PICC placement could be moved to cheaper outpatient department

3.7 Describe any additional tests or investigations needed for selecting or monitoring patients, or particular administration requirements, associated with using this technology that are over and above usual clinical practice.

None

3.8 Describe any additional facilities, technologies or infrastructure that need to be used alongside the technology under evaluation for the claimed benefits to be realised.

None

3.9 Describe any tests, investigations, interventions, facilities or technologies that would no longer be needed with using this technology.

X-ray and fluoroscopy would be reduced significantly and will still be used in a small proportion of patients for whom Sherlock 3CG TCS is not indicated.

3.10 Describe how the NHS in England can disinvest from tests, investigations, interventions, facilities or technologies described in section 3.9 that would no longer be needed with using this technology.

No disinvestment would be necessary as x-ray and fluoroscopy will still be required for other clinical uses.

4 Regulatory information

Provide PDF copies of the following documents:

- instructions for use
- CE mark certificate or equivalent UK regulatory approval such as EC declaration of conformity
- quality systems (ISO 13485) certificate (if required).

4.1 Does the technology have CE mark for the indication(s) specified in the scope issued by NICE? If so, give the date that authorisation was received. If not, state current UK regulatory status, with relevant dates (for example, date of application and/or expected approval dates).

The Sherlock 3CG TCS is classified as Class I, per Annex IX Rule 12. The Sherlock 3CG TCS is used together with the PowerPICC SOLO catheter with the Sherlock 3CG TPS stylet, which is classified as a Class III device under Rule 8 in accordance with Annex IX of the Medical Devices Directive, 93/42/EEC. The Sherlock 3CG TCS received CE marking in December 2011 and this was updated in February 2013. The PowerPICC SOLO catheter with the Sherlock 3CG TPS stylet received CE marking in February 2012. The Sherlock 3CG TCS was launched in the UK in April 2013.

4.2 Does the technology have regulatory approval outside the UK? If so, please provide details.

The Sherlock 3CG has approval in the United States from the Food and Drug Agency.

4.3 If the technology has not been launched in the UK provide the anticipated date of availability in the UK.

Sherlock 3CG was launched in the UK in April 2013.

4.4 If the technology has been launched in the UK provide information on the use in England.

Sherlock 3CG is currently being used at the following clinical sites in the NHS in England.

- Cambridge University Hospitals NHS Foundation Trust (Addenbrooke's Hospital)
- Frimley Park Hospital NHS Foundation Trust
- Heart of England NHS Foundation Trust (Good Hope Hospital)

- Heart of England NHS Foundation Trust (Heartlands Hospital)
- King's College Hospital NHS Foundation Trust (King's College Hospital)
- Maidstone and Tunbridge Wells NHS Trust (Maidstone Hospital)
- Medway NHS Foundation Trust (Medway Maritime Hospital)
- Northampton General Hospital NHS Trust (Northampton General Hospital)
- Oxford University Hospitals NHS Trust (John Radcliffe Hospital)
- Royal Liverpool and Broadgreen University Hospitals NHS Trust (Royal Liverpool)
- The Royal Marsden NHS Foundation Trust (The Royal Marsden Hospital, London site)
- The Royal Marsden NHS Foundation Trust (The Royal Marsden Hospital, Sutton site)
- University Hospitals Birmingham NHS Foundation Trust (Queen Elizabeth Hospital)
- University Hospitals Bristol NHS Foundation Trust (Bristol Haematology and Oncology Centre)

Other NHS sites (Ireland) using Sherlock are:-

- Belfast Health and Social Care Trust (Belfast City Hospital, Belfast)
- Western Health and Social Care Trust (Altnagelvin Area Hospital, Derry).

64% of the NHS England clinical sites named above, (9/14 sites: Royal Marsden Surrey; Royal Marsden London; Frimley; Belfast City; Medway Maritime, Kings College Oncology, Heartlands and Good Hope) are now using

Sherlock 3CG TCS to place and confirm PICCs without x-ray confirmation post PICC insertion, for all suitable patients where the use of Sherlock 3CG TCS is indicated and one other site is awaiting imminent Trust sign-off to eliminate x-ray post PICC insertion (Bristol Oncology).

5 Ongoing studies

5.1 Provide details of all completed and ongoing studies on the technology from which additional evidence relevant to the decision problem is likely to be available in the next 12 months.

A Study to Assess Placement and Confirmation of Peripheral Inserted Central Catheters Tip Position Using a New Electrocardiographic Method (SHERLOCK 3CG). Centre Leon Berard, France. (ClinicalTrials.gov identifier: NCT01969981).

This is a prospective, single centre, observational study of patients aged 18+ requiring a PICC. The purpose of the study is to determine whether Sherlock 3CG TCS, is an adequate, safe and efficient method for the placement and confirmation of the tip of the PICC.

The study was started in October 2013 with an estimated completion date of April 2014 and a target recruitment of 500 patients. The patient's routine care will not be modified and only PICC will be assessed in the study. PICC placement will be performed using the Site Rite ultrasound guidance and tip position will be confirmed using the Sherlock 3CG TCS. Patients won't be followed up in the study.

Inclusion Criteria:

- 18 years-old patient or older
- Patient requiring PICC placement in the vascular access unit
- Patient able to read and understand the French language

- Patient affiliated with a social security system.

Exclusion Criteria:

- Any contraindication to PICC insertion
- Patient unable to lie in the supine position
- Patient with a Body Mass Index > 40
- -Any medical condition that could change the normal presentation of the P-wave such as arrhythmia, atrial flutter, pace maker with permanent stimulation.

Intervention: PICC placement with Sherlock 3CG

Outcomes

All outcomes will be assessed during the procedure (Day 0).

Primary Outcome(s)

- Efficacy of PICC placement using Sherlock 3CG TCS.

Secondary Outcome(s)

- Acute complications rates
- Pain
- Final radiation rate
- Number of punctures in brachial site
- Number of repositions after procedure closed
- Percentage of patients requiring fluoroscopy
- Percentage of patients with good placement as confirmed by X-Ray
- Unique function rate.

5.2 If the technology is, or is planned to be, subject to any other form of assessment in the UK, please give details of the assessment, organisation and expected timescale.

Sherlock 3CG TCS is not subject to any other form of assessment in the UK.

6 Equality

NICE is committed to promoting equality of opportunity and eliminating unlawful discrimination on the grounds of age, disability, gender reassignment, race, religion or belief, sex, and sexual orientation, and to comply fully with legal obligations on equality and human rights.

Equality issues require special attention because of NICE's duties to have due regard to the need to eliminate unlawful discrimination, promote equality and foster good relations between people with a characteristic protected by the equalities legislation and others.

Any issues relating to equality that are relevant to the technology under assessment should be described. This section should identify issues described in the scope and also any equality issues not captured in the final scope.

Further details on equality may be found in section 11.3 of this document.

6.1.1 Describe any equality issues relating to the patient population and condition for which the technology is being used.

Although many patients requiring a PICC would be classed as disabled under the Equality Act 2010, there are no equality issues with the use of Sherlock 3CG TCS.

6.1.2 Describe any equality issues relating to the assessment of the technology that may require special attention.

There are no equality issues relating to the assessment of Sherlock 3CG requiring special attention.

6.1.3 How will the submission address these issues and any equality issues raised in the scope?

There were no equality issues raised in the scope.

Section B – Clinical evidence

7 Published and unpublished clinical evidence

Section B requires sponsors to present published and unpublished clinical evidence for their technology.

Sponsors should read section 6 of the Medical Technologies Evaluation Programme methods guide on published and unpublished evidence, available from www.nice.org.uk/mt

All statements should be evidence-based and directly relevant to the scope. Reasons for deviating from the scope should be clearly stated and explained in table A1.

Sponsors are required to submit section B in advance of the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

7.1 Identification of studies

Published studies

7.1.1 Describe the strategies used to retrieve relevant clinical data from the published literature. Exact details of the search strategy used should be provided in section 10, appendix 1.

The exact details of the search strategy used to identify relevant clinical data from the published literature is presented in Section 8.1, Appendix 1. The search strategy aimed to identify all clinical studies of Sherlock 3CG TCS used in adults undergoing PICC insertion. The strategy was structured to search for two concepts: peripherally inserted central catheters and Sherlock 3CG TCS and its comparators (X-ray; fluoroscopy).

The strategy excluded publication types which were unlikely to yield detailed study reports: news, editorials, comments, and letters. All human studies published in full text, abstract, or poster form were eligible for inclusion. All

studies were of adult patients aged at least 18 years who underwent insertion of a PICC. The strategy also excluded animal studies as well as studies conducted on children because Sherlock 3CG TCS is not indicated for use in this age group. To ensure all relevant studies were identified, a limit was set for the publication year, to identify studies published from 2000 onwards, although Sherlock 3CG TCS first became available in 2006. The searches were conducted in a range of relevant databases of research (documented in Section 10, Appendix 1). The resources searched include databases specified as a minimum for the clinical evidence search in section 80.1 of the NICE MTEP Sponsor Submission Template, plus additional relevant databases of clinical evidence such as clinical trial registers and conference abstract sources.

Searches were conducted in each database or resource listed in Section 8.1.1. All search results were loaded into the EndNote bibliographic software; deduplicated and transferred to Excel for screening and data abstraction.

Unpublished studies

7.1.2 Describe the strategies used to retrieve relevant clinical data from unpublished sources.

The following strategies were utilised to obtain unpublished data.

1). Clinicians in the NHS sites that are using Sherlock 3CG TCS were approached to see if they were conducting an internal studies or were maintain local registries of PICC use or conducting any clinical audits.

2). Authors identified from relevant conference oral and poster presentations were approached.

7.2 Study selection

Published studies

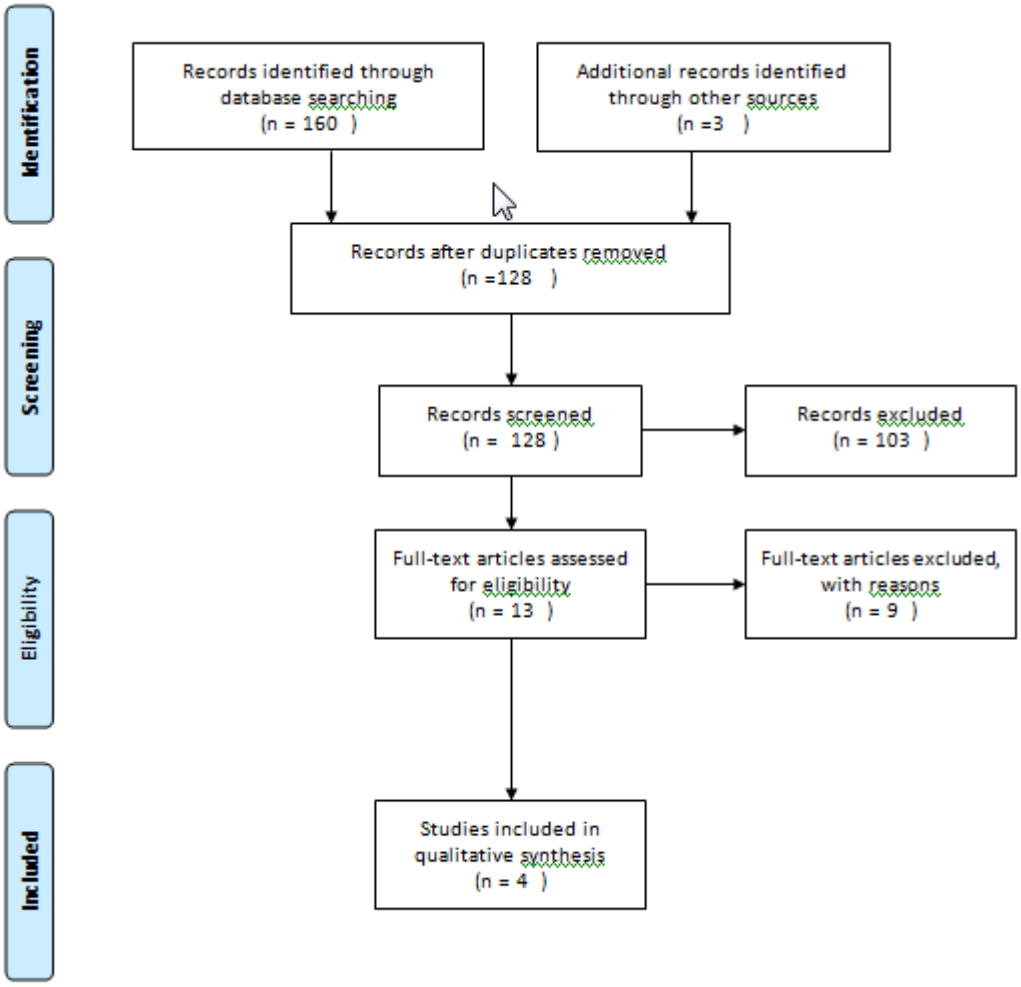
7.2.1 Complete table B1 to describe the inclusion and exclusion criteria used to select studies from the published literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table B1 Selection criteria used for published studies

Inclusion criteria	
Population	Adult patients requiring a PICC
Interventions	Sherlock 3CG, X-ray, fluoroscopy
Outcomes	• accuracy of catheter tip placement • incidence of catheter malposition • need for catheter re-positioning • impact of malposition-related complications such as infection/thrombosis • treatment delay following catheter placement • reduced staff time • reduced in-hospital stay • requirement for confirmatory chest X-ray • requirement for fluoroscopy to correctly place the PICC tip • time taken to insert PICC • PICC failure/re-insertion rates • patient experience measures • quality of life • device-related adverse events.
Study design	Randomised controlled studies, observational studies, case studies
Language restrictions	English language articles only
Search dates	2000 - current
Exclusion criteria	
Population	Children
Interventions	None
Outcomes	None
Study design	None
Language restrictions	Non-English language
Search dates	None

7.2.2 Report the numbers of published studies included and excluded at each stage in an appropriate format.

Figure 1. Prisma Diagram of Included and Excluded studies



Unpublished studies

7.2.3 Complete table B2 to describe the inclusion and exclusion criteria used to select studies from the unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table B2 Selection criteria used for unpublished studies

Inclusion criteria	
Population	Adults requiring a PICC
Interventions	Sherlock 3CG, X-ray, Fluoroscopy
Outcomes	• accuracy of catheter tip placement • incidence of catheter malposition • need for catheter re-positioning • impact of malposition-related complications such as infection/thrombosis • treatment delay following catheter placement • reduced staff time • reduced in-hospital stay • requirement for confirmatory chest X-ray • requirement for fluoroscopy to correctly place the PICC tip • time taken to insert PICC • PICC failure/re-insertion rates • patient experience measures • quality of life • device-related adverse events.
Study design	All study designs
Language restrictions	English language only
Search dates	All dates
Exclusion criteria	
Population	Children
Interventions	None
Outcomes	None
Study design	News, editorials, comments, and letters
Language restrictions	Non English language
Search dates	None

7.2.4 Report the numbers of unpublished studies included and excluded at each stage in an appropriate format.

None

7.3 Complete list of relevant studies

The sponsor should provide a PDF copy of all studies included in the submission if the sponsor is either the copyright owner or has adequate copyright clearance to permit the intended use by NICE. If the sponsor does not have sufficient copyright clearance, they are asked to submit references or links only, or details of contacts for unpublished studies. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

7.3.1 Provide details of all published and unpublished studies identified using the selection criteria described in tables B1 and B2.

Table B3 List of relevant published studies

Primary study reference	Study name (acronym)	Population	Intervention	Comparator
Adams, 2013	The Clinical Efficacy of PICC Tip Confirmation using ECG Tip Locator Technology.	Patients requiring PICC	Sherlock 3CG TCS	X-ray
Barton A, 2014.	Evaluation of ECG and PICC tip location. Is it safe to stop using x-ray?	Adult patients requiring a PICC insertion	Sherlock 3CG TCS	X-ray
Johnston A, 2014	Evaluation of PICC malposition rates and the impact of the Sherlock 3CG TCS.	Adult, intensive care patients requiring a PICC insertion.	Sherlock 3CG TCS	X-ray
Kupka, 2011	Changing nursing practice and improving patient care by using ECG guidance to eliminate post PICC insertion radiograph	Not reported	Not reported	X-ray
Lelkes V, 2013	Analysis of the Sherlock II tip location system for inserting peripherally inserted central venous catheters.	Patients who had a PICC placed at the bedside using the Sherlock II tip locating system.	Sherlock II	X-ray
Naylor C, 2007	Reduction of malposition in peripherally inserted central catheters with tip location system.	Patients requiring a PICC	Sherlock TLS	X-ray
Oakley C, 2011.	PICC journey to CAJ by way of Sapiens.	Not reported	Sapiens TCS	X-ray
Parikh, 2012	Successful Implementation of Electrocardiographic-Guided PICC placement with a Nurse Comprised	Patients with PICCs placed using Sherlock 3CG TCS	Sherlock 3CG TCS	X-ray

	PICC Team			
Pittiruti, 2010	Positioning the tip of central venous catheters by the intracavitary ECG method, using a new specific device.	Patients who underwent positioning of central vascular access devices	Sapiens TLS	X-ray
Pittiruti, 2011	Rapid vein assessment before central venous catheterization: The GAVeCeLT recommendations.	Patients with atrial fibrillation, candidate to PICC or CVC insertion	Sapiens TLS	X-ray
Shukla, 2012	Efficacy of Sherlock II tip location system for bedside peripherally inserted central venous catheter	Patients who had bedside PICC placement	Sherlock II	X-ray
Smith, 2010	Intravenous electrocardiographic evidence	Patients undergoing PowerPICC insertion	ECG	None
Stewart F, 2013.	New Australian Experience: Improvement in PICC insertion techniques using real time tracking and ECG for optimal PICC tip position (without need for CXR).	Patients requiring PICC insertion.	Sherlock 3CG TCS	X-ray
Symington K, 2011	Sherlock 3CG Spokane Trial	Not reported	Sherlock 3CG TCS	X-ray

Table B4 List of relevant unpublished studies

Data source	Study name (acronym)	Population	Intervention	Comparator
N/A				

7.3.2 State the rationale behind excluding any of the published studies listed in tables B3 and B4.

13 relevant studies were identified from the literature search. 9 Studies were excluded for the following reasons:-

- Access to the level of study data needed was not possible.
- The version of Sherlock reported in the study was a predecessor of Sherlock 3CG TCS.
- Study linked from a clinical trials register but full text does not mention explicitly that the device used was Sherlock 3CG TCS.
- Studies were published with different study names but are the same study where one is published as an abstract and then as a full text article.

7.4 Summary of methodology of relevant studies

7.4.1 Describe the study design and methodology for each of the published and unpublished studies using tables B5 and B6 as appropriate. A separate table should be completed for each study.

Table B5 Summary of methodology for randomised controlled trials

No randomised controlled trials were identified.

Table B6 Summary of methodology for observational studies

Study name	**Successful Implementation of Electrocardiographic-Guided PICC Placement with a Nurse-Comprised PICC Team**
Objective	1).To evaluate Sherlock 3CG TCS in the placement of PICCs. 2). To successfully implement use of the Sherlock 3CG to reduce the utilization of chest radiographs for PICC positioning.
Location	USA.
Design	Case Series
Duration of study	October 2011 to April 2012

	November 2012 to May 2013
Patient population	Inpatients and outpatients attending the Mayo Clinic and requiring a PICC. The age range of the patients was from 15 to 100 years, with a mean age of 62.
Sample size	October 2012 – May 2013: 247 PICC lines in 221 patients. After exclusions, 209 PICCs were evaluated. November 2012 – May 2013: 437 PICCs
Inclusion criteria	None reported.
Exclusion criteria	Patients with atrial fibrillation, atrial flutter or lack of an identifiable p wave.
Intervention(s) (n =) and comparator(s) (n =)	Sherlock 3CG = 209 PICC insertions All patients were x-rayed for confirmation of tip position.
Baseline differences	No patient demographics were reported
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	N/A
Statistical tests	N/A
Primary outcomes (including scoring methods and timings of assessments)	Successful placement of the tip of the PICC into the SVC or CAJ. Assessment of outcomes was done during the procedure or immediately after (Day 0).
Secondary outcomes (including scoring methods and timings of assessments)	Reduction in the use of x-ray for PICC confirmation.

Study name	**The Clinical Efficacy of PICC Tip Confirmation Using ECG Tip Locator Technology**
Objective	To validate PICC tip location when utilizing Sherlock 3CG TCS as compared to chest x-ray verification in order to eliminate the mandatory use of chest x-ray.
Location	USA
Design	Case Series
Duration of study	9 months
Patient population	Adults requiring a PICC insertion
Sample size	333 patients.
Inclusion criteria	Patients requiring a PICC
Exclusion criteria	Patients with no identifiable p-wave.

Intervention(s) (n =) and comparator(s) (n =)	Sherlock 3CG TCS X-ray
Baseline differences	Patient demographics were not described.
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	N/A
Statistical tests	None reported
Primary outcomes (including scoring methods and timings of assessments)	Tip location accuracy. Usability of Sherlock 3CG TCS.
Secondary outcomes (including scoring methods and timings of assessments)	1). Cost of insertion 2). Time taken to insert PICC.

Study name	**Evaluation of ECG and PICC Tip Location Technology. Is it Safe to Stop Using X-ray?**
Objective	Clinical trial of Sherlock 3CG TCS
Location	UK
Design	Case Series
Duration of study	3 months (data available for period following initial trial period).
Patient population	Not reported
Sample size	65 patients. (While awaiting approval to stop x-raying; an additional 225 PICCs were placed).
Inclusion criteria	All adults requiring a PICC
Exclusion criteria	Patients with atrial fibrillation
Intervention(s) (n =) and comparator(s) (n =)	Sherlock 3CG TCS = 65 (A further 225 after the initial 3 month trial) All patients were x-rayed post PICC insertion
Baseline differences	Not reported
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	N/A
Statistical tests	N/A

Primary outcomes (including scoring methods and timings of assessments)	Number of PICCs appropriately placed in the SVC.
Secondary outcomes (including scoring methods and timings of assessments)	None reported

Study name	**A New Australian Experience: Improvement in Peripherally Inserted Central Catheter (PICC) Insertion Technique Using Real Time Tracking Technology & Optimal PICC Tip Position (Without the Need for CXR)**
Objective	To assess the accuracy and proficiency of implementing Sherlock 3CG TCS for PICC insertion.
Location	Australia
Design	Case Series
Duration of study	November 2012 to March 2013
Patient population	Patients requiring a PICC
Sample size	65 patients
Inclusion criteria	Not reported
Exclusion criteria	Not reported
Intervention(s) (n =) and comparator(s) (n =)	Sherlock 3CG TCS
Baseline differences	Not reported
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	N/A
Statistical tests	N/A
Primary outcomes (including scoring methods and timings of assessments)	Accuracy of PICC insertion
Secondary outcomes (including scoring methods and timings of assessments)	Cost savings Time saved

Study name	**Analysis of Clinical Audit Data**
Objective	To
Location	UK
Design	Pooled analysis of data gathered from 5 NHS clinical sites using Sherlock 3CG TCS
Duration of study	N/A
Patient population	Patients who have a PICC inserted using Sherlock 3CG TCS
Sample size	
Inclusion criteria	
Exclusion criteria	
Intervention(s) (n =) and comparator(s) (n =)	
Baseline differences	
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	
Statistical tests	
Primary outcomes (including scoring methods and timings of assessments)	
Secondary outcomes (including scoring methods and timings of assessments)	

7.4.2 Provide details on data from any single study that have been drawn from more than one source (for example a poster and unpublished report) and/or when trials are linked this should be made clear (for example, an open-label extension to randomised controlled trial).

N/A

7.4.3 Highlight any differences between patient populations and methodology in all included studies.

It is not possible to comment on any differences between the patient populations and methodology of the included studies as information on patient demographics is not reported in all of the abstracts for the studies and no full text articles were available.

7.4.4 Provide details of any subgroup analyses that were undertaken in the studies included in section 7.4.1. Specify the rationale and state whether these analyses were pre-planned or post-hoc.

N/A

7.4.5 If applicable, provide details of the numbers of patients who were eligible to enter the study(s), randomised, and allocated to each treatment in an appropriate format.

N/A

7.4.6 If applicable provide details of and the rationale for, patients that were lost to follow-up or withdrew from the studies.

N/A

7.5 Critical appraisal of relevant studies

7.5.1 Complete a *External Assessment Centre.* separate quality assessment table for each study. A suggested format for the quality assessment results is shown in tables B7 and B8.

Table B7 Critical appraisal of randomised control trials

No randomised control trials identified.

Table B8 Critical appraisal of observational studies

Study name: Successful Implementation of Electrocardiographic-Guided PICC Placement with a Nurse-Comprised PICC Team		
Study question	**Response yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Not clear	No details of the patient recruitment process are reported in the abstract.
Was the exposure accurately measured to minimise bias?	Not clear	No details of the PICC insertion process were reported in the poster abstract.
Was the outcome accurately measured to minimise bias?	Not clear	
Have the authors identified all important confounding factors?	N/A	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	
How precise (for example, in terms of confidence interval and p values) are the results?	N/A	
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

Study name: The Clinical Efficacy of PICC Tip Confirmation Using ECG Tip Locator Technology.		
Study question	**Response yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Not clear	No details of the patient recruitment process are reported in the abstract.
Was the exposure	Not clear	No details of the PICC insertion process were

accurately measured to minimise bias?		reported in the poster abstract.
Was the outcome accurately measured to minimise bias?	Yes	Tip location accuracy - For all PICCs that were successfully placed using the Sherlock 3CG TCS, a subsequent x-ray was performed on all patients. Usability of Sherlock 3CG TCS – No details reported on how this was measured.
Have the authors identified all important confounding factors?	N/A	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	
How precise (for example, in terms of confidence interval and p values) are the results?	N/A	
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

Study name: Evaluation of ECG and PICC Tip Location Technology. Is it Safe to Stop Using X-ray?		
Study question	**Response yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Yes	All adult patients requiring a PICC were recruited for the study. The inclusion and exclusion criteria are described.
Was the exposure accurately measured to minimise bias?	Not clear	No details of the PICC insertion process were reported in the poster abstract.
Was the outcome accurately measured to minimise bias?	Not clear	The abstract does not report explicitly state how PICC position accuracy was measured.
Have the authors identified all important confounding	N/A	

factors?		
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	
How precise (for example, in terms of confidence interval and p values) are the results?		
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

Study name: A New Australian Experience: Improvement in Peripherally Inserted Central Catheter (PICC) Insertion Technique Using Real Time Tracking Technology & Optimal PICC Tip Position (Without the Need for CXR)		
Study question	**Response yes/no/not clear/N/A)**	**How is the question addressed in the study?**
Was the cohort recruited in an acceptable way?	Not clear	No details of the patient recruitment process are reported in the abstract.
Was the exposure accurately measured to minimise bias?		All PICCs were inserted as per hospital and manufacturer guidelines and Sherlock 3CG TCS was used to track the PICC using real time navigation and position the catheter tip at the CAJ using ECG technology.
Was the outcome accurately measured to minimise bias?		Tip position accuracy - When a max P wave was achieved the PICC was secured and the tip confirmed using CXR.
Have the authors identified all important confounding factors?	N/A	
Have the authors taken account of the confounding factors in the design and/or analysis?	N/A	
Was the follow-up of patients complete?	N/A	
How precise (for example, in terms of		

confidence interval and p values) are the results?		
Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study		

7.6 Results of the relevant studies

7.6.1 Complete a results table for each study with all relevant outcome measures pertinent to the decision problem. A suggested format is given in table B9.

Table B9 Outcomes from published and unpublished studies

Study name		**Successful Implementation of Electrocardiographic-Guided PICC Placement with a Nurse-Comprised PICC Team**
Size of study groups	**Treatment**	437
	Control	N/A
Study duration	**Time unit**	Phase 1- 6 months Phase 2 – 6 months
Type of analysis	**Intention-to -treat/per protocol**	N/A
Outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Other outcome	**Name**	N/A
	Unit	
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Comments		Phase I – 83% of PICC tips were placed in the SVC or CAJ. Phase II – 96% of PICC tips were placed in the SVC or CAJ.

Study name		The Clinical Efficacy of PICC Tip Confirmation Using ECG Tip Locator Technology
Size of study groups	Treatment	333
	Control	N/A
Study duration	Time unit	9 months
Type of analysis	Intention-to-treat/per protocol	N/A
Outcome	Name	
	Unit	
Effect size	Value	N/A
	95% CI	N/A
Statistical test	Type	N/A
	p value	N/A
Other outcome	Name	N/A
	Unit	
Effect size	Value	N/A
	95% CI	N/A
Statistical test	Type	N/A
	p value	N/A
Comments		Usability of Sherlock 3CG TCS – The device was utilized in 83.5% of patients. Sherlock could not be used on 13.5% of patients due to abnormal p-waves, loose connections or poor lead placement. Accuracy of Sherlock 3CG TCS = 98.2% of PICC placements. Malposition rate = 1.8%. Time to infusion: PICC verified by x-ray = 101 minutes compared to 39.5 minutes with Sherlock 3CG TCS.

Study name		Evaluation of ECG and PICC Tip Location Technology. Is it Safe to Stop Using X-ray?
Size of study groups	Treatment	65 (225 post evaluation completion)
	Control	N/A
Study duration	Time unit	3 months
Type of analysis	Intention-to-treat/per protocol	N/A
Outcome	Name	N/A
	Unit	N/A
Effect size	Value	N/A
	95% CI	N/A
Statistical test	Type	N/A
	p value	N/A
Other outcome	Name	N/A
	Unit	
Effect size	Value	N/A
	95% CI	N/A
Statistical test	Type	N/A
	p value	N/A
Comments		100% of all PICC insertions were appropriately placed in the SVC.

Study name		**A New Australian Experience: Improvement in Peripherally Inserted Central Catheter (PICC) Insertion Technique Using Real Time Tracking Technology & Optimal PICC Tip Position (Without the Need for CXR)**
Size of study groups	**Treatment**	160
	Control	N/A
Study duration	**Time unit**	
Type of analysis	**Intention-to-treat/per protocol**	N/A
Outcome	**Name**	N/A
	Unit	N/A
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Other outcome	**Name**	N/A
	Unit	
Effect size	**Value**	N/A
	95% CI	N/A
Statistical test	**Type**	N/A
	p value	N/A
Comments		1hr 51min average wait time for x-ray removed per PICC insertion. 96% of ECG guided placements were successfully position within the CAJ with maximum P wave achieved. 4% of tips were reported to be in the Right Atrium.

7.6.2 Justify the inclusion of outcomes in table B9 from any analyses other than intention-to-treat.

7.7 Adverse events

In section 7.7 the sponsor is required to provide information on the adverse events experienced with the technology being evaluated in relation to the scope.

For example, post-marketing surveillance data may demonstrate that the technology shows a relative lack of adverse events commonly associated with the comparator.

7.7.1 Using the previous instructions in sections 7.1 to 7.6, provide details of the identification of studies on adverse events, study selection, study methodologies, critical appraisal and results.

The exact details of the search strategy used to identify relevant clinical data from the published literature is presented in Section 8.2, Appendix 2. The search strategy aimed to identify all clinical studies of Sherlock 3CG TCS used in adults undergoing PICC insertion. The strategy was structured to search for three concepts: peripherally inserted central catheters, Sherlock 3CG TCS and its comparators (X-ray; fluoroscopy) and adverse effects.

The strategy excluded publication types which were unlikely to yield detailed study reports: news, editorials, comments, and letters. All human studies published in full text, abstract, or poster form were eligible for inclusion. All studies were of adult patients aged at least 18 years who underwent insertion of a PICC. The strategy also excluded animal studies as well as studies conducted on children because Sherlock 3CG TCS is not indicated for use in this age group. To ensure all relevant studies were identified, a limit was set for the publication year, to identify studies published from 2000 onwards, although Sherlock 3CG TCS first became available in 2006. The searches were conducted in a range of relevant databases of research (documented in Section 10, Appendix 1). The resources searched include databases specified as a minimum for the clinical evidence search in section 8.1 of the NICE MTEP Sponsor Submission Template, plus additional relevant databases of clinical evidence such as clinical trial registers and conference abstract sources.

Searches were conducted in each database or resource listed in Section 8.2. All search results were loaded into the EndNote bibliographic software; deduplicated and transferred to Excel for screening and data abstraction.

7.7.2 Provide details of all important adverse events reported for each study. A suggested format is shown in table B10.

No adverse events were reported in any studies

Table B10 Adverse events across patient groups

	Time period 1			***Time period 2 etc.***		
	Intervention **% of patients (n = *x*)**	***Comparator*** **% of patients (n = *x*)**	**Relative risk (95% CI)**	***Intervention*** **% of patients (n = *x*)**	***Comparator*** **% of patients (n = *x*)**	**Relative risk (95% CI)**
Class 1 (for example, nervous system disorders)						
Adverse event 1						
Adverse event 2						
Class 2 (for example, vascular disorders)						
Adverse event 3						
Adverse event 4						
CI, confidence interval Adapted from European Public Assessment Reports published by the European Medicines Agency						

7.7.3 Describe all adverse events and outcomes associated with the technology in national regulatory databases such as those maintained by the MHRA and FDA (Maude).

No adverse events and outcomes were reported in the MHRA database.

A search of Sherlock 3CG or Sapiens on FDA (Maude) retrieved 51 records. The incidents reported are not necessarily device-related complications or adverse events but rather are technical issues related to the device.

7.7.4 Provide a brief overview of the safety of the technology in relation to the scope.

Sherlock 3CG TCS provides a safe method for PICC tip placement and confirmation.

7.8 Evidence synthesis and meta-analysis

When more than one study is available and the methodology is comparable, a meta-analysis should be considered.

Section 7.8 should be read in conjunction with the 'Medical Technologies Evaluation Programme Methods Guide', available from www.nice.org.uk/mt

7.8.1 Describe the technique used for evidence synthesis and/or meta-analysis. Include a rationale for the studies selected, details of the methodology used and the results of the analysis.

Direct comparison of studies is not appropriate.

7.8.2 If evidence synthesis is not considered appropriate, give a rationale and provide a qualitative review. The review should summarise the overall results of the individual studies with reference to their critical appraisal.

All the studies that were identified as relevant for inclusion were clinical case series of evaluations of the accuracy of Sherlock 3CG TCS. None of the studies employed statistical tests to evaluate outcomes and as such it is not appropriate to combine the data from these multiple sources of data. In addition, all the studies were abstracts or poster presentations for which no full text was available. The absence of the full text of the studies together with the study designs (clinical evaluations of Sherlock 3CG TCS) are factors that present limitations in critically appraising the studies and objectively assessing the quality and robustness of the studies.

Data from the included studies shows that the accuracy of Sherlock 3CG TCS in determining the tip location ranged from 83% in the study conducted by Parikh (2012) and 100% in the study by Barton (2014). Studies by Stewart (2014) and Adams (2013) reported accuracy as 96% and 98.2% respectively. The study by Parikh (2012) was conducted in two phases: Phase I and Phase

II. The accuracy of Sherlock in Phase I was reported as unsatisfactory at 83% but this increased to 96% in Phase II. Parikh (2012) highlight how the lack of adequate training of PICC placers may have contributed to the unsatisfactory results seen in Phase I and with increased training accuracy improved.

Consequently, malposition rates of Sherlock 3CG TCS ranged between 17 and 0%.

The studies by Stewart (2013) and Adams (2013) also attempted to determine the time savings of using Sherlock 3CG TCS to confirm PICC tip placement compared to using x-ray for confirmation. Adams (2013) report that by using Sherlock 3CG TCS, a time saving of 61 minutes is made compared to waiting for an x-ray procedure and radiologist report to verify the x-ray. Stewart (2013) reports this time saving as 111 minutes.

Sherlock 3CG TCS is not indicated for use in patients without an identifiable p-wave. In their study, Adams (2013) report that Sherlock 3CG TCS was not used in approximately 18% of patients. This figure included patients with an abnormal p-wave, loose connections and poor ECG lead placement.

7.9 Interpretation of clinical evidence

7.9.1 Provide a statement of principal findings from the clinical evidence highlighting the clinical benefit and any risks relating to adverse events from the technology.

The principal findings of the studies indicate that Sherlock 3CG TCS is an accurate method of placing PICCs and confirming the final tip position of the PICC and it is time saving when compared to tip confirmation with x-ray. The results also indicate that Sherlock 3CG TCS is safe to use and is not associated with any adverse effects or complications.

The results of the studies demonstrate that Sherlock 3CG TCS provides clinical benefit by reducing the incidence of PICC malpositions and subsequent repositioning; eliminates the need for post insertion x-ray which

results in a shortened care pathway and reduction in staff requirements for PICC tip confirmation.

7.9.2 Provide a summary of the strengths and limitations of the clinical-evidence base of the technology.

Strengths

The studies were conducted in a ‘real-life’, non-controlled environment and as such the results provide an insight into the use of Sherlock 3CG TCS in a normal clinical setting.

Limitations

As no full text papers were available, conducting a meaningful quality assessment and critique of the studies was not possible.

The design of the studies is considered as low-level evidence which can be influenced by bias and in some cases relies on the availability and accuracy of data records.

7.9.3 Provide a brief statement on the relevance of the evidence base to the scope. This should focus on the claimed patient- and system-benefits described in the scope.

The evidence presented is relevant to the scope prepared by NICE. With the exception of data on reductions in hospital stay and patient experience, the results of the clinical studies supports the claims made in the scope.

7.9.4 Identify any factors that may influence the external validity of study results to patients in routine clinical practice.

None

7.9.5 Based on external validity factors identified in 7.9.4 describe any criteria that would be used in clinical practice to select patients for whom the technology would be suitable.

N/A

Section C – Economic evidence

Section C requires sponsors to present economic evidence for their technology.

All statements should be evidence-based and directly relevant to the decision problem.

The approach to the de novo cost analysis expected to be appropriate for most technologies is cost-consequence analysis. Sponsors should read section 7 of the Medical Technologies Evaluation Programme Methods guide on cost-consequences analysis, available from www.nice.org.uk/mt

Sponsors are requested to submit section C with the full submission. For details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

8 Existing economic evaluations

8.1 Identification of studies

The review of the economic evidence should be systematic and transparent and a suitable instrument for reporting such as the PRISMA statement (www.prisma-statement.org/statement.htm).

A PDF copy of all included studies should be provided by the sponsor.

8.1.1 Describe the strategies used to retrieve relevant health economics studies from the published literature and to identify all unpublished data. The search strategy used should be provided as in section 10, appendix 3.

The literature search was designed to identify cost and cost-effectiveness studies of Sherlock 3CG TCS used in adults undergoing PICC insertion. The strategy was developed for MEDLINE (Ovid interface). The strategy was structured to search for three concepts:

- Peripherally inserted central catheters
- Sherlock 3CG TCS
- Economic evaluations

The search strategy was devised using a combination of subject indexing terms and free text search terms in the title, abstract and keyword heading word fields. The search terms were identified through discussion between the research team, by scanning background literature, and by browsing database thesauri. The Sherlock 3CG TCS concept was captured by text words and subject headings to denote electrocardiography, magnetics and real-time tip positioning, as these are features of the technology. The device name was also searched on. The search terms for economic evaluations are based on the filter developed and used by the University of York Centre for Reviews and Dissemination to identify studies for inclusion in the NHS Economic Evaluation Database (NHS EED).

The strategy excluded publication types which were unlikely to yield detailed study reports: news, comments, and editorials. The strategy also excluded animal studies. Searches were limited to studies published in English from 2000 to date. 2000 was identified by the research team as an appropriate date cut off point as the technology was launched in 2006.

The MEDLINE strategy was translated appropriately for other databases. The search was conducted in a range of relevant databases of published and unpublished research. The resources included those databases specified as a minimum for the economic evidence search in section 10.3 of the NICE MTEP Sponsor Submission Template, plus the Health Technology Assessment Database, and additional relevant databases of economic evaluations (Health Economic Evaluations Database and Cost-Effectiveness Analysis Registry).

Additional methods used to identify ongoing and recently completed research included searching trial registers, searching the websites of key conferences to identify conference abstracts for the last 3 years, searching the websites of relevant organisations and searching Google.

Searching a number of databases produces a degree of duplication in the results. To manage this issue, the titles and abstracts of bibliographic records were downloaded and imported into EndNote bibliographic management software and duplicate

records were removed using several algorithms. For records where efficient importing into EndNote was not possible, results were downloaded into a Word document.

The searches identified 1451 records. Following deduplication 1184 records were assessed for relevance.

The full search strategies for all search sources (including search dates and result numbers) are included in Appendix 3/Section 10.3.

8.1.2 Describe the inclusion and exclusion criteria used to select studies from the published and unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

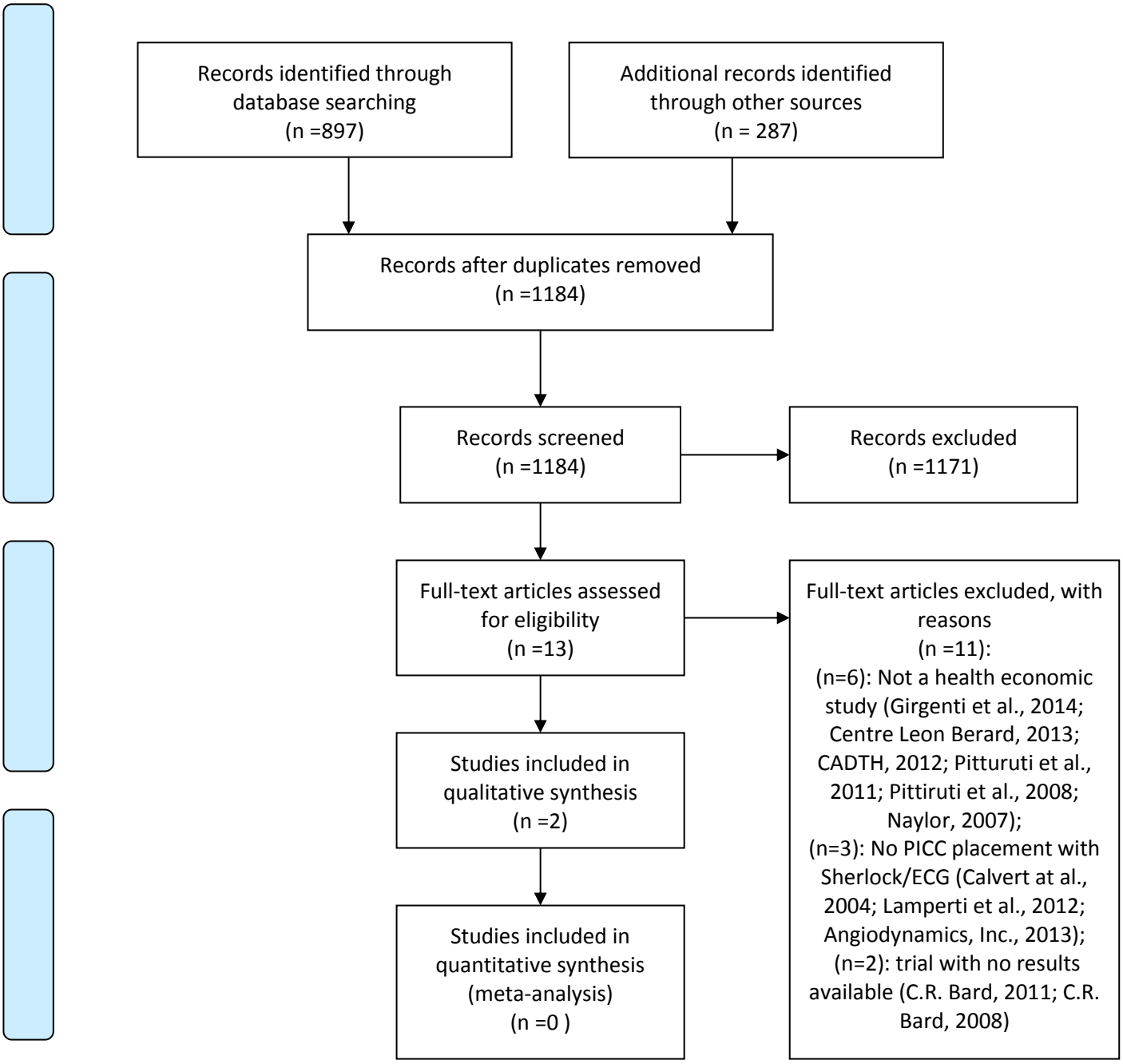
Table C1 Selection criteria used for health economic studies

Inclusion criteria	
Population	Adult patient undergoing PICC insertion
Interventions	Sherlock 3CG Tip Confirmation System
Outcomes	Any
Study design	All types of economic evaluations and cost studies including cost analyses and cost-effectiveness and budget-impact analyses.
Language restrictions	English
Search dates	2000 - present
Exclusion criteria	
Population	Children
Interventions	None
Outcomes	None
Study design	Animal studies
Language restrictions	Non-English
Search dates	Pre-2000

8.1.3 Report the numbers of published studies included and excluded at each stage in an appropriate format.

The numbers of studies included and excluded at each stage of the health economic study review are shown in Figure C1.

Figure C1 PRISMA flow diagram of health economic studies



8.2 Description of identified studies

8.2.1 Provide a brief review of each study, stating the methods, results and relevance to the scope. A suggested format is provided in table C2.

Two health economic studies were identified which are summarised in Table C2.

Table C2 Summary list of all evaluations involving costs

Study name (year)	**Location of study**	**Summary of model and comparators**	**Patient population *(key characteristics, average age)***	**Costs *(intervention and comparator)***	***Patient outcomes (clinical outcomes, utilities, life expectancy, time to recurrence)***	***Results (annual cost savings, annual savings per patient, incremental cost per QALY)***
Adams, (2013)	USA	Simple cost comparison between ECG tip location and blind insertion with chest X-ray verification	Adults requiring PICC insertion. No other information reported.	Cost of insertion with ECG = $273 Cost of insertion with X-ray = $350 Further cost savings generated by lower malposition rate (and therefore malposition costs)	Not reported	Total cost saving/PICC with ECG = $82.57
Stewart (2013)	Australia	Simple cost comparison between ECG tip location and blind insertion with chest X-ray verification	Adults requiring PICC insertion. No other information reported.	Cost of insertion with ECG (per 800 PICC insertions) = (AUS)$168,000 Cost of insertion with X-ray (per 800 PICC insertions) = (AUS)$482,400	Not reported	Total cost saving with ECG (per 800 PICC insertions) = (AUS)$314,400

8.2.2 Provide a complete quality assessment for each health economic study identified. A suggested format is shown in table C3.

Two health economic studies were identified; both are quality assessed in Table C3. Both studies are low quality cost-comparison studies based outside of the UK. Therefore they are of limited relevance and have methodological limitations which negate their use in answering the current decision problem.

Table C3 Quality assessment of health economic studies

Study name: The Clinical Efficacy of PICC Tip Confirmation Using ECG Tip Locator Technology (Adams, 2013)		
Study design	**Cost comparison study**	
Study question	**Response (yes/no/ not clear/N/A)**	**Comments**
1. Was the research question stated?	Yes	
2. Was the economic importance of the research question stated?	Yes	
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	Not clear	Appears to be medical centre at which authors are based
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes	
5. Were the alternatives being compared clearly described?	Yes	
6. Was the form of economic evaluation stated?	Yes	
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	Yes	
8. Was/were the source(s) of effectiveness estimates used stated?	Yes	
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	Not clear	The results of the effectiveness study were provided, but there is little detail relating to the study design
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	N/A	
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	Yes	
12. Were the methods used to value health states and other benefits stated?	N/A	
13. Were the details of the subjects from whom valuations were obtained given?	N/A	

14. Were productivity changes (if included) reported separately?	N/A	
15. Was the relevance of productivity changes to the study question discussed?	N/A	
16. Were quantities of resources reported separately from their unit cost?	No	
17. Were the methods for the estimation of quantities and unit costs described?	No	
18. Were currency and price data recorded?	No	
19. Were details of price adjustments for inflation or currency conversion given?	No	
20. Were details of any model used given?	N/A	
21. Was there a justification for the choice of model used and the key parameters on which it was based?	No	
22. Was the time horizon of cost and benefits stated?	No	
23. Was the discount rate stated?	No	
24. Was the choice of rate justified?	No	
25. Was an explanation given if cost or benefits were not discounted?	No	
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	No	
27. Was the approach to sensitivity analysis described?	N/A	No sensitivity analysis was undertaken
28. Was the choice of variables for sensitivity analysis justified?	N/A	
29. Were the ranges over which the parameters were varied stated?	N/A	
30. Were relevant alternatives compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)	Yes	
31. Was an incremental analysis reported?	Yes	
32. Were major outcomes presented in a disaggregated as well as aggregated form?	No	Cost of PICC insertion was disaggregated, but malposition costs were not
33. Was the answer to the study question given?	Yes	
34. Did conclusions follow from the data reported?	Yes	
35. Were conclusions accompanied by the appropriate caveats?	No	
36. Were generalisability issues addressed?	No	
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. British Medical Journal 313 (7052): 275–83. Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Study name: A New Australian Experience: Improvement in Peripherally Inserted Central Catheter (PICC) Insertion Technique Using Real Time Tracking Technology & Optimal PICC Tip Position (Without the Need for CXR) (Stewart, 2013)		
Study design	**Cost comparison study**	
Study question	**Response (yes/no/not clear/N/A)**	**Comments**
1. Was the research question stated?	Yes	
2. Was the economic importance of the research question stated?	Yes	
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	Not clear	
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes	
5. Were the alternatives being compared clearly described?	Yes	
6. Was the form of economic evaluation stated?	Not clear	
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	Yes	
8. Was/were the source(s) of effectiveness estimates used stated?	Not clear	Assumptions appear to have been used to inform radiologist time, proportion of patients requiring second X-ray, additional nurse time and additional time spent in hospital
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	No	It is assumed that placement with ECG is 100% effective
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	N/A	
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	Yes	
12. Were the methods used to value health states and other benefits stated?	N/A	
13. Were the details of the subjects from whom valuations were obtained given?	N/A	
14. Were productivity changes (if included) reported separately?	N/A	
15. Was the relevance of productivity changes to the study question discussed?	N/A	

16. Were quantities of resources reported separately from their unit cost?	No	
17. Were the methods for the estimation of quantities and unit costs described?	No	
18. Were currency and price data recorded?	No	
19. Were details of price adjustments for inflation or currency conversion given?	No	
20. Were details of any model used given?	N/A	
21. Was there a justification for the choice of model used and the key parameters on which it was based?	No	
22. Was the time horizon of cost and benefits stated?	No	
23. Was the discount rate stated?	No	
24. Was the choice of rate justified?	No	
25. Was an explanation given if cost or benefits were not discounted?	No	
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	No	
27. Was the approach to sensitivity analysis described?	N/A	No sensitivity analysis was undertaken
28. Was the choice of variables for sensitivity analysis justified?	N/A	
29. Were the ranges over which the parameters were varied stated?	N/A	
30. Were relevant alternatives compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)	Yes	
31. Was an incremental analysis reported?	Yes	
32. Were major outcomes presented in a disaggregated as well as aggregated form?	Yes	
33. Was the answer to the study question given?	Yes	
34. Did conclusions follow from the data reported?	Yes	
35. Were conclusions accompanied by the appropriate caveats?	No	
36. Were generalisability issues	No	

addressed?		
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. British Medical Journal 313 (7052): 275–83. Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

9 De novo cost analysis

Section 9 requires the sponsor to provide information on the de novo cost analysis.

The de novo cost analysis developed should be relevant to the scope.

All costs resulting from or associated with the use of the technology should be estimated using processes relevant to the NHS and personal social services.

Note that NICE cites the price of the product used in the model in the Medical Technology guidance.

9.1 Description of the de novo cost analysis

9.1.1 Provide the rationale for undertaking further cost analysis in relation to the scope.

Two health economic studies were identified informing the cost-consequences of the use of Sherlock 3CG TCS; however, both of these studies were of low quality and of limited relevance to the current NHS setting. Therefore, a de novo cost analysis was undertaken in order to ascertain this.

The use of Sherlock 3CG TCS potentially has a higher initial procedural cost than PICC placement without the system as a special catheter is required as are ECG leads and the Sherlock 3CG TCS machine. In addition staff need training to operate the system appropriately which potentially further increases the cost of the procedure compared to current practice.

Sherlock 3CG TCS could increase the percentage of patients who have successful PICC placement at the bedside reducing the number of patients requiring PICC placement with fluoroscopy in theatre or a radiology suite. This saving in fluoroscopy costs could offset the additional costs of using Sherlock 3CG TCS. In addition, Sherlock 3CG TCS may remove the need for an X-ray to confirm tip placement altogether. Nine of the 14 NHS Trusts currently using Sherlock do so without a confirmation X-ray which may allow for the savings of additional resources and allow administration of desired drugs more quickly.

The purpose of this cost analysis was to determine the net costs of introducing the use of:

- Bedside placement with Sherlock 3CG TCS with confirmation X-ray;
- Bedside placement with Sherlock 3CG TCS without confirmation X-ray.

Patients

9.1.2 What patient group(s) is (are) included in the cost analysis?

The cost analysis includes adults undergoing PICC insertion who do not have medical conditions that contraindicate them for insertion with Sherlock 3CG TCS.

Technology and comparator

9.1.3 Provide a justification if the comparator used in the cost analysis is different from the scope.

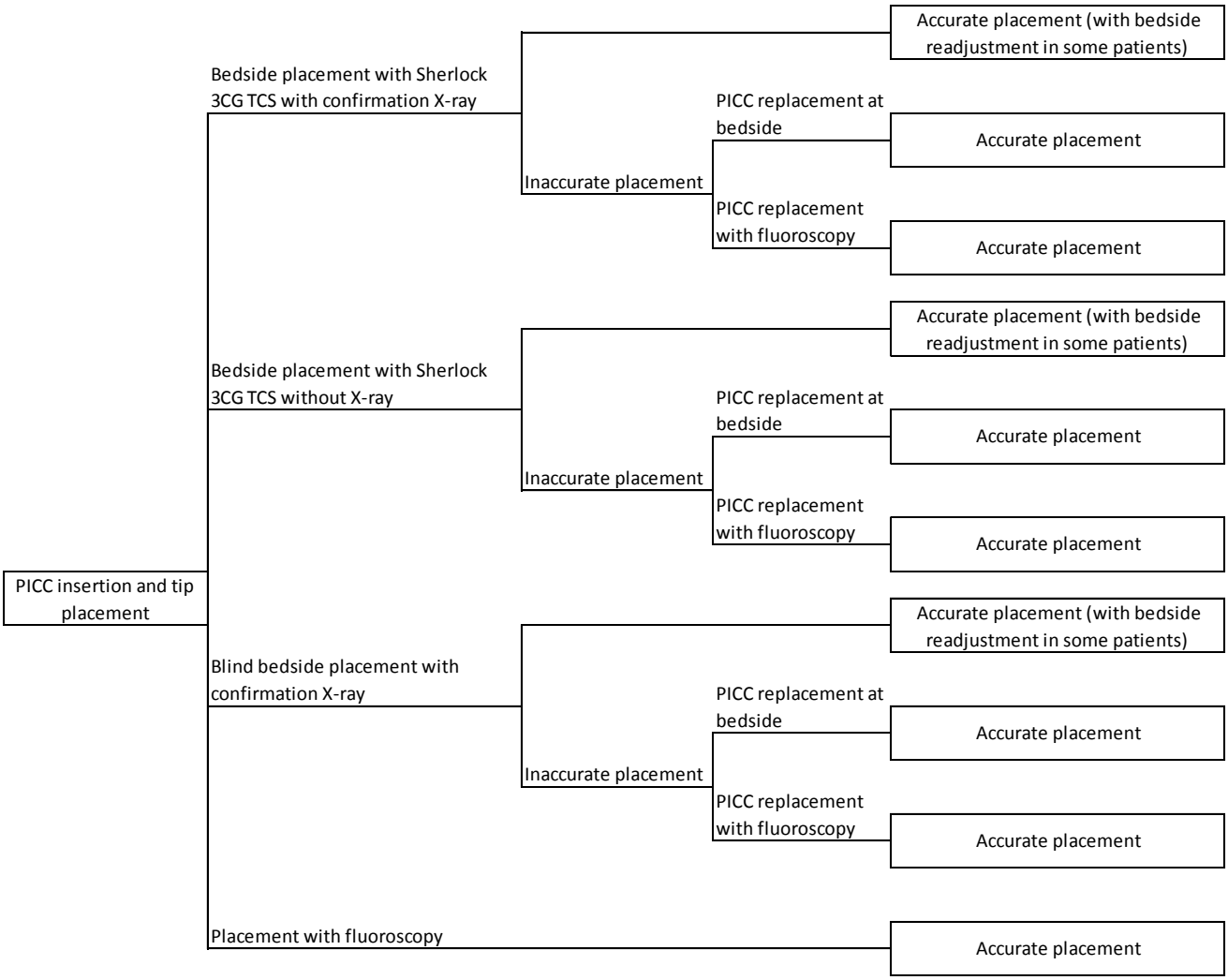
The comparators used in the cost analysis are:

- Blind bedside placement with confirmation X-ray (i.e. no use of Sherlock 3CG TCS);
- Fluoroscopy to guide PICC insertion and confirm tip placement.

Other NHS settings (tertiary care and outpatient) were tested in sensitivity analysis.

Model structure

9.1.4 Provide a diagram of the model structure you have chosen.



9.1.5 Justify the chosen structure in line with the clinical pathway of care identified in response to question 3.3.

The model structure as displayed in Section 9.1.4 reflects the clinical pathway of patients undergoing PICC insertion as described in Section 3.3. PICC line insertion and tip placement may be achieved through:

- Bedside placement with Sherlock 3CG TCS with confirmation X-ray;
- Bedside placement with Sherlock 3CG TCS without confirmation X-ray;
- Blind bedside placement with confirmation X-ray;
- Fluoroscopy to guide PICC insertion and confirm tip placement.

PICC lines inserted at the bedside (both with and without Sherlock 3CG TCS) may have their tips placed either accurately or inaccurately. Depending on the how the PICC has been inaccurately placed, it may be readjusted at bedside following x-ray or it may need to be replaced either at the bedside or under fluoroscopy.

In the base case all PICC tip replacements are carried out under fluoroscopy (Barton, 2013 and Walker *et al*., 2013). However, advice from a clinician stated that at his Trust patients who experience failed PICC line insertion with Sherlock 3CG TCS have blind PICC line reinsertion at the bedside with an X-ray (Section 9.2.5). Therefore, sensitivity analysis explored the impact of a proportion of patients having a second placement attempt at the bedside rather than immediately being sent to fluoroscopy.

For patients undergoing initial insertion under fluoroscopy, no malposition occurs and accurate insertion is achieved at the first attempt (Walker at al., 2013). The model considers those patients who are able to have a PICC line inserted.

All patients end the model with accurate PICC line insertion.

Both bedside placement with Sherlock 3CG TCS and a confirmation X-ray and bedside placement with Sherlock 3CG TCS without a confirmation X-ray are considered in the model. This reflects current practice in the NHS as described in Section 4.4.

9.1.6 Provide a list of all assumptions in the cost model and a justification for each assumption.

The cost model has the following assumptions:

- The time taken for achieve successful placement with Sherlock 3CG TCS is equal to the time taken for successful placement at the bedside without the technology.
- There is no benefit to patients resulting from more rapid PICC line placement with Sherlock 3CG TCS in the scenario where no confirmatory x-ray is required. This is a conservative assumption as there may be benefit to some patients of receiving required drugs sooner.
- X-rays are assumed to read with 100% accuracy, meaning that no consequences of misread X-rays are captured in the model. This

assumption was made as the clinical evidence did not provide information on the consequence of misread X-rays. .

- All model inputs are the same for bedside insertion with Sherlock 3CG TCS with X-ray and bedside insertion with Sherlock 3CG without X-ray, with the exception of the initial cost of PICC insertion and tip placement.

- Reinsertion of PICC lines following failure with other methods (bedside placement with Sherlock 3CG TCS (with or without X-ray) or blind bedside placement with X-ray) does not involve an additional overnight stay in hospital. This is a conservative assumption as more patients in the bedside placement arm without Sherlock 3CG TCS require reinsertion due to higher failure rates and could therefore incur additional costs due to potential overnight stays.

- Where insertion with Sherlock 3CG TCS is unsuccessful reinsertion is assumed to take place with fluoroscopy. Clinical advice has indicated that in some cases patients may have reinsertion at the bedside (with X-ray), however as the cost of bedside placement is lower than fluoroscopy (and still effective in around 93% of patients at first insertion attempt) using the cost of fluoroscopy insertion in the model is a conservative assumption.

- Costs other than those included are assumed to be the same for Sherlock 3CG TCS and the comparators.

- The cost of an X-ray for placement with Sherlock 3CG TCS (Table C6) is assumed to consist of the time cost of the radiographer (i.e. no equipment costs) as is the case in the cost analysis conducted by Walker *et al.* The cost for X-ray is not listed within NHS reference costs due to the high volume and low cost nature of the procedure. A NHS Scotland cost for X-ray was identified (£54.79); however this cost includes a number of radiological procedures and is likely to be an overestimation (ISD Scotland, 2013). Therefore, to ensure consistency between the treatment and comparator only the staff cost has been included.

- It is assumed in the base case that 3 nurses are trained per Sherlock 3CG TCS device. This is explored in the sensitivity analysis.

- The cost of an ultrasound scan used in the micro costing all PICC placement (Table C6 and C7) was assumed to be equivalent to the NHS reference cost for diagnostic imaging cost for anaesthetics (RA23Z: Ultrasound scan, less than 20 minutes). The ultrasound required to locate the vein in PICC placement will be short and of a small area, therefore this cost was judged to be most appropriate.

- Complications occurring post PICC line insertion, such as infection, were not included within the model and are therefore assumed to be equal for each comparator. Walker *et al.* state that infections should not occur if staff and patients are educated on the best ways to minimise infection risk. Therefore, it was judged there are confounding factors influencing infection rates (aside from the method of PICC tip placement).

- Device risks are not included within the model and are therefore assumed to be equal for each comparator. These were not included within the clinical evidence.

- Within the model it is assumed that nurses and radiologists are trained in PICC line insertion and additional training required relates to learning how to use Sherlock 3CG TCS only.

- The Sherlock 3CG TCS device is assumed to either be stored within the ward or department where it is used and therefore time is not spent fetching it. Or, in hospitals running a mobile intravenous service the device will be brought to the ward with the specialist nurse using it meaning no additional time is required to fetch the device. This assumption has been made as in current NHS practice the small device is carried around with the nurse responsible for inserting PICC lines.

- All other assumptions that have been made to populate model input parameters are specified in Tables C5, C6 and C7.

9.1.7 Define what the model's health states are intended to capture.

There are no health states in the decision tree analytic model.

9.1.8 Describe any key features of the cost model not previously reported. A suggested format is presented below.

Table C4 Key features of model not previously reported

Factor	Chosen values	Justification	Reference
Time horizon of model	Time taken for PICC to be successfully inserted	Consistent with clinical evidence	Adams *et al*., 2013, Barton *et al*., 2014, Johnston *et al*., 2014 Parikh *et al.,* 2012, Pittiruti *et al*., 2011. and Stewart *et al*., 2013.
Discount of 3.5% for costs	N/A	Short time horizon of the model means that discounting is not required.	
Perspective (NHS/PSS)	NHS and PSS perspective	Specified in NICE Methods guide	(NICE, 2011)
Cycle length	N/A	Model takes the form of a decision tree	
NHS, National Health Service; PSS, Personal Social Services			

9.2 Clinical parameters and variables

9.2.1 Describe how the data from the clinical evidence were used in the cost analysis.

Data from the clinical evidence review was utilised within the model to populate the proportion of successful PICC line placements with Sherlock 3CG TCS as provided in Section 7.6.1.

Four studies were identified in the clinical evidence review: Adams *et al*., 2013, Barton *et al*., 2014, Parikh *et al.,* 2012 and Stewart *et al*., 2013. All four studies were unpublished. A further two studies (relating to the previous version of Sherlock) were identified after the submission of the clinical evidence review. Following discussions with NICE, they were included: Johnston *et al*., 2014 and Pittiruti *et al*., 2011. All six studies were considered for use to populate the costing model, specifically the proportion of successful tip placements with Sherlock 3CG TCS.

Johnston *et al*. undertook a relatively large UK based study and reported malposition rates following tip placement with Sherlock 3CG TCS. The proportion of patients specifically requiring reinsertion was not reported and therefore this study could not be included within the model. Further, this study included all critically ill patients in intensive care units who required PICC line insertion, regardless of whether or not they were suitable for insertion using Sherlock 3CG TCS, or not. Within the cost

model the proportion of patients suitable for PICC placement with Sherlock 3CG TCS is included, thus the effectiveness data required for the model should only relate to those patients who are suitable for the device.

Pittiruti *et al*. studied various methods of catheter placement and did not report results for tip placement following PICC line insertion specifically. Therefore, this study was also unable to be used within the cost analysis.

The remaining four case series provided the appropriate information for the cost model. Of these the study by Parikh *et al*. was judged to be most appropriate for use in the base case despite being a US study as this case series included the largest number of patients. The results from phase 2 of this study (post training) were used as training costs are incorporated into the cost model and therefore it can be assumed that all nurses carrying out the procedure are trained appropriately.

The success rates from the three remaining case series: Adams *et al.* 2013, Barton *et al.* 2014 and Stewart *et al.* 2013 are considered in sensitivity analysis.

9.2.2 Are costs and clinical outcomes extrapolated beyond the study follow-up period(s)? If so, what are the assumptions that underpin this extrapolation and how are they justified?

No extrapolation beyond study follow-up was carried out.

9.2.3 Were intermediate outcome measures linked to final outcomes (for example, was a change in a surrogate outcome linked to a final clinical outcome)? If so, how was this relationship estimated, what sources of evidence were used and what other evidence is there to support it?

No, intermediate outcome measures were not linked to final outcomes.

9.2.4 Were adverse events such as those described in section 7.7 included in the cost analysis? If appropriate, provide a rationale for the calculation of the risk of each adverse event.

No adverse events were described in the clinical evidence and therefore were not included in section 7.7 or the cost analysis.

9.2.5 Provide details of the process used when the sponsor's clinical advisers assessed the applicability of available or estimated clinical model parameter and inputs used in the analysis.

Clinical advice was provided by Andrew Barton, clinical nurse specialist in vascular access at Frimley Park Hospital NHS Foundation Trust, who has experience of PICC placement both with and without Sherlock 3CG TCS. The questions were asked by email and both the questions asked and answers received are documented below.

1) After the PICC is initially placed but before the x-ray is taken what care does the patient receive? Would they occupy a bed and what level of care would a nurse have to provide (e.g. would the nurse have to stay with the patent until the x-ray results came back or how often would the nurse return to check on the patient?)

Once the PICC line is placed and awaiting a chest x-ray it is safe to leave the Patient. Care must be taken to cover the ends of the PICC so that it is not used until confirmation of the TIP is documented. This can be done by taping gauze on the end of the PICC or by allowing an IV cap to the hub. With Sherlock 3CG TCS this is not a problem because the PICC tip location can be confirmed at the time of insertion.

2) If the PICC is not placed accurately first time what proportion of failed placements resulted in:

a. Successful adjustment second time (if so how long would a nurse need to adjust and would a second x-ray be taken?)

Prior to Sherlock 3CG TCS most of the PICCs (80%) I placed would need to be pulled back slightly after the x-ray was done. This would be done using a measurement and a second x-ray would not be indicated.

b. Complete replacement with ultrasound and x-ray second time?

Prior to Sherlock 3CG TCS 1 out of every 10 PICCs or 10% would require replacement because the PICC was placed in the IJ or contra laterally. Removing and reintroducing the same PICC is not acceptable because of the risk of infection.

c. Complete replacement with fluoroscopy without an inpatient stay?

If the PICC was placed in an outpatient they would not have to stay overnight provided that a fluoroscopy slot could be found.

d. Complete replacement with fluoroscopy with an inpatient stay?

If the patient was an inpatient they would not be discharged until another PICC was placed with Fluoroscopy.

3) Would there be any difference in resource use and nurse time in placement of a PICC between a tertiary or acute centre?

This would depend on the technique and technology used as outlined above, I would say no difference

4) Would there be any difference in resource use and nurse time in if placement of a PICC was done in an outpatient clinic?

This would depend on the technique and technology used as outlined above, I would say no difference

5) If accurate insertion with Sherlock 3CG TCS is not possible following the first attempt would all patients undergo insertion with fluoroscopy rather than reinsertion with Sherlock 3CG TCS?

In the rare occasion that Sherlock 3CG tip navigation system does not work, the insertion strategy reverts to a traditional PICC insertion using neck and arm manoeuvres and USS and CXR to check position. Fluoroscopy would only be indicated if the PICC was unable to lead into the vessel because of an obstruction if the line kept going into the neck.

6) Could you provide an estimate of how many nurses (or other healthcare professionals) would be trained to use a Sherlock 3CG TCS device in a 'typical' hospital?

It would depend on how many PICC placers there are.

7) Is the PICC kit here https://my.supplychain.nhs.uk/catalogue/product/fsu499 the one that would be used in practice and if not which PICC kits are commonly used?

The link you provided above referred me to a COOK PICC line which is an open ended PICC line. In my trust we use the BARD Solo power PICC with the Sherlock ECG machine. Before we used Sherlock we used the BARD Groshong PICC. Below

is the list of consumables which were required before the SOLO Power PICC and after. The SOLO Power PICC pack comes with everything inside it.

8) What other consumable resources (if any) outside of this kit would be needed for a nurse to place a PICC?

BARD Groshong PICC – Separate PICC insertion Pack; Drapes; Gloves; Chloraprep 3ml applicator; Syringes; Needles; Scissors; Scalpel; Statlock; Dressing; Gauze; Steristrips; Probe cover; USS Gel; Sterile gown; Tourniquet; Saline 10mls; Lidocaine.

BARD SOLO Power PICC pack - Gloves; Chloraprep 3ml applicator; Lidocaine; Saline 10mls; ECG Electrodes.

Some further questions were asked of Andrew Barton by email and the question and responses are detailed below:

9) Would the radiographer taking the confirmatory x-ray be about a band 5? Also would it be normal for the radiographer to have an assistant present during the x-ray?

The radiographer would be a qualified radiographer, the band would depend on who was available, they usually work alone.

10) Similarly would the radiographer[2] undertaking fluoroscopy be a grade 5 and would an assistant be present?

The radiographer undertaking the fluoroscopy would be a qualified radiographer, the band would depend on who was available, there would be just one of them.

11) Where would insertion with fluoroscopy be undertaken?

Fluoroscopy for PICC insertion in my trust would be undertaken in the interventional radiology suit unless the patient was a child undergoing anaesthetic then the procedure would be undertaken in a theatre using a C arm for fluoroscopy.

[2] Published literature and information online suggests that a radiologist rather than radiographer would insert PICC lines with fluoroscopy.

9.2.6 Summarise all the variables included in the cost analysis. Provide cross-references to other parts of the submission. A suggested format is provided in table C5 below.

All model input parameters and their values are displayed in Table C5.1.

Table C5.1 Summary of variables applied in the cost model

Variable	Value	Range or 95% CI	Source
Proportion of successful placements (Sherlock 3CG TCS with or without confirmation X-ray)	96%	-	Parikh *et al*., 2012
Proportion of successful adjustments at bedside (Sherlock 3CG TCS)	0%	-	Assumption - after failure with Sherlock 3CG TCS patients have reinsertion under fluoroscopy (in base case)
Proportion of successful placements (blind placement at bedside with X-ray)	93%	-	Walker *et al*., 2013. This will include patients requiring some readjustment following X-ray.
Proportion of successful adjustments at bedside (bedside)	0%	-	Walker *et al.,* 2013 - all patients go for reinsertion with fluoroscopy after bedside failure (in base case).
Proportion of successful insertions (fluoroscopy)	100%	-	Walker *et al*., 2013
Cost of insertion (Sherlock 3CG TCS with confirmation x-ray)	£310.15	-	See Table C6 for details
Cost of insertion Sherlock 3CG TCS with no x-ray	£272.30	-	See Table C6 for details
Cost of insertion (blind insertion at bedside with X-ray)	£274.33	-	See Table C7a for details
Cost of insertion (with fluoroscopy)	£814.93	-	See Table C7b for details
Cost of PICC adjustment with Sherlock 3CG TCS	£310.15	-	Assumed to be equal to initial insertion cost with X-ray (cost only used in sensitivity analysis)
Cost of PICC adjustment at bedside	£274.33	-	Assumed to be equal to initial insertion cost (cost only used in sensitivity analysis)
Cost of reinsertion with fluoroscopy after failure with Sherlock 3CG TCS	£814.93	-	Assumed to be equal to insertion cost with fluoroscopy
Cost of reinsertion with fluoroscopy after failure at bedside	£814.93	-	Assumed to be equal to insertion cost with fluoroscopy
CI, confidence interval			

9.3 Resource identification, measurement and valuation

NHS costs

9.3.1 Describe how the clinical management of the condition is currently costed in the NHS in terms of reference costs and the payment by results (PbR) tariff.

PICC insertion does not have a specific HRG code and therefore reference cost, but is included within other HRG codes and reference costs. Examples of HRGs which include PICC insertion costs within the procedure costs are provided in the following screenshot (NHS Information Centre, 2014):

Procedure Code and Description

L997
Percutaneous transluminal peripheral insertion of central catheter

Procedure Hierarchy Band

8
Sixteen bands have been established (running from 0 to 15 inclusive) with band 3 representing the lowest resource use and band 15 representing the most resource intensive procedures.

Root HRGs and Criteria

VA15
MT Procedure sum greater than 44

VA14
MT procedure sum in the range 30 to 44

VA13
MT procedure sum in the range 19 to 29

QZ13
Requires a diagnosis of renal failure from list QZ_Renalfailure in any position and length of stay of 1 day or less

VA12
MT procedure sum in the range 9 to 18

QZ14
Requires a primary diagnosis of T824 mechanical complication of vascular dialysis catheter and length of stay of 1 day or less

VA11
MT procedure sum in the range 1 to 8

Select the first HRG in the above list (from top-bottom) where the criteria matches that of the FCE/Spell. If additional criteria lists are required, press the Action button at the top right of the screen and select Reference Lists.

These HRG codes relate to expensive procedures of which PICC insertion is likely to be a small proportion of the total cost.

9.3.2 State the Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS) codes for the operations, procedures and interventions relevant to

the use of the technology for the clinical management of the condition.

The OPCS 4.6 code for the procedure in which Sherlock 3CG TCS may be used is L99.7: Percutaneous transluminal peripheral insertion of central catheter.

Resource identification, measurement and valuation studies

9.3.3 Provide a systematic search of relevant resource data for the NHS in England. Include a search strategy and inclusion criteria, and consider published and unpublished studies.

Studies on cost resources were searched for through the economic evidence search (detailed in section 8.1). The research team identified time resource needs in relation to PICC positioning and re-positioning as the relevant resource issue which required additional searching.

A systematic, focussed literature search was designed to identify published studies reporting on time resource requirements in relation to PICC positioning and re-positioning. The strategy was developed for MEDLINE (Ovid interface). The strategy was structured to search for three concepts:

- peripherally inserted central catheters
- positioning
- time resource issues

The research team agreed that the strategy would be focussed and pragmatic, aiming to retrieve records which clearly included key terms for the concepts of interest. The search strategy was devised using a combination of subject indexing terms and free text search terms in the title, abstract and keyword heading word fields.

The strategy excluded publication types which were unlikely to yield detailed study reports: news, comments, editorials and letters. The strategy also excluded animal studies. Searches were limited to studies published in English, but no date restriction was applied.

The MEDLINE strategy was translated appropriately for other databases. The search was conducted in a range of relevant databases of published research. The resources included those databases specified as a minimum for the search on resource identification, measurement and valuation in section 10.4 of the NICE MTEP Sponsor Submission Template, plus the Health Technology Assessment Database and Health Economic Evaluations Database.

Searching a number of databases produces a degree of duplication in the results. To manage this issue, the titles and abstracts of bibliographic records were downloaded and imported into EndNote bibliographic management software and duplicate records were removed using several algorithms.

The searches identified 1181 records. Following deduplication 788 records were assessed for relevance. The full search strategies for all search sources (including search dates and result numbers) are included in the appendix. The following selection criteria were applied to the search results to identify relevant studies:

Inclusion criteria (resource use review)	
Population	Adult patient undergoing PICC insertion
Interventions	PICC insertion (at bedside, under fluoroscopy or with Sherlock 3CG TCS)
Outcomes	Resource use in PICC placement, repositioning or replacement
Study design	Any
Language restrictions	English
Search dates	No limit
Exclusion criteria	
Population	Children
Interventions	None
Outcomes	None
Study design	Animal studies
Language restrictions	Non-English
Search dates	No limit

A rapid review of the search records was undertaken and 8 studies were identified as containing relevant information. Relevant information from these studies is displayed in Table C5.2. Of these, the study by Walker *et al*. was deemed to be the most relevant as it was the only study identified that was undertaken within a UK NHS setting. The study was also recent and likely to reflect current NHS practices.

Table C5.2 Summary list of resource use studies

Study name (year)	Location of study	Summary of intervention and comparator	Patient population *(key characteristics, average age)*	Time taken to insert PICC	Other resource use information useful to model
Costantino et al. (2005)	US	Intervention: PICC insertion with ultrasongraphic (not relevant) Control: PICC insertion without ultrasongraphic guidance	Patient with difficult-to-obtain intravenous access (3 failed attempts). N=21 in control group	Mean (SD) = 30+/- 21 minutes (from notification by a nurse until successful cannulation)	NR
Cowl et al (2000)	US	Intervention: insertion of PICC at bedside Comparator: insertion of central venous catheter (not relevant)	N=51 in PICC group. Median age = 58 (21-81) Male = 62.7%	Mean (SD) = 41.2 +/- 17.2 minutes from time of opening catheter kit to catheter secured and covered with sterile dressing.	2 to 5 catheter insertion attempt = 21.6%
Davis et al. (2004)	US	Review paper about PICC line placement	All patients undergoing PICC line placement	Average time (range) = 2 hours (60-180 minutes)	Costs of consumables reported (US costs)
Hahn et al. (1995)	US	Intervention: PICC insertion under fluoroscopy with CO2 Control: PICC insertion under fluoroscopy with iodinated contrast medium	N=41 in intervention group N=33 in control group Mean age = 51 years	Intervention group: Mean (range) = 22.8 (13-64) minutes Control group = 23.2 (12-60) minutes	NR
Hockley et al. (2007)	Australia	Intervention: PICC insertion with CathRite (not relevant) Control: PICC insertion at bedside (blind placement)	Blind placement group: N=19; Mean age = 55.9 +/-4.7 Male = 79%	Mean (SD) = 24.6 +/-14.5 minutes	NR
Schweickert et al. (2009)	US	Intervention: PICC insertion with ultrasound inspection	PICC insertion at bedside group: N=149;	Median (range) = 9.0 (7-11) minutes. No information is	NR

		(not relevant) Control: PICC insertion at bedside	Mean age = 52 (39-65) Male = 49%	provided around what is included within this timeframe (how it was measured).	
Walker et al. (2013)	UK NHS	Intervention: PICC insertion by radiologist under fluoroscopy, nurse at bedside or consultant anaesthetists in ICU	N=141 PICC line insertions. N=48 by radiologist, N=91 by nurse-led teams and N=2 by consultant anaesthetists in ICU.	Mean insertion time (radiologist) = 40.125 minutes (plus 10 minutes nurse preparation time). Mean insertion time (nurse) = 62.49 minutes Mean insertion time (ICU) = 18 minutes	All times include both insertion and patient consent. ICU time was shortest due to lack of patient transfer required and lack of surgical safety checklist
Yamada et al. (2010)	Japan	Intervention: PICC insertion at bedside by physician	N=44 PICC insertions in 39 patients. Patients were terminally ill cancer patients.	Mean insertion time (SD) = 23+/-7.9 minutes. Defined as the period from when the patient's skin was cleaned with a disinfectant solution to when the catheter was fixed with sutures	NR

9.3.4 Provide details of the process used when clinical advisers assessed the applicability of the resources used in the model[3].

Clinical advice was provided by Andrew Barton, clinical nurse specialist in vascular access at Frimley Park Hospital NHS Foundation Trust. The questions asked and answers received are provided in Section 9.2.5. Questions 2-4 and 7-11 include information on resource use.

Technology and comparators' costs

9.3.5 Provide the list price for the technology.

The acquisition cost of Sherlock 3CG TCS System with stand and printer is £9,990 +VAT.

9.3.6 If the list price is not used in the de novo cost model, provide the alternative price and a justification.

Not applicable

9.3.7 Summarise the annual costs associated with the technology and the comparator technology (if applicable) applied in the cost model. A suggested format is provided in tables C6 and C7. Table C7 should only be completed when the most relevant UK comparator for the cost analysis refers to another technology.

The cost per patient of PICC insertion with Sherlock 3CG TCS is displayed in Table C6. The costs per patient of insertion at the bedside are displayed in Table C7a and insertion under fluoroscopy in Table C7b. The costs calculated in these tables were used as inputs within the economic model (Table C5).

Of key note is the time taken by a nurse to insert the PICC at the bedside. Walker *et al.* reported mean nurse time for successful insertion as 62.49 minutes. Adams *et al*. reported the mean time taken to insert a PICC line with Sherlock 3CG TCS (with no X-ray) as 39.5 minutes. A conservative assumption was taken to use 62.49 minutes for bedside insertion with Sherlock 3CG TCS plus x-ray confirmation in the base

[3] Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee.

case, i.e. equal to blind bedside insertion as reported by Walker *et al*. (2013). Therefore any time savings resulting from the use of Sherlock 3CG TCS at the bedside were not captured in the base case. For PICC tip placement with Sherlock 3CG TCS without X-ray, the figure of 39.5 minutes from Adams *et al*. was used.

The cost of ultrasound was added for each insertion method, including the comparators (blind beside insertion with X-ray and insertion with fluoroscopy) as ultrasound is required to visualise a vessel in the upper arm prior to PICC line insertion. Walker *et al.* did not include the cost of ultrasound within their costing calculations. Introducing a cost of ultrasound across each insertion method may result in double counting of nurse time; however this will occur in both the treatment and comparator arms and given the short time required for ultrasound in PICC line insertion patients is likely to be minimal.

Table C6.1 Costs per PICC line insertion associated with Sherlock 3CG TCS and X-ray

Items	Value	Source
Price of the technology per PICC line insertion	£6.39	Unit cost of Sherlock 3CG = £9,990 (Bard, 2013). Life span = 4 years (conservative assumption, usually last 8 years) 468 potential uses per year per Sherlock 3CG TCS device (mid-value from survey conducted by Bard). 83.5% of patients requiring PICC lines are suitable for Sherlock 3CG TCS (Adams, 2013). This is known pre-ante, so consumables are not wasted on these patients. (£9,990/4)/(468*0.835) = £6.39
Consumables (if applicable)	£189.91	Pack including PICC, sterile maximum barrier, procedure tray and ECG leads (£175-£200). Mid-point of £187.50 used in base case Printer paper: £120 for 1,000 sheets (12p each and 2 sheets per insertion). Other consumables not included in PICC pack = gloves, lidocaine, saline 10ml, 2 ECG electors and Chloraprep 3ml applicator = £2.17
Maintenance cost	£1.52	Annual maintenance cost = £595 (Bard, 2013). 468 attempted uses per year (mid-value from survey conducted by Bard). 83.5% of attempted patients are suitable (Adams, 2013) £595/(468*0.835) = £1.52
Training cost	£1.42	Training cost covered by Bard. Requires 4.5 hours of nurse time: £34 per hour of non-face-to-face contact time (PSSRU, 2013) 4.5*41 = £184.50 to train one nurse (in use of Sherlock 3CG TCS). Assumed 3 new nurses trained per year per device = £553.5. 83.5% of 468 PICCs placed per year with Sherlock 3CG TCS. 615/391 = £1.42 per patient to train nurses
Other costs	£111.15	Ultrasound = £18 (NHS reference costs (2012-13). Diagnostic imaging, anaesthetics. RA23Z - ultrasound scan, less than 20 minutes Radiographer time for X-ray = 10 minutes (Walker *et al*., 2013) multiplied by the cost of radiographer = £34 per hour - Hospital radiologist PSSRU, 2013) = £5.67 Nurse day ward: £84 per hour of face-to-face contact (PSSRU, 2013) multiplied by 62.49 minutes (assumed to be equal to bedside placement time reported by Walker *et al*., 2013) = £104.15
Total cost per insertion	£310.15	

Table C6.2 Costs per PICC line insertion associated with Sherlock 3CG TCS without X-ray

Items	Value	Source
Price of the technology per PICC line insertion	£6.39	Unit cost of Sherlock 3CG = £9,990 (Bard, 2013). Life span = 4 years (conservative assumption, usually last 8 years) 468 potential uses per year per Sherlock 3CG TCS device (mid-value from survey conducted by Bard). 83.5% of patients requiring PICC lines are suitable for Sherlock 3CG TCS (Adams, 2013). This is known pre-ante, so consumables are not wasted on these patients. (£9,990/4)/(468*0.835) = £6.39
Consumables (if applicable)	£189.91	Pack including PICC, sterile maximum barrier, procedure tray and ECG leads (£175-£200). Mid-point of £187.50 used in base case Printer paper: £120 for 1,000 sheets (12p each and 2 sheets per insertion). Other consumables not included in PICC pack = gloves, lidocaine, saline 10ml, 2 ECG electors and Chloraprep 3ml applicator = £2.17
Maintenance cost	£1.52	Annual maintenance cost = £595 (Bard, 2013). 468 attempted uses per year (mid-value from survey conducted by Bard). 83.5% of attempted patients are suitable (Adams, 2013) £595/(468*0.835) = £1.52
Training cost	£1.42	Training cost covered by Bard. Requires 4.5 hours of nurse time: £34 per hour of non-face-to-face contact time (PSSRU, 2013) 4.5*41 = £184.50 to train one nurse. Assumed 3 nurses trained per year per device = £553.5. 83.5% of 468 PICCs placed per year with Sherlock 3CG TCS. 615/391 = £1.42 per patient to train nurses
Other costs	£83.83	Ultrasound = £18 (NHS reference costs (2012-13). Diagnostic imaging, anaesthetics. RA23Z - ultrasound scan, less than 20 minutes Nurse day ward: £84 per hour of face-to-face contact (PSSRU, 2013) multiplied by 39.5 minutes (Adams *et al*., 2013)= £65.83
Total cost per insertion	£272.30	

Table C7.1 Costs per PICC line insertion associated with the comparator technology in the cost model (bedside insertion)

Items	Value	Source
Cost of the comparator	N/A	
Consumables (if applicable)	£163.18	Equipment cost for nurses £195.81 (Walker *et al*., 2013) with VAT (at 20% removed) This includes the cost of additional consumables that may be required during adjustment as calculated by Walker *et al,* for example if a PICC is too long and has to be pulled back and an additional sterile pack may be required.
Maintenance cost	N/A	
Training cost	N/A	
Other costs	£111.15	Ultrasound = £18 (NHS reference costs (2012-13). Diagnostic imaging, anaesthetics. RA23Z - ultrasound scan, less than 20 minutes Radiographer time for X-ray = 10 minutes (Walker *et al*., 2013) multiplied by the cost of radiographer = £34 per hour - Hospital radiographer PSSRU, 2013) = £5.67 Nurse day ward: £84 per hour of face-to-face contact (PSSRU, 2013) multiplied by 62.49 minutes (Walker *et al*., 2013) = £87.49 It is unclear if this time includes time taken for PICC lines to be pulled back (i.e. adjusted), however as the time taken for PICC placement used to cost successful PICC placement at the bedside and the proportion of successful PICC lines placed we both taken from Walker *et al*., 2013 we can assumed they defined and calculated consistently.
Total cost per treatment/patient	£274.33	

Table C7.2 Costs per PICC line insertion associated with the comparator technology in the cost model (fluoroscope insertion)

Items	Value	Source
Cost of the comparator	N/A	
Consumables (if applicable)	£217.88	Equipment cost for radiology (Walker *et al*., 2013) with VAT (at 20% removed)
Maintenance cost	N/A	
Training cost	N/A	
Other costs	£579.05	Radiologist time to insert PICC = 40.13 minutes (Walker *et al*., 2013) multiplied by the cost of radiologist = £99 per hour - Hospital consultant (PSSRU, 2013) = £66.21 Nurse team set up of room: 10 minutes to set up room (Walker *et al*., 2013) multiplied by cost of nurse = £34 per hour – Nurse day ward non face-to-face time (PSSRU, 2013) = £5.67 Theatre cost = £507.18 (Walker *et al*., 2013)
Total cost per treatment/patient	£814.93	

Health-state costs

9.3.8 If the cost model presents health states, the costs related to each health state should be presented in table C8. The health states should refer to the states in section 9.1.7. Provide a rationale for the choice of values used in the cost model.

The model does not present health states.

Adverse-event costs

9.3.9 Complete table C9 with details of the costs associated with each adverse event referred to in 9.2.4 included in the cost model. Include all adverse events and complication costs, both during and after longer-term use of the technology.

For patients requiring reinsertion with fluoroscopy after failure with either Sherlock 3CG TCS or bedside placement, the cost of insertion with fluoroscopy as displayed in Table C7b was used.

The cost of adjustment of PICC line with Sherlock 3CG TCS or at the bedside is assumed to be the same as the initial cost of insertion. This cost is not used in the base case as all patients have reinsertion with fluoroscopy, but in sensitivity analysis only.

Adverse events were assumed to be constant across the treatment and comparators as adverse events were not reported within the clinical evidence. Walker *et al*. reported higher infection rates for insertion with fluoroscopy compared with blind insertion at bedside, however as no clinical evidence was identified reporting on infection with Sherlock 3CG TCS this could not be incorporated within the model.

Miscellaneous costs

9.3.10 Describe any additional costs and cost savings that have not been covered anywhere else (for example, PSS costs, and patient and carer costs). If none, please state.

None

9.3.11 Are there any other opportunities for resource savings or redirection of resources that it has not been possible to quantify?

Various potential resource savings were unable to be quantified and included within the cost analysis.

For patients requiring drugs rapidly benefits may exist by using Sherlock 3CG TCS (particularly with no X-ray) for PICC placement as it may result in more rapid PICC placement and so more rapid delivery of required drug therapy. Due to an absence of data on the benefits of the system in this regard this potential benefit could not be quantified and thus was not included within the cost model.

Patients requiring multiple X-rays following various adjustments during PICC placement may incur resources during movement around the hospital. This is likely to vary locally depending on the layout of the hospital. Further, those patients who experience initial PICC placement failure and required reinsertion with fluoroscopy may in some cases incur an additional overnight stay in hospital. This scenario would occur in the event that a fluoroscopy slot could not be found, the likelihood of which may differ between NHS settings. As the placement success rate is higher with Sherlock 3CG TCS compared with blind bedside placement this potential benefit may provide an opportunity for resource savings.

In addition, the model does not capture adverse events such as infections which may occur as a result of PICC line insertion and may incur significant costs. Walker *et al*. reported the infection rates were higher for insertion with fluoroscopy compared with blind bedside placement perhaps due to aftercare of the PICC line. It is possible moving the patient away from sterile areas (for example for X-rays) may also increase the risk of infection. Infections were not reported in the clinical evidence identified for PICC insertion with Sherlock 3CG TCS (either with or without X-ray) and could therefore not be included within the model.

Finally, the model assumes that all X-rays are read with 100% accuracy. Harako *et al*. (2004) note that X-rays to determine PICC tip location can sometimes be hard to read and discrepancies can exist between readings by different individuals. The use of Sherlock 3CG TCS allows PICC tip location to be confirmed without X-ray and therefore some potential for resource use savings caused by complications resulting from misreading of X-rays may exist. It should be noted, however, that the use of computed radiography can improve X-ray reading accuracy and therefore this potential benefit is likely to be smaller now than previously where films were used (Harako *et al*., 2004).

9.4 Approach to sensitivity analysis

Section 9.4 requires the sponsor to carry out sensitivity analyses to explore uncertainty around the structural assumptions and parameters used in the analysis. All inputs used in the analysis will be estimated with a degree of imprecision. For technologies whose final price/acquisition cost has not been confirmed, sensitivity analysis should be conducted over a plausible range of prices.

Analysis of a representative range of plausible scenarios should be presented and each alternative analysis should present separate results.

9.4.1 Has the uncertainty around structural assumptions been investigated? State the types of sensitivity analysis that have been carried out in the cost analysis.

It was assumed in the base case that those patients experiencing unsuccessful PICC tip placement with either Sherlock 3CG TCS or bedside placement would have their PICC line removed and reinserted with fluoroscopy. This structural assumption was investigated through consideration of a scenario whereby a proportion of patients has their PICC lines repositioned using the initial insertion method, rather than fluoroscopy. Naylor (2007) conducted a case series of patients undergoing PICC insertion with a previous version of Sherlock and reported that 25% of initial misplaced PICC lines could be successfully adjusted on a second attempt with the previous version Sherlock. In order to consider all scenarios, the proportion of patients having PICC replacement with their initial method or fluoroscopy was varied between 0% and 100%. The results are reported in Section 9.5.7.

In addition, advice from a clinician stated that at his Trust patients who experience failed PICC line insertion with Sherlock 3CG TCS have PICC line reinsertion with blind placement at the bedside with an X-ray (Section 9.2.5). In the base case reinsertion with fluoroscopy was used as this was the more expensive and therefore more conservative option. Scenario analysis explored the advice provided by the clinician for patients undergoing initial insertion at the bedside with Sherlock 3CG TCS with or without an X-ray (described in Section 9.4.2).

The remaining model structure was judged to be a fair representation of current clinical practice (simplified due to the paucity of data available to populate the model) and as such sensitivity analysis focused on varying input parameters as described in Section 9.4.2.

9.4.2 Was a deterministic and/or probabilistic sensitivity analysis undertaken? If not, why not? How were variables varied and what was the rationale for this? If relevant, the distributions and their sources should be clearly stated.

One-way sensitivity analysis

One-way deterministic sensitivity analysis was undertaken around model input parameters to assess the impact on the model of changing input value and to identify the key drivers of the model.

The ranges for effectiveness of both insertion with Sherlock 3CG TCS and insertion at the bedside were derived where possible from the highest and lowest values reported in the clinical evidence.

For the remaining inputs, where possible, ranges of costs and resource usage were obtained from the published literature. Where this was not possible ranges were based on assumptions. The rationale behind the range for each input parameter is provided in Table C10.1.

Two-way sensitivity analysis

Two-way sensitivity analysis was undertaken around the following:

- proportion of patients requiring replacement of their PICC line with fluoroscopy or where the initial insertion method could be used for replacement;
- PICC placement accuracy with Sherlock 3CG TCS and bedside placement;
- Cost of PICC reinsertion with fluoroscopy after failure with Sherlock 3CG TCS or bedside placement;
- The proportion of successful tip placements and the initial cost of insertion at bedside with either Sherlock 3CG TCS (with and without X-ray) or blind placement.

Scenario analysis

Multi-way scenario analysis was undertaken to consider settings whereby costs may be higher or lower (this may include tertiary care or outpatient settings as specified for consideration in the scope). This included:

- Patients having PICC line insertion in tertiary care. No evidence could be identified to determine the difference in costs in secondary and tertiary care during PICC placement. Therefore, scenario analysis was undertaken where costs for all procedures were increased and decreased by 25% to assess the

impact on the overall results and where the costs relating to insertion with Sherlock 3CG TCS only were increased and decreased by 25%. Patients who experienced PICC line insertion failure in the base case had reinsertion with fluoroscopy. A scenario was considered whereby these patients have reinsertion at the bedside using blind insertion and an X-ray to confirm placement.

- Patients who experienced PICC line insertion failure in the base case had reinsertion with fluoroscopy. A scenario was considered whereby these patients have reinsertion at the bedside using blind insertion and an X-ray to confirm placement regardless of the initial method used for placement.
- A scenario considering unit costs with qualification costs for healthcare professionals was considered (PSSRU, 2013).
- Scenario analysis was conducted whereby the theatre cost was removed for both insertion with fluoroscopy and reinsertion with fluoroscopy. Walker *et al*. included the cost of theatre, as a patient undergoing insertion under fluoroscopy would be blocking a slot for another procedure to take place in the radiology department, but acknowledged there was some doubt as to whether this cost should be included.

Consideration of scenario analysis using the data provided by Walker *et al*. for a Macmillan suite (as a proxy for a tertiary setting) and outpatient setting was made. However, concerns existed as to whether the differences between departments specified by Walker *et al*. were specific to the logistics of Raigmore hospital. Further, details such as the time taken for PICC line insertion in each department were not provided with overall costs given. Therefore these analyses were not undertaken.

Table C10.2 only lists those variables that are changed from their base case value within the scenario analysis; all other input parameters remain consistent with their base case value.

Threshold analysis

A number of threshold analysis were also carried out to provide information on how much certain parameters could change from their baseline values whilst generating cost savings with the use of Sherlock 3CG TCS. The results of these are shown in Section 9.5.7.

9.4.3 Complete table C10.1, C10.2 and/or C10.3 as appropriate to summarise the variables used in the sensitivity analysis.

Table C10.1 Variables used in one-way scenario-based deterministic sensitivity analysis

Variable	Base-case value	Range of values	Explanation of range used
Bedside insertion with Sherlock 3CG TCS (with or without X-ray)			
Proportion of successful placements	96%	92%-100%	Highest value in literature = 100% (Barton *et al*., 2014) and lowest = 96% (Parikh *et al*., 2012 and Stewart *et al.*, 2013) for trained staff. Lower values were considered to represent clinical practice that may be poorer than those in studies.
Proportion of successful adjustments/replacements after initial misplacement	0%	0-100%	In base case all go to fluoroscopy after initial failure. Range considers scenario where all patients have replacement with Sherlock 3CG TCS and cost is £310.15 with X-ray and £272.30 without X-ray.
Cost of insertion at bedside (with X-ray)	£310.15	£227.40 - £499.24	In order to calculate the range, each the following inputs have been varied as follows: Number of insertions per year per device: +/-10%; Proportion of patients utilising device: +/- 10 percentage points; Life span of device: 2 to 8 years; Nurses using device: 2 to 8; Hours of training: 4 to 5; Ultrasound cost: £0 to £51; Consumables: £178-203; Time to insert PICC: 30-120 minutes; X-ray cost: £3 - £54.79.
Cost of insertion at bedside (no X-ray)	£272.30	£210.40 - £374.45	In order to calculate the range, each the following inputs have been varied as follows: Number of insertions per year per device: +/-10%; Proportion of patients utilising device: +/- 10 percentage points; Life span of device: 2 to 8 years; Nurses using device: 2 to 8; Hours of training: 4 to 5;

			Ultrasound cost: £18 to £51; Consumables: £178-203 Time to insert PICC: 20-70 minutes.
Cost of reinsertion with fluoroscopy after initial failure	£814.93	£607.78 - 1,054.67	Range calculated as specified below.
<u>Blind insertion at bedside with X-ray</u>			
Proportion of successful placements	93.1%	91%-95%	Reported in Walker *et al*., 2013 introduction.
Proportion of successful adjustments/replacements after initial misplacement	0%	0-100%	In base case all go to fluoroscopy after initial failure. Range considers scenario where all patients have replacement at bedside and cost is £274.33
Cost of insertion	£274.33	£209.86 - £453.29	In order to calculate the range, each the following inputs have been varied as follows: Equipment cost: +/-10% Time to insert PICC: 30-120 minutes; Ultrasound cost: £18 to £51; X-ray cost: £3 - £54.79.
Cost of reinsertion with fluoroscopy initial failure	£814.93	£607.78 - 1,054.67	Range calculated as specified below.
<u>Insertion with fluoroscopy</u>			
Cost of insertion with fluoroscopy	£814.93	£607.78 - 1,054.67	In order to calculate the range, each the following inputs have been varied as follows: Equipment cost: +/-10% Radiologist time: 20-60 minutes; Ultrasound cost: £18 to £51; Theatre cost: +/-30%

Table C10.2 Variables used in multi-way scenario-based sensitivity analysis

Variable	*Base case*	All costs increased from base case by 25%	All costs reduced from base case by 25%	Costs relating to Sherlock 3CG TCS increased from base case by 25%	Costs relating to Sherlock 3CG TCS reduced from base case by 25%	Theatre cost excluded	Bedside replacement of PICC line for failed Sherlock 3CG TCS patients	Unit costs with qualification costs for healthcare professionals
Cost of insertion with Sherlock 3CG TCS and X-ray	£310.15	£388	£233	£388	£233	Same as base case	Same as base case	£327.56
Cost of insertion with Sherlock 3CG TCS (no X-ray)	£272.30	£340	£204	£340	£204	Same as base case	Same as base case	£283.07
Cost of blind insertion at bedside with X-ray	£274.33	£343	£206	Same as base case	Same as base case	Same as base case	Same as base case	£291.50
Cost of insertion with fluoroscopy	£814.93	£1,019	£611	Same as base case	Same as base case	£307.75	Same as base case	£842.85
Cost of reinsertion with fluoroscopy after initial failure	£814.93	£1,019	£611	£1,019 for Sherlock 3CG TCS arm only. Same as base case for blind bedside placement.	£611 for Sherlock 3CG TCS arm only. Same as base case for blind bedside placement.	£307.75	Equal to the total cost per patient for bedside insertion for Sherlock 3CG TCS patients = £330.56 (to incorporate patients requiring fluoroscopy after failure at bedside). Same as base case for blind bedside insertion patients.	£842.85

9.4.4 If any parameters or variables listed in section 9.2.6 were omitted from the sensitivity analysis, provide the rationale.

The following variables were omitted from sensitivity analysis:

- Proportion of successful insertions with fluoroscopy. This method is deemed to be the gold standard of PICC insertion and current clinical evidence from an NHS setting (Walker *et al*., 2013) suggested this to be the case. Therefore, within the analysis insertion with fluoroscopy always has a 100% success rate.

- All variables on the model 'set up' sheet were included within the sensitivity analysis when varying the cost of PICC line insertion with Sherlock 3CG TCS (as they feed into this cost), but were not independently considered. This is with the exception of number of patients utilising each Sherlock 3CG TCS device in the threshold analysis.

9.5 Results of de novo cost analysis

Section 9.5 requires the sponsor to report the de novo cost analysis results. These should include the following:

- costs
- disaggregated results such as costs associated with treatment, costs associated with adverse events, and costs associated with follow-up/subsequent treatment
- a tabulation of the mean cost results
- results of the sensitivity analysis.

Base-case analysis

9.5.1 Report the total costs associated with use of the technology and the comparator(s) in the base-case analysis. A suggested format is presented in table C11.

Table C11 Base-case results

	Total per patient cost (£)
PICC insertion with Sherlock 3CG TCS and X-ray to confirm tip placement	£342.75
Blind PICC insertion at bedside with X-ray to confirm tip placement	£330.56
PICC insertion with fluoroscopy	£814.93
PICC insertion with Sherlock 3CG TCS and no X-ray	£304.90

9.5.2 Report the total difference in costs between the technology and comparator(s).

At baseline, PICC insertion with Sherlock 3CG TCS and an X-ray to confirm tip placement is cost incurring of £12.19 per patient versus blind placement at the bedside with X-ray, and cost saving of £472.18 per patient versus placement with fluoroscopy.

At baseline, PICC insertion with Sherlock 3CG TCS and no X-ray to confirm tip placement generates cost savings of £25.67 per patient versus blind placement at the bedside with X-ray and cost savings of £510.04 per patient versus placement with fluoroscopy.

9.5.3 Provide details of the costs for the technology and its comparator by category of cost. A suggested format is presented in table C12.

Table C12.1 Summary of costs by category of cost per patient (Sherlock 3CG TCS plus X-ray v. blind bedside insertion plus X-ray)

Item	Cost *intervention (Sherlock plus X-ray)*	Cost *comparator (Bedside insertion plus X-ray)*	Increment	Absolute increment	% of absolute increment
Equipment costs	£215.82	£181.18	£34.64	£34.64	58.27%
Staff costs	£94.33	£93.15	£1.17	£1.17	1.98%
Reinsertion cost	£32.60	£56.23	-£23.63	£23.63	39.75%
Theatre costs	£0.00	£0.00	£0.00	£0.00	0%
Total	£342.75	£330.56	£12.19	£59.45	100%
Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee					

Table C12.2 Summary of costs by category of cost per patient (Sherlock 3CG TCS plus X-ray v. fluoroscope insertion)

Item	Cost *intervention (Sherlock plus X-ray)*	Cost *comparator (fluoroscope)*	Increment	Absolute increment	% of absolute increment
Equipment costs	£215.82	£235.88	-£20.06	£20.06	3.44%
Staff costs	£94.33	£71.87	£22.45	£22.45	3.86%
Reinsertion cost	£32.60	£0.00	£32.60	£32.60	5.60%
Theatre costs	£0.00	£507.18	-£507.18	£507.18	87.10%
Total	£342.75	£814.93	-£472.18	£582.29	100%
Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee					

Table C12.3 Summary of costs by category of cost per patient (Sherlock 3CG TCS with no X-ray v. blind bedside insertion plus X-ray)

Item	Cost *intervention (Sherlock no X-ray)*	Cost *comparator (Bedside insertion plus X-ray)*	Increment	Absolute increment	% of absolute increment
Equipment costs	£215.82	£181.18	£34.64	£34.64	36.48%
Staff costs	£56.47	£93.15	-£36.68	£36.68	38.63%
Reinsertion cost	£32.60	£56.23	-£23.63	£23.63	24.89%
Theatre costs	£0.00	£0.00	£0.00	£0.00	0.00%
Total	£304.90	£330.56	-£25.67	£94.95	*100%*
Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee					

Table C12.4 Summary of costs by category of cost per patient (Sherlock 3CG TCS with no X-ray v. fluoroscope insertion)

Item	Cost *intervention (Sherlock no X-ray)*	Cost *comparator (fluoroscopy)*	Increment	Absolute increment	% of absolute increment
Equipment costs	£215.82	£235.88	-£20.06	£20.06	3.49%
Staff costs	£56.47	£71.87	-£15.40	£15.40	2.68%
Reinsertion cost	£32.60	£0.00	£32.60	£32.60	5.67%
Theatre costs	£0.00	£507.18	-£507.18	£507.18	88.17%
Total	£304.90	£814.93	-£510.04	£575.23	*100%*
Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee					

9.5.4 If appropriate, provide details of the costs for the technology and its comparator by health state. A suggested format is presented in table C13.

No health states were included within the model.

9.5.5 If appropriate, provide details of the costs for the technology and its comparator by adverse event. A suggested format is provided in table C14.

No adverse events were included within the cost model.

Sensitivity analysis results

9.5.6 Present results of deterministic one-way sensitivity analysis of the variables described in table C10.1.

Figures C2 to C20 display the cost difference per patient when one-way sensitivity analysis is undertaken around the variables described in table C10.1.

One-way sensitivity analysis: PICC insertion at bedside with Sherlock 3CG TCS plus X-ray v. blind PICC insertion at bedside with X-ray

Figure C2 Proportion of successful placements with Sherlock 3CG TCS

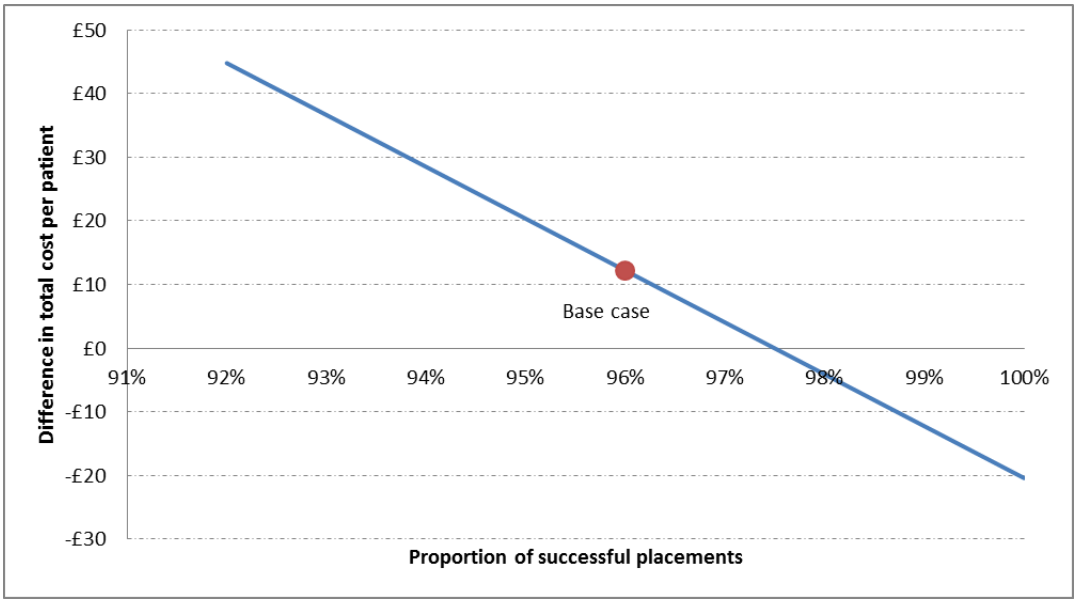


Figure C3 Proportion of successful blind placements at bedside with X-ray

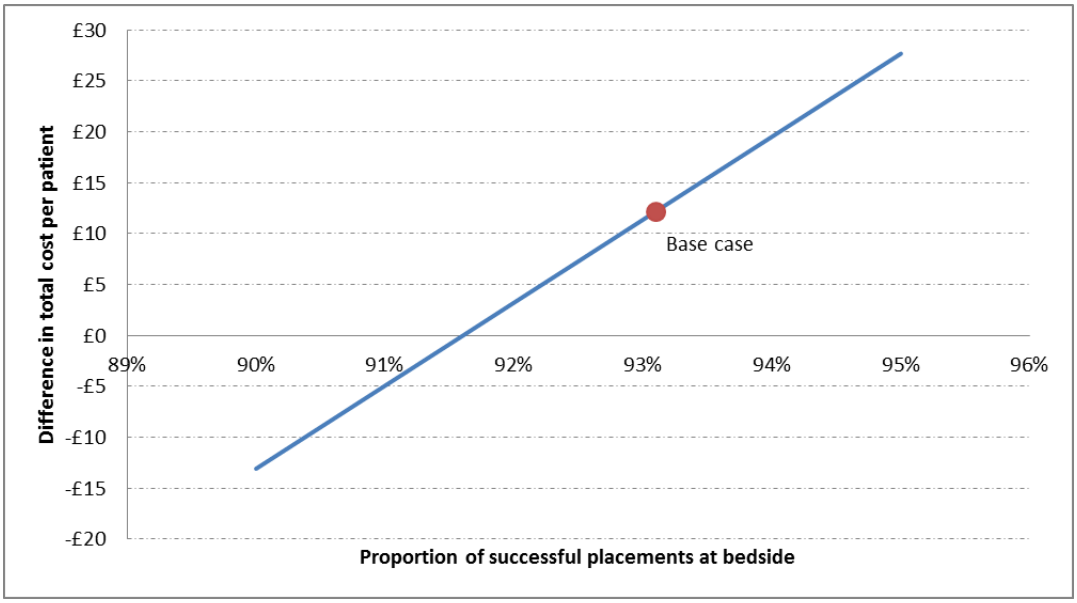


Figure C4 Cost of insertion with Sherlock 3CG TCS plus X-ray

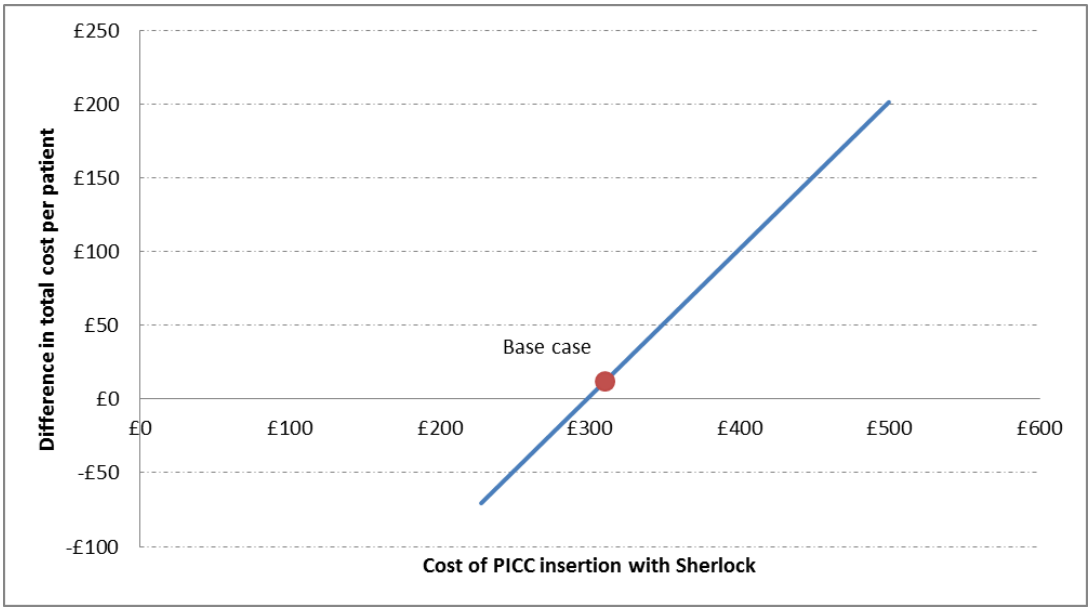


Figure C5 Cost of insertion at bedside plus X-ray

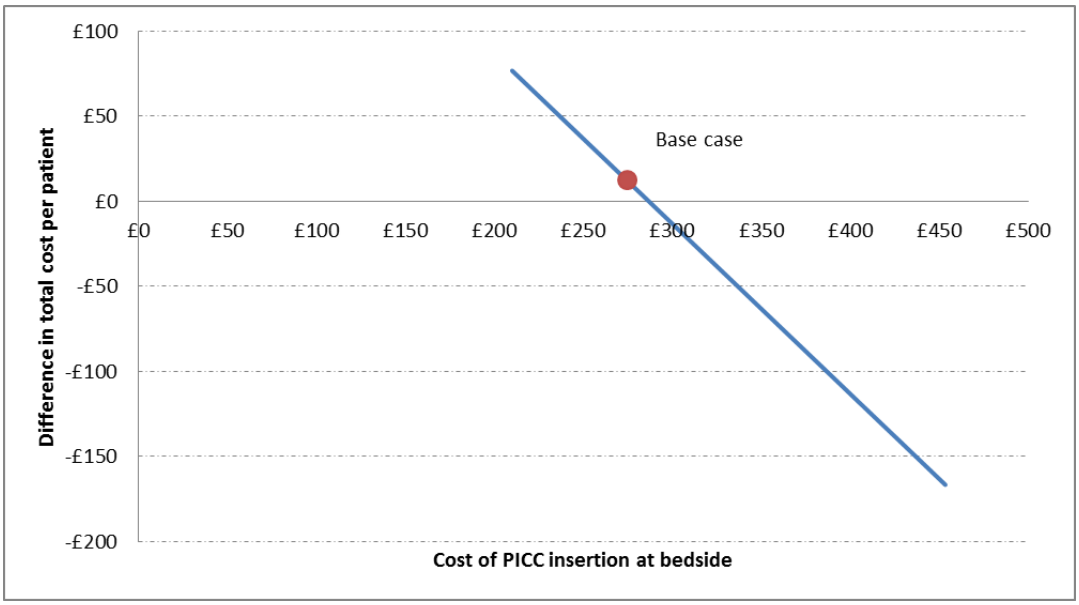


Figure C6: Proportion of successful adjustments after malposition identified on X-ray with Sherlock 3CG TCS (instead of with fluoroscopy)

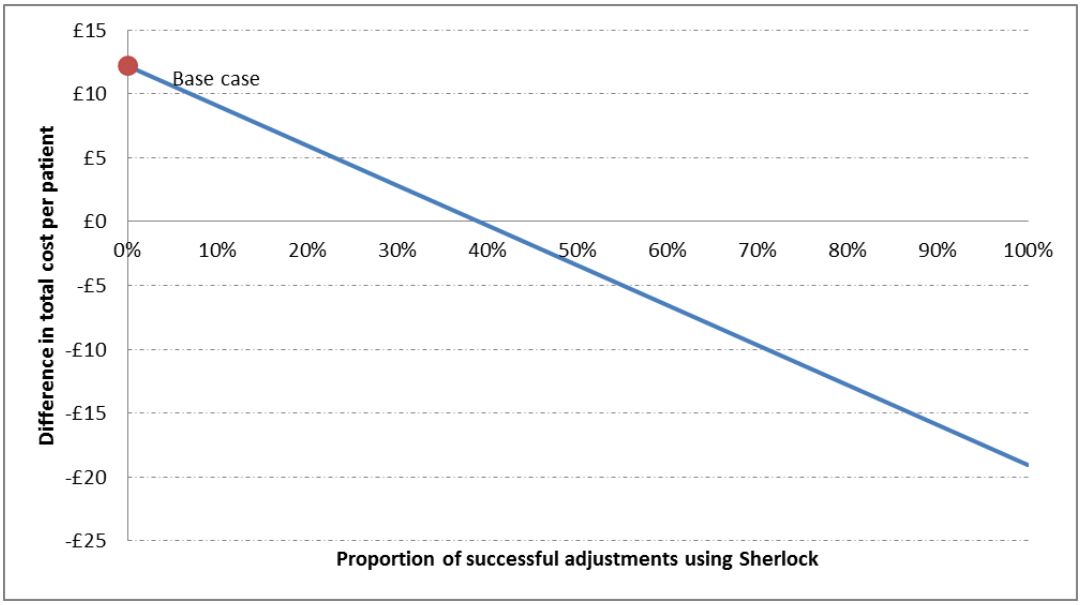
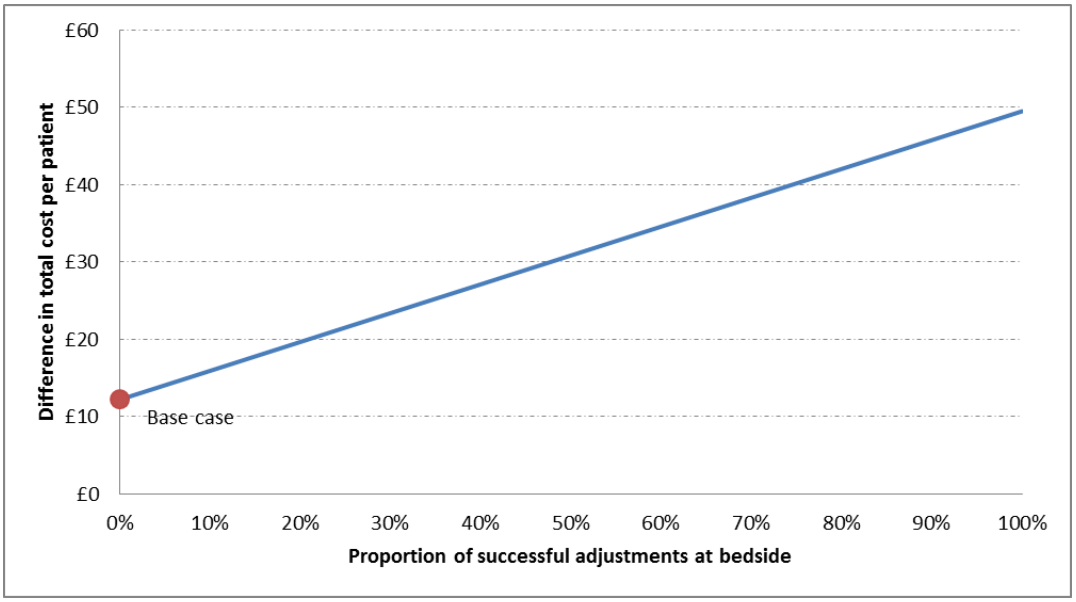


Figure C7: Proportion of successful adjustments at bedside without Sherlock 3CG TCS (instead of with fluoroscopy)



<u>One-way sensitivity analysis: PICC insertion at bedside with Sherlock 3CG TCS plus X-ray v. PICC insertion with fluoroscopy</u>

Figure C8 Proportion of successful placements with Sherlock 3CG TCS

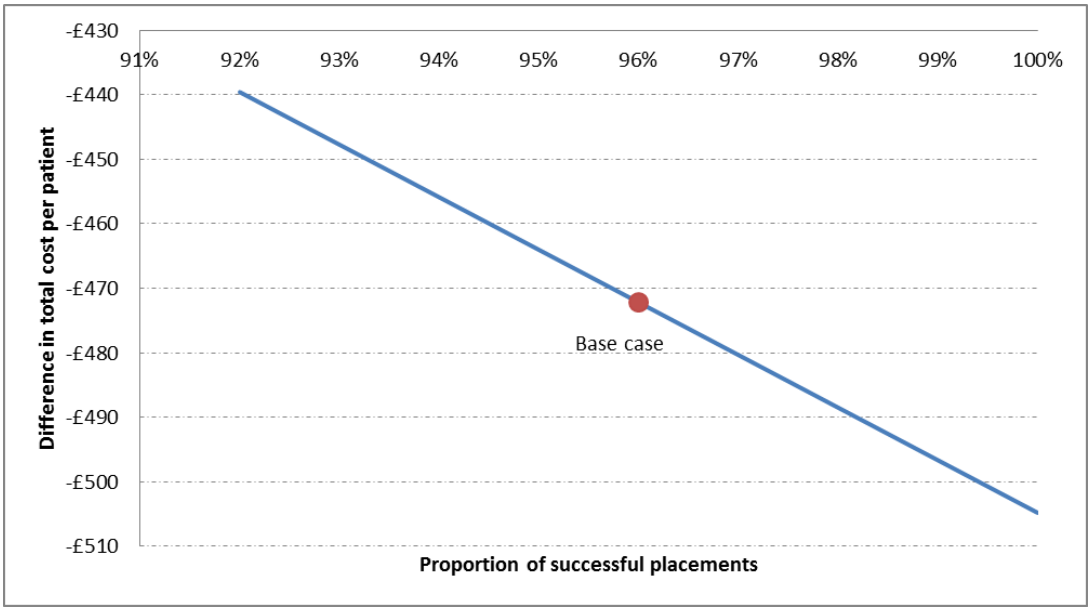


Figure C9 Cost of insertion with Sherlock 3CG TCS

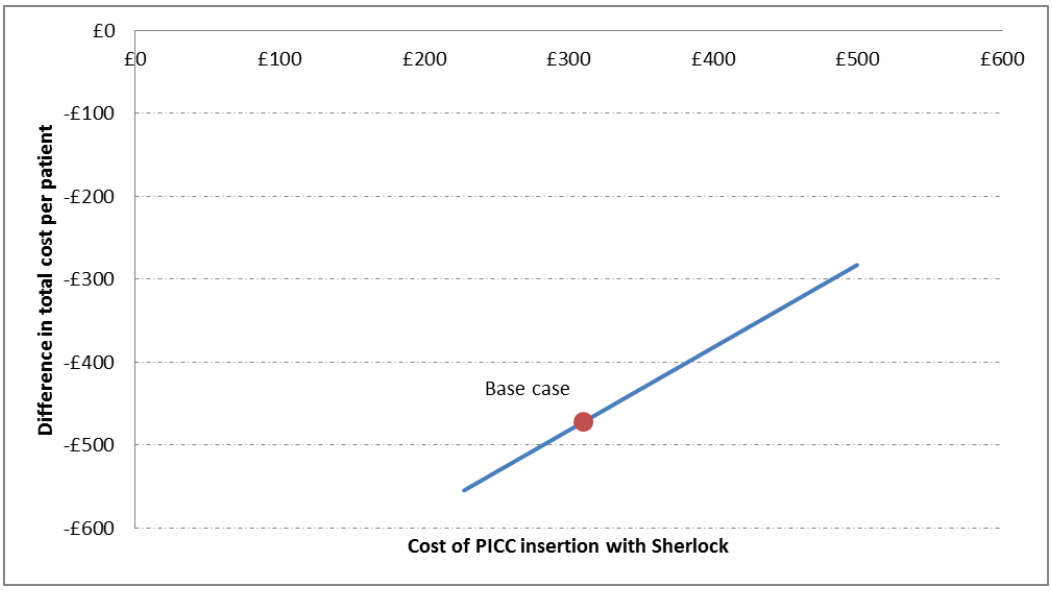


Figure C10 Cost of insertion with fluoroscopy

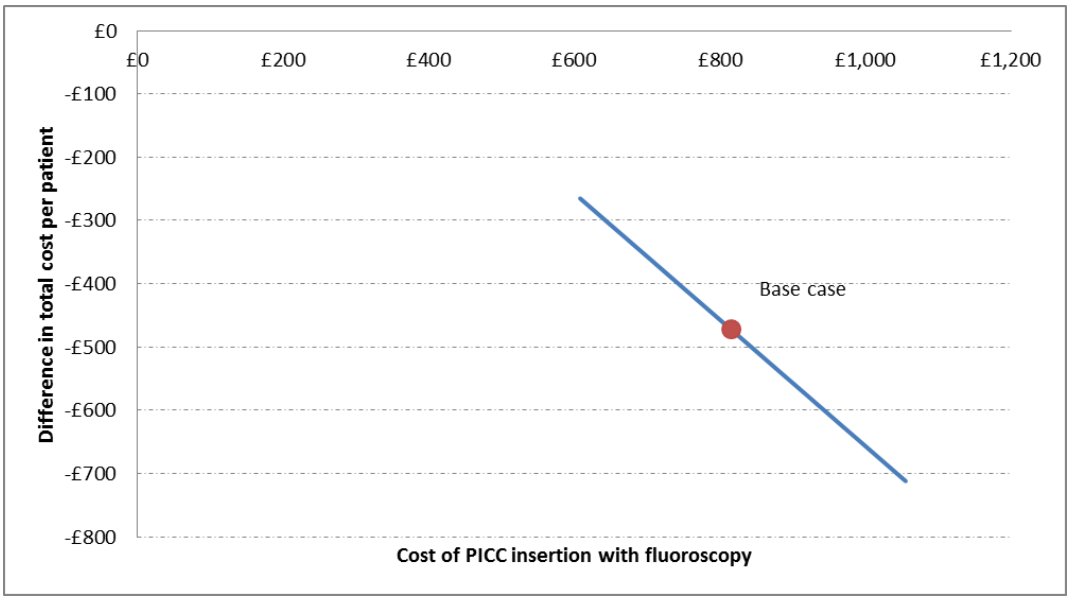
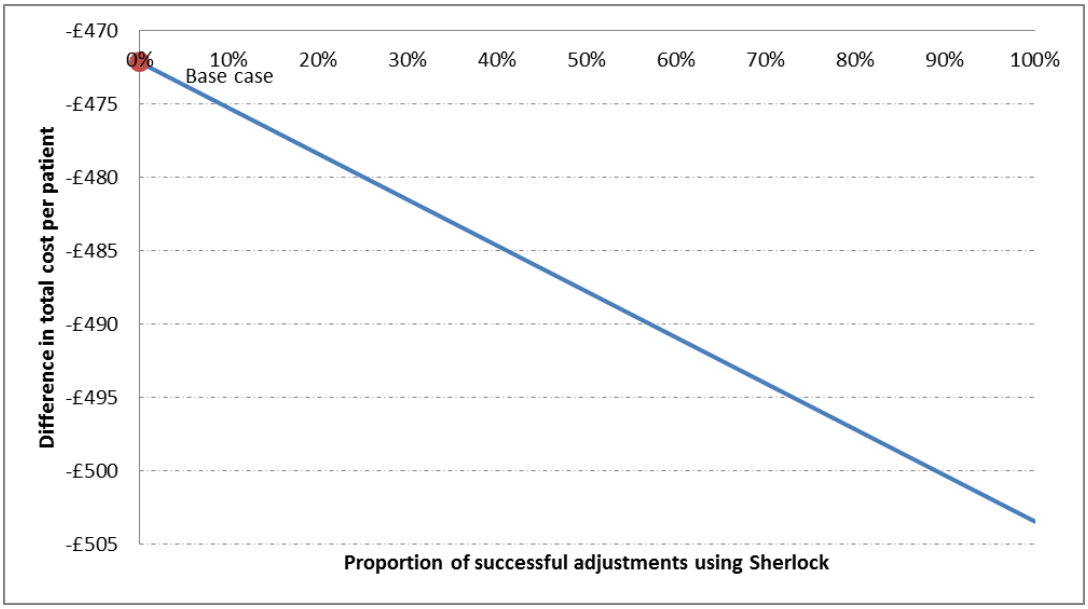


Figure C11: Proportion of successful adjustments with Sherlock 3CG TCS (instead of with fluoroscopy)



<u>One-way sensitivity analysis: PICC insertion at bedside with Sherlock 3CG TCS with no X-ray v. blind PICC insertion at bedside with X-ray</u>

Figure C12 Proportion of successful placements with Sherlock 3CG TCS (no X-ray)

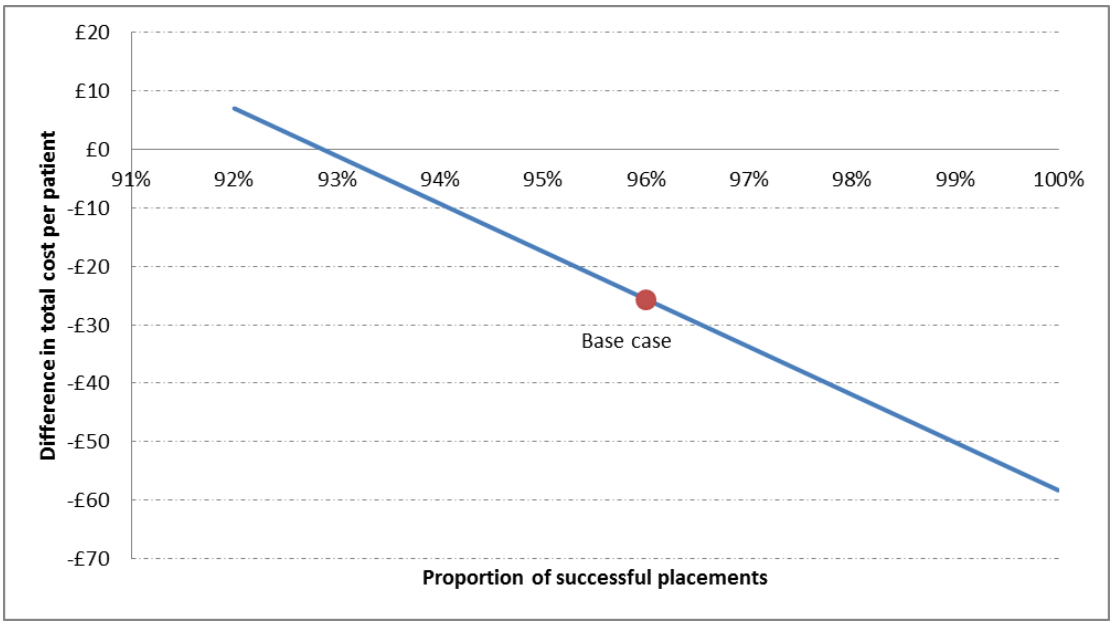


Figure C13 Proportion of successful placements at bedside

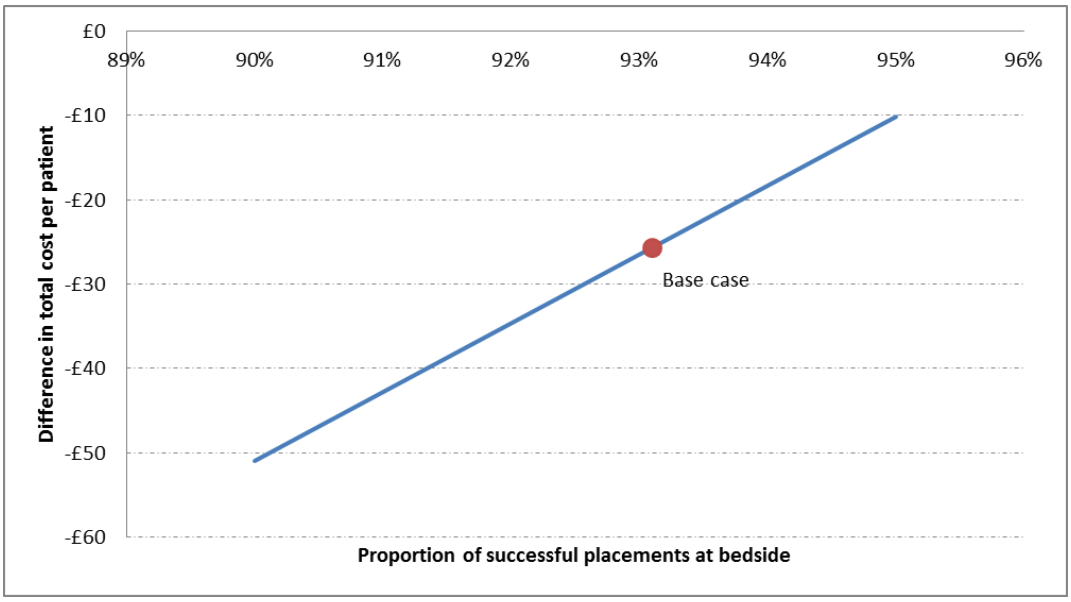


Figure C14 Cost of insertion with Sherlock 3CG TCS (no X-ray)

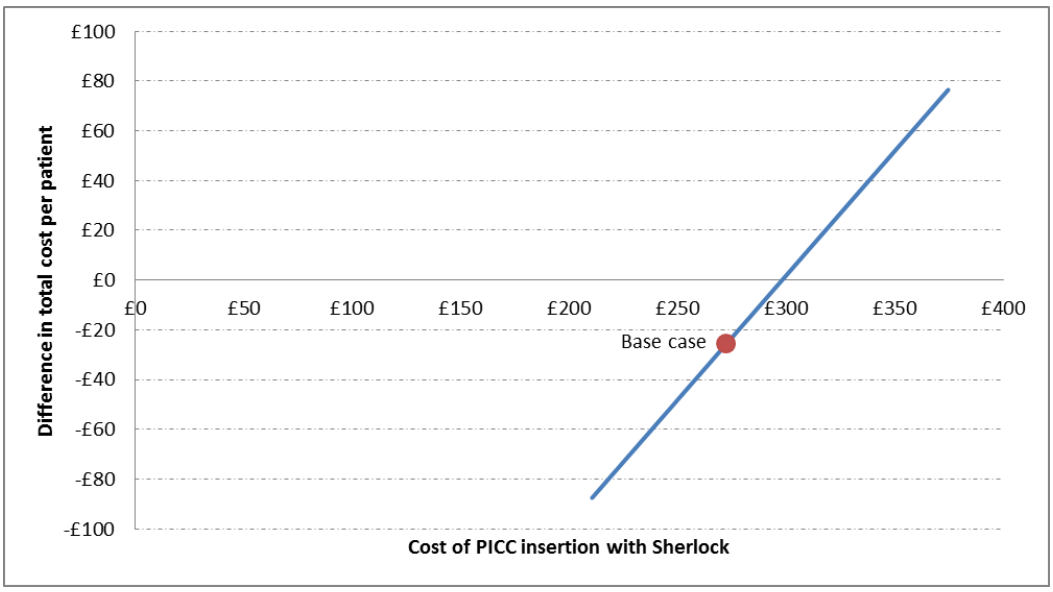


Figure C15 Cost of insertion at bedside plus X ray

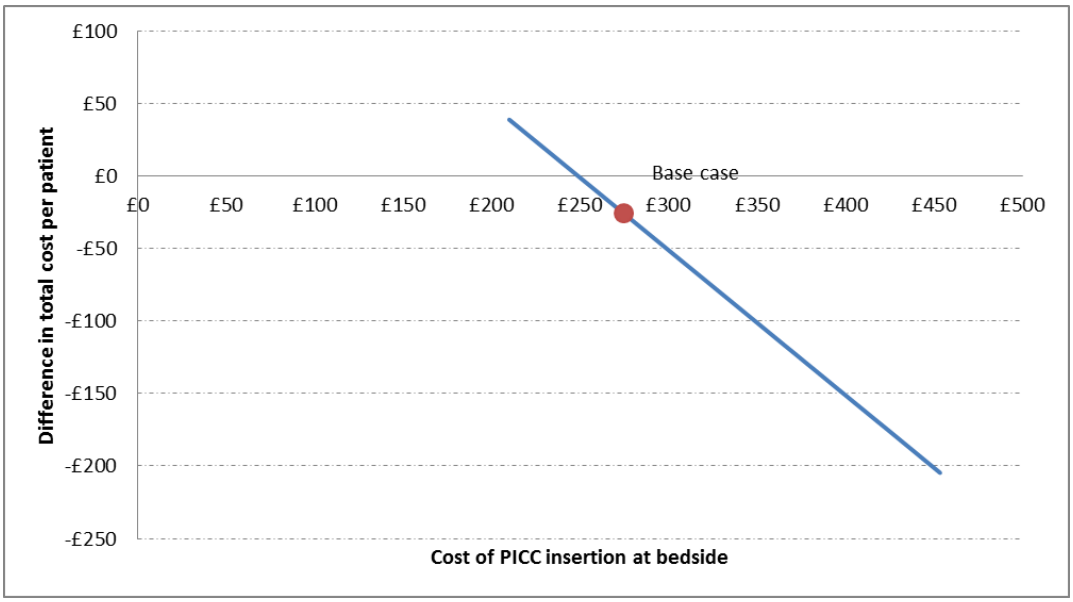


Figure C16 Proportion of successful adjustments with Sherlock 3CG TCS (instead of with fluoroscopy) after failure with Sherlock 3CG TCS (no X-ray)

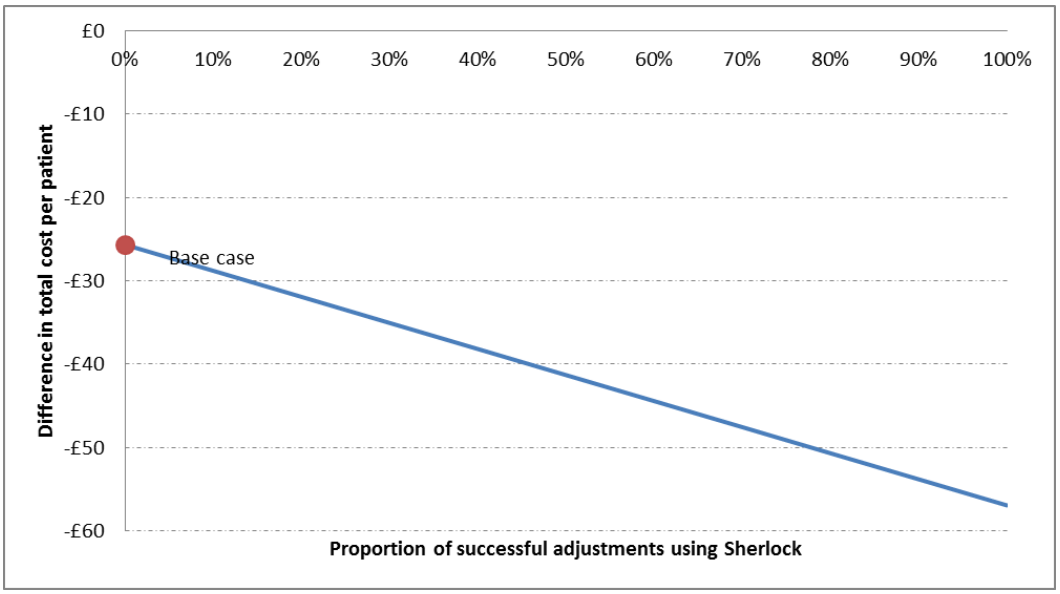
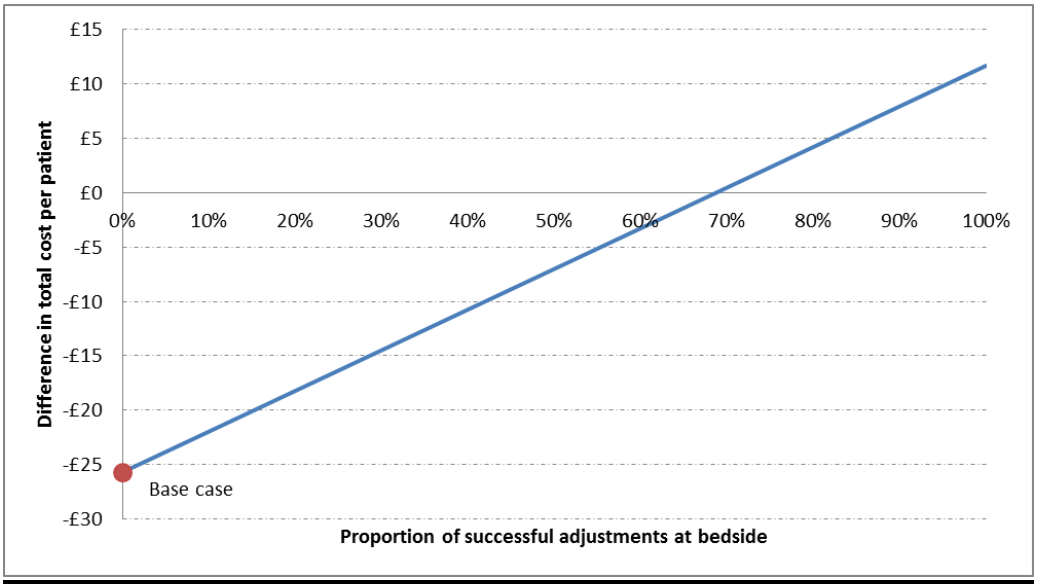


Figure C17 Proportion of successful adjustments at bedside (instead of with fluoroscopy)



<u>One-way sensitivity analysis: PICC insertion with Sherlock 3CG TCS with no X-ray v. PICC insertion with fluoroscopy</u>

Figure C18 Proportion of successful placements with Sherlock 3CG TCS (no X-ray)

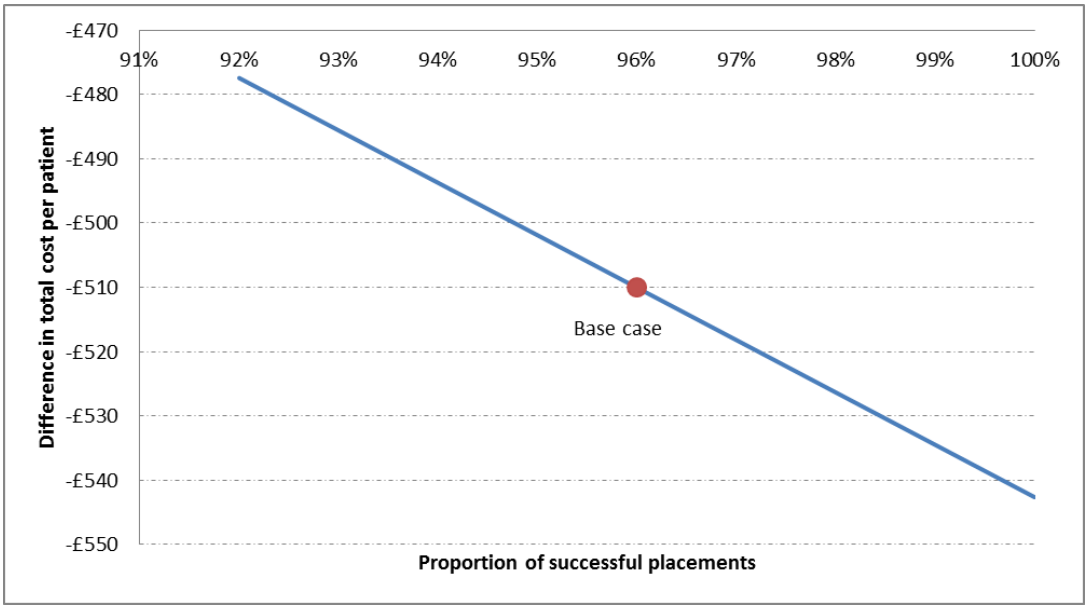


Figure C19 Cost of insertion with Sherlock 3CG TCS (no X-ray)

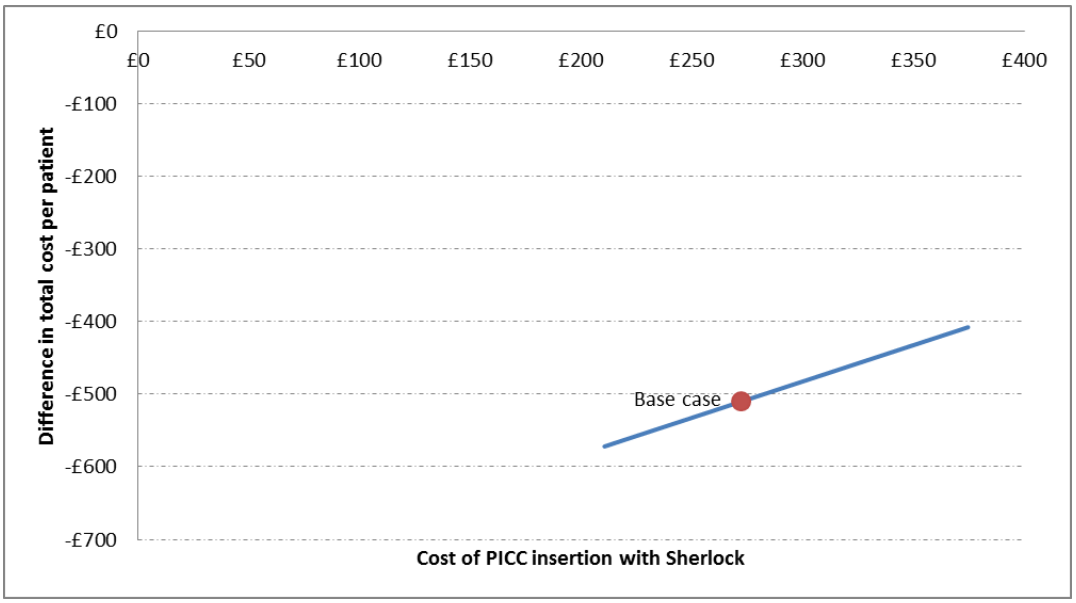


Figure C120 Cost of insertion with fluoroscopy

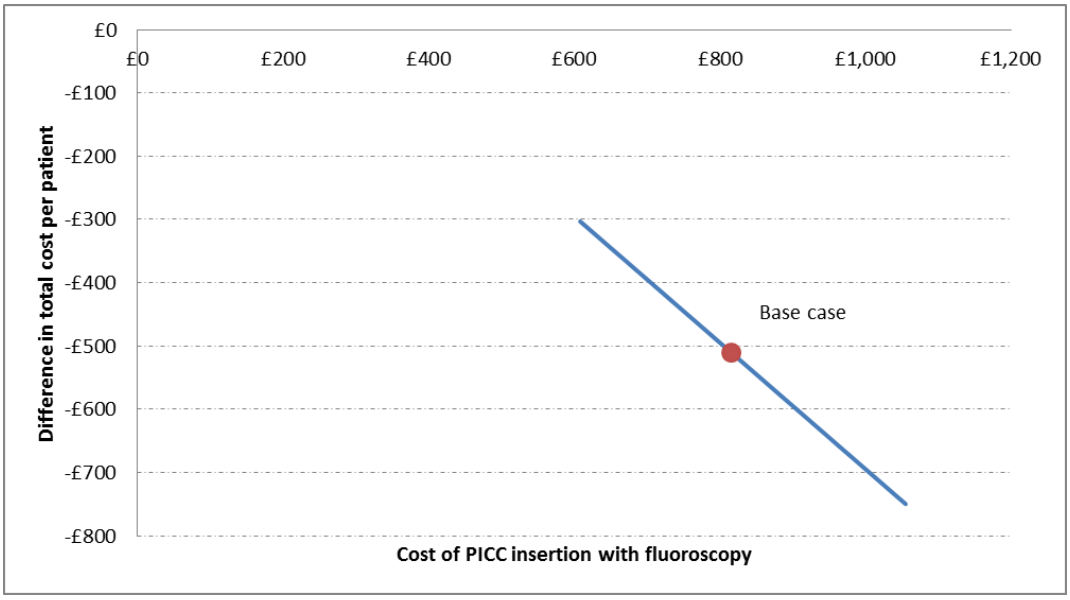
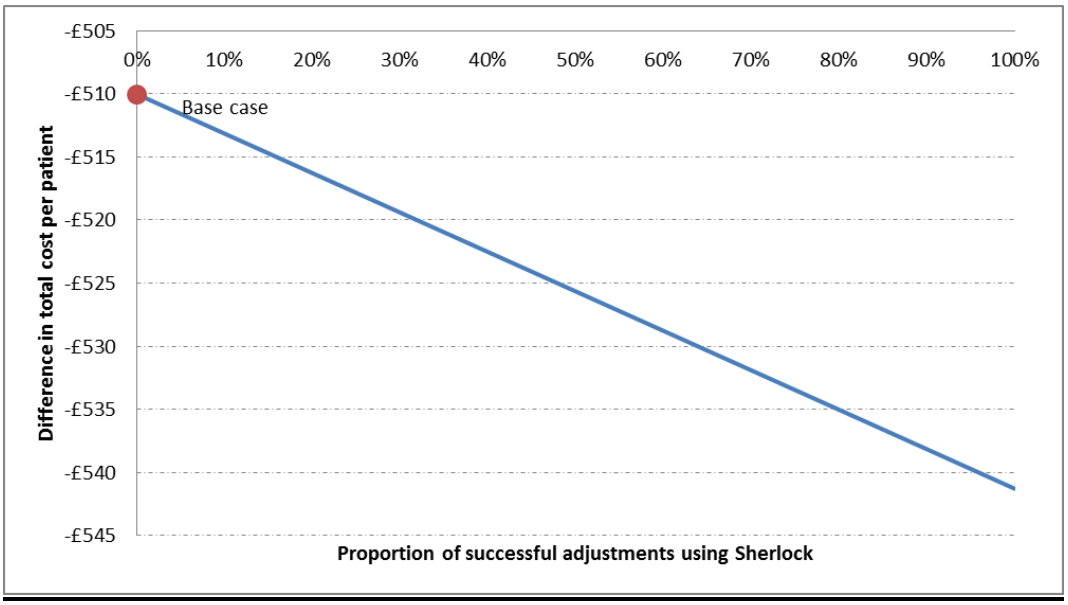


Figure C21 Proportion of successful adjustments with Sherlock 3CG TCS (instead of with fluoroscopy) after failure with Sherlock 3CG TCS (no X-ray)



9.5.7 Present results of deterministic multi-way scenario sensitivity analysis described in table C10.2.

<u>Two-way sensitivity analysis:</u> <u>PICC insertion at bedside with Sherlock 3CG TCS with X-ray v. blind PICC insertion at the bedside with X-ray</u>

Figure C22 Proportion of successful placements with Sherlock 3CG TCS and proportion of successful blind placements at the bedside

		Proportion of successful blind placements at bedside										
		90.0%	90.5%	91.0%	91.5%	92.0%	92.5%	93.0%	93.5%	94.0%	94.5%	95.0%
Proportion of successful placements with Sherlock	92%	£20	£24	£28	£32	£36	£40	£44	£48	£52	£56	£60
	93%	£11	£15	£20	£24	£28	£32	£36	£40	£44	£48	£52
	94%	£3	£7	£11	£15	£20	£24	£28	£32	£36	£40	£44
	95%	-£5	-£1	£3	£7	£11	£15	£20	£24	£28	£32	£36
	96%	-£13	-£9	-£5	-£1	£3	£7	£11	£15	£20	£24	£28
	97%	-£21	-£17	-£13	-£9	-£5	-£1	£3	£7	£11	£15	£20
	98%	-£29	-£25	-£21	-£17	-£13	-£9	-£5	-£1	£3	£7	£11
	99%	-£38	-£33	-£29	-£25	-£21	-£17	-£13	-£9	-£5	-£1	£3
	100%	-£46	-£42	-£38	-£33	-£29	-£25	-£21	-£17	-£13	-£9	-£5

Figure C23 Proportion of successful replacements with Sherlock 3CG TCS and proportion of successful replacements at the bedside (as opposed to requiring fluoroscopy)

		Proportion of successful replacements at bedside										
		0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
Proportion of successful replacements with Sherlock	0%	£12	£16	£20	£23	£27	£31	£35	£38	£42	£46	£49
	10%	£9	£13	£17	£20	£24	£28	£31	£35	£39	£43	£46
	20%	£6	£10	£13	£17	£21	£25	£28	£32	£36	£40	£43
	30%	£3	£7	£10	£14	£18	£21	£25	£29	£33	£36	£40
	40%	£0	£3	£7	£11	£15	£18	£22	£26	£30	£33	£37
	50%	-£3	£0	£4	£8	£11	£15	£19	£23	£26	£30	£34
	60%	-£7	-£3	£1	£5	£8	£12	£16	£20	£23	£27	£31
	70%	-£10	-£6	-£2	£2	£5	£9	£13	£16	£20	£24	£28
	80%	-£13	-£9	-£5	-£2	£2	£6	£10	£13	£17	£21	£24
	90%	-£16	-£12	-£8	-£5	-£1	£3	£6	£10	£14	£18	£21
	100%	-£19	-£15	-£12	-£8	-£4	£0	£3	£7	£11	£15	£18

Figure C24 Cost of PICC reinsertion with fluoroscopy after Sherlock 3CG TCS or bedside failure

		Cost of fluoroscope insertion (after bedside failure)										
		£608	£650	£690	£720	£760	£800	£840	£880	£920	£960	£1,055
Cost of fluoroscope insertion (after Sherlock failure)	£608	£18	£15	£13	£10	£8	£5	£2	-£1	-£3	-£6	-£13
	£650	£20	£17	£14	£12	£9	£7	£4	£1	-£2	-£4	-£11
	£690	£21	£19	£16	£14	£11	£8	£5	£3	£0	-£3	-£9
	£720	£23	£20	£17	£15	£12	£9	£7	£4	£1	-£2	-£8
	£760	£24	£21	£19	£17	£14	£11	£8	£5	£3	£0	-£7
	£800	£26	£23	£20	£18	£15	£13	£10	£7	£4	£2	-£5
	£840	£27	£25	£22	£20	£17	£14	£11	£9	£6	£3	-£3
	£880	£29	£26	£23	£21	£19	£16	£13	£10	£8	£5	-£2
	£920	£31	£28	£25	£23	£20	£17	£15	£12	£9	£6	£0
	£960	£32	£29	£27	£25	£22	£19	£16	£13	£11	£8	£1
	£1,055	£36	£33	£30	£28	£26	£23	£20	£17	£15	£12	£5

Figure C25 Proportion of successful placements and cost of insertion with Sherlock 3CG TCS plus X-ray

		Cost of insertion with Sherlock										
		£227	£250	£280	£310	£330	£360	£380	£410	£440	£470	£499
Proportion of successful tip placements	92%	-£38	-£15	£15	£45	£65	£95	£115	£145	£175	£205	£234
	93%	-£46	-£24	£6	£36	£56	£86	£106	£136	£166	£196	£226
	94%	-£54	-£32	-£2	£28	£48	£78	£98	£128	£158	£188	£218
	95%	-£62	-£40	-£10	£20	£40	£70	£90	£120	£150	£180	£209
	96%	-£71	-£48	-£18	£12	£32	£62	£82	£112	£142	£172	£201
	97%	-£79	-£56	-£26	£4	£24	£54	£74	£104	£134	£164	£193
	98%	-£87	-£64	-£34	-£4	£16	£46	£66	£96	£126	£156	£185
	99%	-£95	-£72	-£42	-£12	£8	£38	£58	£88	£118	£148	£177
	100%	-£103	-£81	-£51	-£21	-£1	£29	£49	£79	£109	£139	£169

Two-way sensitivity analysis: PICC insertion at bedside with Sherlock 3CG TCS no X-ray v. blind PICC insertion at the bedside with X-ray

Figure C26 Proportion of successful placements with Sherlock 3CG TCS and proportion of successful blind placements at the bedside

		Proportion of successful blind placements at bedside										
		90.0%	90.5%	91.0%	91.5%	92.0%	92.5%	93.0%	93.5%	94.0%	94.5%	95.0%
Proportion of successful placements with Sherlock	92%	-£18	-£14	-£10	-£6	-£2	£2	£6	£10	£14	£18	£22
	93%	-£26	-£22	-£18	-£14	-£10	-£6	-£2	£2	£6	£10	£14
	94%	-£35	-£31	-£26	-£22	-£18	-£14	-£10	-£6	-£2	£2	£6
	95%	-£43	-£39	-£35	-£31	-£26	-£22	-£18	-£14	-£10	-£6	-£2
	96%	-£51	-£47	-£43	-£39	-£35	-£31	-£26	-£22	-£18	-£14	-£10
	97%	-£59	-£55	-£51	-£47	-£43	-£39	-£35	-£31	-£26	-£22	-£18
	98%	-£67	-£63	-£59	-£55	-£51	-£47	-£43	-£39	-£35	-£31	-£26
	99%	-£75	-£71	-£67	-£63	-£59	-£55	-£51	-£47	-£43	-£39	-£35
	100%	-£84	-£79	-£75	-£71	-£67	-£63	-£59	-£55	-£51	-£47	-£43

Figure C27 Proportion of successful replacements with Sherlock 3CG TCS and proportion of successful replacements at the bedside (as opposed to requiring fluoroscopy)

		Proportion of successful replacements at bedside										
		0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
Proportion of successful replacements with Sherlock	0%	-£26	-£22	-£18	-£14	-£11	-£7	-£3	£0	£4	£8	£12
	10%	-£29	-£25	-£21	-£18	-£14	-£10	-£6	-£3	£1	£5	£9
	20%	-£32	-£28	-£24	-£21	-£17	-£13	-£10	-£6	-£2	£2	£5
	30%	-£35	-£31	-£28	-£24	-£20	-£16	-£13	-£9	-£5	-£1	£2
	40%	-£38	-£34	-£31	-£27	-£23	-£20	-£16	-£12	-£8	-£5	-£1
	50%	-£41	-£38	-£34	-£30	-£26	-£23	-£19	-£15	-£11	-£8	-£4
	60%	-£44	-£41	-£37	-£33	-£29	-£26	-£22	-£18	-£15	-£11	-£7
	70%	-£48	-£44	-£40	-£36	-£33	-£29	-£25	-£21	-£18	-£14	-£10
	80%	-£51	-£47	-£43	-£39	-£36	-£32	-£28	-£25	-£21	-£17	-£13
	90%	-£54	-£50	-£46	-£43	-£39	-£35	-£31	-£28	-£24	-£20	-£16
	100%	-£57	-£53	-£49	-£46	-£42	-£38	-£35	-£31	-£27	-£23	-£20

Figure C28 Cost of PICC reinsertion with fluoroscopy after Sherlock 3CG TCS or bedside failure

		Cost of fluoroscope insertion (after bedside failure)										
		£608	£650	£690	£720	£760	£800	£840	£880	£920	£960	£1,055
Cost of fluoroscope insertion (after Sherlock failure)	£608	-£20	-£23	-£25	-£27	-£30	-£33	-£36	-£38	-£41	-£44	-£50
	£650	-£18	-£21	-£24	-£26	-£28	-£31	-£34	-£37	-£40	-£42	-£49
	£690	-£16	-£19	-£22	-£24	-£27	-£30	-£32	-£35	-£38	-£41	-£47
	£720	-£15	-£18	-£21	-£23	-£26	-£28	-£31	-£34	-£37	-£39	-£46
	£760	-£14	-£16	-£19	-£21	-£24	-£27	-£30	-£32	-£35	-£38	-£44
	£800	-£12	-£15	-£18	-£20	-£22	-£25	-£28	-£31	-£34	-£36	-£43
	£840	-£10	-£13	-£16	-£18	-£21	-£24	-£26	-£29	-£32	-£35	-£41
	£880	-£9	-£12	-£14	-£17	-£19	-£22	-£25	-£28	-£30	-£33	-£40
	£920	-£7	-£10	-£13	-£15	-£18	-£20	-£23	-£26	-£29	-£31	-£38
	£960	-£6	-£8	-£11	-£13	-£16	-£19	-£22	-£24	-£27	-£30	-£36
	£1,055	-£2	-£5	-£7	-£10	-£12	-£15	-£18	-£21	-£23	-£26	-£33

Figure C29 Proportion of succesful placements and cost of insertion with Sherlock 3CG TCS (no X-ray)

		Cost of insertion with Sherlock										
		£210	£220	£240	£252	£270	£288	£306	£324	£342	£360	£374
Proportion of successful tip placements	92%	-£55	-£45	-£25	-£13	£5	£23	£41	£59	£77	£95	£109
	93%	-£63	-£54	-£34	-£22	-£4	£14	£32	£50	£68	£86	£101
	94%	-£71	-£62	-£42	-£30	-£12	£6	£24	£42	£60	£78	£93
	95%	-£79	-£70	-£50	-£38	-£20	-£2	£16	£34	£52	£70	£85
	96%	-£88	-£78	-£58	-£46	-£28	-£10	£8	£26	£44	£62	£76
	97%	-£96	-£86	-£66	-£54	-£36	-£18	£0	£18	£36	£54	£68
	98%	-£104	-£94	-£74	-£62	-£44	-£26	-£8	£10	£28	£46	£60
	99%	-£112	-£102	-£82	-£70	-£52	-£34	-£16	£2	£20	£38	£52
	100%	-£120	-£111	-£91	-£79	-£61	-£43	-£25	-£7	£11	£29	£44

Scenario analysis results

The results of scenario analyses conducted are displayed in Table C13. Information on the parameters used within each scenario are shown in Table C10.2.

Table C13 Scenario analyses results

	Sherlock 3CG with X-ray v. blind bedside placement with X-ray	Sherlock 3CG with X-ray v. fluoroscopy placement	Sherlock 3CG (no X-ray) v. blind bedside placement with X-ray	Sherlock 3CG (no X-ray) v. fluoroscopy placement
Costs increased from base case by 25%	£15.45 per patient	-£590.24 per patient	-£32.55 per patient	-£638.24 per patient
Costs reduced from base case by 25%	£9.28 per patient	-£353.56 per patient	-£19.72 per patient	-£382.56 per patient
Costs relating to Sherlock 3CG TCS increased from base case by 25%	£98.20 per patient	-£386.24 per patient	£50.20 per patient	-£434.17 per patient
Costs relating to Sherlock 3CG TCS reduced from base case by 25%	-£73.12 per patient	-£557.49 per patient	-£102.12 per patient	-£586.49 per patient
Theatre cost excluded	£26.89 per patient	£14.71 per patient	-£10.96 per patient	-£23.14 per patient
Bedside replacement of PICC line for failed Sherlock 3CG TCS patients	-£7.19 per patient	-£491.56 per patient	-£45.04 per patient	-£529.41 per patient
Healthcare professional costs using costs with qualification costs included	£11.62 per patient	-£481.58 per patient	-£32.87 per patient	-£526.07 per patient

Threshold analysis results

Threshold analysis was carried out to establish the limit of certain input parameters for Sherlock 3CG TCS (with or without X-ray) to be cost saving. The following input parameters are considered and the results set out for each of the four insertion method comparisons carried out. The results are reported as the parameter limit for Sherlock 3CG TCS to be cost saving.

1. Minimum number of patients utilising each Sherlock 3CG TCS device per year:

- Sherlock 3CG TCS with X-ray v. blind bedside placement with X-ray: this input does not drive the results enough in order to generate cost savings;
- Sherlock 3CG TCS with X-ray v. fluoroscopy placement: 8 patients;
- Sherlock 3CG TCS (no X-ray) v. bedside placement: 103 patients;
- Sherlock 3CG TCS (no X-ray) v. fluoroscopy placement: 7 patients.

2. Maximum number of nurses trained per device:

- Sherlock 3CG TCS with X-ray v. bedside placement: this input does not drive the results enough in order to generate cost savings;
- Sherlock 3CG TCS with X-ray v. fluoroscopy placement: 1209 nurses;
- Sherlock 3CG TCS (no X-ray) v. bedside placement: 68 nurses;
- Sherlock 3CG TCS (no X-ray) v. fluoroscopy placement: 1305 nurses.

3. Maximum time to insert the PICC line with Sherlock 3CG TCS (compared with 62.49 minutes nurse time for bedside placement and 40.13 minutes of radiographer time with fluoroscopy:

- Sherlock 3CG TCS with X-ray v. bedside placement: 53 minutes
- Sherlock 3CG TCS with X-ray v. fluoroscopy placement: 399 minutes;
- Sherlock 3CG TCS (no X-ray) v. bedside placement: 57 minutes;
- Sherlock 3CG TCS (no X-ray) v. fluoroscopy placement: 403 minutes.

4. Minimum cost of insertion with fluoroscopy for Sherlock 3CG TCS (with or without X-ray) to be cost saving (to the nearest whole pound):

- Sherlock 3CG TCS with X-ray v. bedside placement: £1,235 per insertion (in this case reinsertion following initial failure);
- Sherlock 3CG TCS with X-ray v. fluoroscopy placement: £324 per insertion;
- Sherlock 3CG TCS (no X-ray) v. bedside placement: Cost go as low as £0 and insertion with Sherlock 3CG TCS (no X-ray remains cost-saving);
- Sherlock 3CG TCS (no X-ray) v. fluoroscopy placement: £284 per insertion.

9.5.8 Present results of the probabilistic sensitivity analysis described in table C10.3.

Probabilistic sensitivity analysis was not carried out.

9.5.9 What were the main findings of each of the sensitivity analyses?

<u>One-way sensitivity analysis</u>

PICC placement with Sherlock 3CG plus X-ray

The results of the one-way sensitivity analysis showed that when comparing bedside placement with Sherlock 3CG TCS plus X-ray to blind insertion at the bedside the results were sensitive to a number of parameters. Sherlock 3CG TCS with X-ray becomes cost-saving the base case when:

- The proportion of successful placements with Sherlock 3CG TCS is above 97.5%;
- The proportion of successful blind placements at the bedside is below 91.5%;
- The cost of insertion with Sherlock 3CG TCS is less than £298 per patient;
- The cost of insertion at bedside placement without Sherlock 3CG TCS is greater than £287 per patient;

- The proportion of patients able to have reinsertion at the bedside without Sherlock, instead of with fluoroscopy following failure to insert the PICC is greater than 40%.

All five of these scenarios are explored further in the two-way sensitivity analysis or threshold analysis.

PICC placement with Sherlock 3CG with no X-ray

Where no X-ray is required to confirm PICC tip placement, Sherlock 3CG TCS is cost saving compared to bedside placement in the base case and one-way sensitivity analysis around some input parameters. Sherlock 3CG TCS with no X-ray becomes cost-incurring when:

- The proportion of successful placements with Sherlock 3CG TCS is below 93%;
- The cost of insertion with Sherlock 3CG TCS is greater than £300 per patient;
- The cost of insertion at the bedside without Sherlock 3CG TCS is less than £250 per patient;
- The proportion of patients able to have reinsertion at the bedside without Sherlock, instead of with fluoroscopy following failure to insert the PICC is greater than 69%.

These scenarios are explored further in the two-way sensitivity analysis and threshold analysis.

Where Sherlock 3CG TCS (either with or without a confirmation X-ray) is compared to insertion with fluoroscopy, Sherlock 3CG TCS is always cost-saving across the parameter ranges considered in sensitivity analysis.

<u>Two-way sensitivity analysis</u>

PICC placement with Sherlock 3CG plus X-ray

The results of the two-way analysis show that where Sherlock 3CG TCS with X-ray is compared to bedside placement there are situations in which insertion with Sherlock 3CG TCS is cost incurring and situations where cost savings are generated.

Firstly, where the proportion of successful placements with Sherlock 3CG TCS is at 100% (Barton, 2014) insertion with Sherlock 3CG TCS plus X-ray is always cost saving regardless of the success of blind placements at the bedside (Figure C22). As the success rate for Sherlock 3CG TCS plus X-ray falls, blind placement at the bedside is more likely to be cost saving, particularly where this success rate is highest. This suggests that in order for Sherlock 3CG TCS to be cost-saving compared to bedside placement in an NHS organisation, placement success rates must be at least 4.5 percentage points higher with Sherlock 3CG TCS plus X-ray than bedside placement.

Second, the two-way sensitivity analysis considering the proportion of successful replacement with the original insertion method (rather than with fluoroscopy) suggests that provided the proportion of Sherlock 3CG TCS patients requiring reinsertion with fluoroscopy is no more than 50% less than the with bedside placement, Sherlock 3CG TCS will be cost saving (Figure C23). Likewise, the two-way sensitivity analysis considering the cost of fluoroscopy for those patients requiring reinsertion with fluoroscopy shows that where the cost of insertion with fluoroscopy is in the range considered, Sherlock 3CG TCS is always cost incurring (Figure C24). Only where the cost of insertion with fluoroscopy following failure with Sherlock 3CG TCS plus X-ray is cheaper than that following blind bedside placement can Sherlock 3CG TCS plus X-ray generate cost savings. Clinical advice suggested that in the UK NHS some patients may have reinsertion at the bedside with blind placement plus X-ray if insertion with Sherlock 3CG TCS fails, in this case Sherlock 3CG TCS plus X-ray can generate cost savings (see scenario results in Section 9.5.7).

Two-way sensitivity analysis considering the cost of PICC insertion and tip placement with Sherlock 3CG TCS plus X-ray shows that where the cost of insertion is below £330 per patient placement with Sherlock 3CG TCS plus X-ray, this method has the potential to generate cost-savings (Figure C25). These cost savings are dependent upon the success rate of initial placement.

PICC placement with Sherlock 3CG with no X-ray

When comparing placement with Sherlock 3CG TCS (no x-ray) v. blind bedside placement with X-ray there are situations in which Sherlock 3CG TCS (no X-ray) becomes cost incurring.

Figure C26 shows that where the proportion of successful placements with Sherlock 3CG TCS is at 94% or below, insertion with Sherlock 3CG TCS may become cost incurring provided the success rate of blind placement is high. In order for placement with Sherlock 3CG TCS with no X-ray to generate cost-savings, the success rate with this method must be around 1.5 percentage points higher than that of blind bedside placement.

The two-way sensitivity analysis considering the proportion of successful replacements with the original insertion method (rather than with fluoroscopy) suggests that provided the proportion of Sherlock 3CG TCS patients (no X-ray) requiring reinsertion with fluoroscopy is no more than 70% less than the with bedside placement, Sherlock 3CG TCS will be cost saving (Figure C27). The cost of insertion with fluoroscopy after initial insertion did not affect the direction of results for the range considered (Figure C28).

Finally, two-way sensitivity analysis considering the cost and accuracy of PICC insertion and tip placement with Sherlock 3CG TCS (no X-ray) shows that where placement with the technology is 100% accurate the cost of insertion can be as high as below £324 per patient placement and still generate cost savings compared to placement without the technology.

Scenario analysis

The scenario analysis shows firstly that where all costs were increased or reduced by 25% the outcome of the results (in terms of whether Sherlock was cost incurring or cost saving) remained the same as in the base case (Table C13). Increasing and decreasing costs across the board may represent NHS settings with higher or lower costs than those used in the base case. Secondly, where the costs relating to insertion with Sherlock 3CG TCS only were increased or reduced by 25% the direction of results changed. Increasing Sherlock 3CG TCS related costs by 25% meant that insertion with Sherlock 3CG TCS (with or without X-ray) was cost incurring versus blind beside placement with X-ray. Cost savings compared with insertion with fluoroscopy remained. Where the costs related to Sherlock 3CG TCS reduced by 25% cost savings were generated against both blind bedside placement with X-ray and insertion with fluoroscopy regardless of whether or not insertion with Sherlock 3CG TCS required an X-ray.

Further, in the scenario where patients who experience tip placement failure with Sherlock 3CG TCS and therefore have blind insertion at the bedside, Sherlock 3CG TCS becomes cost-saving compared to both bedside placement and insertion with fluoroscopy. This occurs because the second procedure required by 4% of patients in this scenario (insertion at the bedside) is cheaper than procedure used in the base case (insertion with fluoroscopy).

Using costs of healthcare professionals with qualification costs (PSSRU, 2013) has little impact on any of the results.

Finally, we considered the cost of insertion with fluoroscopy with the theatre cost removed (Walker *et al*., 2013). This exploratory analysis was carried out as in the costs taken from Walker *et al.* the theatre cost for fluoroscopy is included, however there was some doubt around the inclusion of this cost. This theatre cost may not be generalisable to the NHS more widely. Firstly, the costs calculated by Walker *et al*. were specific to Raigmore hospital and the angiography laboratory in which PICC lines are inserted under fluoroscopy. There may be large variation in this cost across NHS settings dependent on where the procedure is carried out. Secondly, Walker *et al*. state that at Ragimore hospital PICC insertion with fluoroscopy prevents other procedures occurring. This may not be the case in every NHS hospital.

In this analysis, inclusion of the theatre cost means that the cost for insertion with fluoroscopy is much higher than for the other insertion methods. However, other sources (albeit from outside of the UK) have provided evidence to suggest that PICC insertion with fluoroscopy is substantially more expensive than insertion at the bedside and insertion with Sherlock 3CG TCS (Naylor, 2007). Naylor calculated the cost of insertion with fluoroscopy to be $700 compared with $305 for a previous version of Sherlock. Pittiruti *et al*., state that fluoroscopy is not cost-effective and carried safety concerns due to X-ray exposure (Pittiruti *et al*., 2012). Further, Walker *et al*. included theatre costs as these are genuine costs that were incurred to the hospital, meaning had we have excluded these costs in the base case we would have ignored costs that a hospital based analysis thought should be considered.

The results of the scenario analysis with theatre costs removed in the insertion of PICC lines with fluoroscopy show that Sherlock 3CG TCS with X-ray is cost-incurring compared with both blind bedside insertion with X-ray and insertion with fluoroscopy. PICC line insertion with Sherlock 3CG (no X-ray) is cost saving over both

comparators with theatre costs removed. The magnitudes of these cost savings are reduced compared to the base case, however.

Threshold analysis

The threshold analysis on the number of patients needing to utilise one Sherlock 3CG TCS device per year demonstrates that where annual patient numbers suitable for device are less than 103, Sherlock 3CG TCS (no X-ray) will not be cost saving compared to bedside placement without the machine. This occurs because the cost of purchasing the device and training nurses to use the device is not spread across enough patients to make the initial expenditure worthwhile.

Changing the number of patients whilst lowering the unit cost of the machine and training does not alter the results of the model enough to generate cost-savings with Sherlock 3CG TCS plus X-ray. Essentially this shows even if the machine had zero cost and required no training Sherlock 3CG TCS with confirmatory x-ray would not be cost saving compared to placement without the technology.

The number of nurses trained per Sherlock 3CG TCS device has little impact of the results. As this parameter does not substantially impact upon overall costs, the number of numbers trained can be very high and Sherlock 3CG TCS will remain cost saving versus insertion with fluoroscopy. Similarly, a reduction in the number of nurses trained does not generate cost savings for Sherlock 3CG TCS plus X-ray compared with blind placement.

Threshold analysis on the time taken to insert a PICC line with Sherlock 3CG TCS shows that providing PICC tip placement with Sherlock 3CG TCS (either with or without an X-ray) does not take longer than 53 minutes (compared with 62.49 minutes in the base case for blind bedside insertion), then Sherlock is cost saving. Compared with insertion with fluoroscopy, the time taken to insert and place a PICC line with Sherlock 3CG TCS can get very long (over 6 hours) and remain cost saving.

Finally, threshold analysis was conducted to determine how low the cost of insertion with fluoroscopy could be whilst maintaining a cost-saving with Sherlock 3CG TCS both with and without an X-ray compared to the procedure. This analysis was carried out to explore further situations whereby theatre costs may not be at the same level as calculated by Walker *et al*, 2013. Compared with insertion with fluoroscopy, Sherlock 3CG TCS plus X-ray generates cost savings where insertion with fluoroscopy costs at least £324 per insertion. Insertion with Sherlock 3CG TCS (no

X-ray) generates cost savings provided insertion with fluoroscopy costs at least £284 per insertion.

The cost of fluoroscopy also influences the cost savings generated by insertion with Sherlock 3CG TCS compared with blind bedside placement as this is the second line method for those patients experiencing initial failure. As this affects less than 10% of patients the model is not that sensitive to changes in this cost in terms of insertion with Sherlock versus blind bedside placement. The cost of fluoroscopy has to be above £1,235 for insertion with Sherlock 3CG TCS plus X-ray to be cost saving over blind bedside placement plus X-ray. For insertion with Sherlock 3CG TCS (no X-ray), even with a cost of fluoroscopy of £0, Sherlock 3CG TCS (no X-ray) is cost saving over blind bedside placement with X-ray.

9.5.10 What are the key drivers of the cost results?

The key drivers of the model are the cost of PICC line insertion (for each insertion method) and the success rate of placement at initial insertion with Sherlock 3CG TCS plus X-ray and with blind insertion at the bedside plus X-ray. Although in the base case, Sherlock 3CG TCS is cost incurring versus blind bedside placement plus X-ray, where the success rate of Sherlock 3CG TCS is above 97.5% it becomes cost saving. This was the case in two of the studies included in the clinical evidence submission: Barton, 2014 and Adams, 2013. When considering insertion with Sherlock 3CG TCS plus X-ray with fluoroscopy the key driver is the cost of fluoroscopy (driven by inclusion or exclusion of theatre costs).

The results for PICC placement with Sherlock 3CG TCS (no X-ray) are more robustly supportive of the technology being cost-saving. This was the case even where theatre costs were excluded for the cost of PICC insertion and placement with fluoroscopy. The key driver of this analysis was the cost of PICC insertion with Sherlock 3CG TCS.

Miscellaneous results

9.5.11 Describe any additional results that have not been specifically requested in this template. If none, please state.

There are no additional results.

9.6 Subgroup analysis

For many technologies, the capacity to benefit from treatment will differ for patients with differing characteristics. Sponsors are required to complete section 9.6 in accordance with the subgroups identified in the scope and for any additional subgroups considered relevant.

Types of subgroups that are not considered relevant are those based solely on the following factors.

- Subgroups based solely on differential treatment costs for individuals according to their social characteristics.
- Subgroups specified in relation to the costs of providing treatment in different geographical locations within the UK (for example, if the costs of facilities available for providing the technology vary according to location).

No subgroups were defined within the scope and therefore no subgroup analysis has been carried out.

9.7 Validation

9.7.1 Describe the methods used to validate and cross-validate (for example with external evidence sources) and quality-assure the model. Provide references to the results produced and cross-reference to evidence identified in the clinical and resources sections.

The economic model was created in Microsoft Excel by one economist and checked by a second economist. A third economist who had not been previously involved with the submission quality assessed the economic submission.

An external clinical expert was used to validate the key resource assumptions within the model.

Whilst the available published economic evidence described previously was limited, the findings here are consistent with that seen in those studies i.e. The introduction of Sherlock 3CG TCS was cost saving compared to bedside placement without use of this technology.

9.8 Interpretation of economic evidence

9.8.1 Are the results from this cost analysis consistent with the published economic literature? If not, why do the results from this evaluation differ, and why should the results in the submission be given more credence than those in the published literature?

Two economic studies were identified within the economic evidence review (Adams *et al*., 2013 and Stewart *et al*., 2013). As both studies were unpublished, limited information was provided around the methods utilised. However, the available information suggested that the studies were of low methodological quality. Further, both studies were undertaken outside of the UK NHS and therefore have limited relevance to this submission. In both studies PICC placement using Sherlock 3CG TCS with no X-ray to confirm tip location was compared with PICC placement at the bedside and both found the use of Sherlock 3CG TCS to be cost-saving. In the current analysis, where PICC placement with Sherlock 3CG TCS and no confirmation

X-ray is compared with blind bedside placement plus X-ray cost-savings are generated. The limited relevance to the UK NHS and the poor methodological quality of both Adams *et al*., 2013 and Stewart *et al*., 2013 precludes the ability to cross-validate the results of this analysis with these studies, however the overall result of both this analysis and the two unpublished studies find Sherlock 3CG TCS (no X-ray) to be cost saving compared with bedside placement. Naylor (2007) compared a previous version of Sherlock with fluoroscopy and similar to this analysis found Sherlock to be cost saving.

9.8.2 Is the cost analysis relevant to all groups of patients and NHS settings in England that could potentially use the technology as identified in the scope?

The scope specifies that analysis should be conducted for adults requiring PICC insertion. Both inpatients and outpatients in secondary and tertiary care should be considered. Scenario and sensitivity analysis has been conducted to attempt to explore cost differences that may exist between these settings. By varying input parameters it is hoped that the analysis covers all NHS settings in which a PICC line may be placed.

9.8.3 What are the main strengths and weaknesses of the analysis? How might these affect the interpretation of the results?

The key strength of this analysis is the conservative approach to parameter values in the model. For example, the only UK based clinical study of Sherlock 3CG TCS reported a success rate of 100% accurate PICC placement (Barton, 2014). Had this value, rather than 96%, been used the base case results would be more favourable for Sherlock 3CG TCS. In addition, in questionnaires provided by NHS organisations currently using Sherlock 3CG TCS organisations reported either no or less than 1% malposition PICC tip placement with Sherlock 3CG TCS. Prior to the use of Sherlock 3CG TC, i.e. with blind beside placement plus X-ray, malposition rates were far higher (up to 40%). The proportion of this requiring PICC line replacement (as opposed to adjustment) is unclear, however.

A further strength of the submission is that extensive sensitivity and scenario analyses have been undertaken in an attempt to mitigate against the quality of data and generalisability of included studies.

There are various weaknesses of the analysis. Firstly, there is a lack of head to head trial data to incorporate into the model. However, all studies reported higher accuracy rates between Sherlock 3CG TCS and conventional placement even if this was only discussed qualitatively. As insertion with Sherlock 3CG (no X-ray) only has to be as effective as blind bedside placement in to be cost saving the evidence available, albeit not gold standard, supports our conclusions. Second, the absence of any data from tertiary or outpatient use is a weakness of the analysis, however clinical advice has assured that this would make no difference to findings and Walker *et al.* find little difference in the cost of conventional placement between settings (Walker *et al*., 2013).

The final weakness of the analysis is the uncertainty around cost input parameters and the generalisability of Raigmore hospital to the NHS more widely. We have carried out extensive sensitivity analysis in an attempt to overcome this.

9.8.4 What further analyses could be undertaken to enhance the robustness/completeness of the results?

We contacted Walker for a breakdown of costs within his study, but as of submission to NICE a response had not been received. A breakdown of the costs calculated by Walker *et al*. would have allowed us to better understand his calculations and ensure we applied his costs accurately.

Extensive sensitivity analysis was conducted in an attempt to mitigate against the paucity of good quality data available to populate the model and against variation in clinical practice that is likely to exist.

10 References

References for clinical submission

Adams T, (2013). The Clinical Efficacy of PICC Tip Confirmation using ECG Tip Locator Technology. Poster Presentation at the Association of Vascular Access Annual Scientific Meeting 2013.

Barton A (2014). Evaluation of ECG and PICC Tip Location Technology; is it Safe to Stop Using X-Ray. *Journal of Vascular Access*. 15 (3): 202

iData Research Inc (2014). *European Markets for Vascular Access Devices. iData European Union Vascular Access 2014 Report: Austria, Belgium, Denmark, Finland, France, Germany, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, U.K*. British Colombia, iData Research Inc)

Johnston A (2014). Evaluation of Peripherally Inserted Central Catheter (PICC) Malposition Rates and the Impact of the Sherlock 3CG Tip Confirmation System. *Journal of Vascular Access*. 15 (3): 225

Kupka D (2011). Changing nursing practice and improving patient care by using ECG guidance to eliminate post PICC insertion radiograph. *Journal of the Association for Vascular Access.* 16(4): 209.

Lelkes V (2013). Analysis of the Sherlock II tip location system for inserting peripherally inserted central venous catheters. Clinical Imaging. 37 (5): 917-21.

Naylor C, (2007). Reduction of malposition in peripherally inserted central catheters with tip location system. *Journal of the Association for Vascular Access.*12(1). 29-31.

Oakley C (2011). PICC journey to CAJ by way of Sapiens. *Journal of the Association for Vascular Access.* 16(4): 204.

Parikh A, Babcock L, Brumble L, Williams H and McComb B (2012). Successful Implementation of Electrocardiocardiographic-Guided PICC

placement with a Nurse-Comprised PICC Team. Poster Presentation at Radiological Society of North America.

Pittiruti M, (2010). Rapid vein assessment before central venous catheterization: The GAVeCeLT recommendations. *Journal of the Association for Vascular Access.* 16(4): 205.

Pittiruti, M., La Greca, A., Emoli, A. and Scoppettuolo, G., (2011). Positioning the tip of central venous catheters by the intracavitary ECG method, using a new specific device. Intensive Care Medicine. 36: S145.

Shukla, P., Lelkes, V., Kumar, A. and Contractor, S. (2012). Efficacy of Sherlock II tip location system for bedside peripherally inserted central venous catheter. *Journal of Vascular and Interventional Radiology*. 1: S115-S116.

Smith B, Neuharth B, Hendrix A, McDonnall D and Michaels A (2010). Intravenous electrocardiographic guidance for placement of peripherally inserted central catheters. Journal of Electrocardiology. 43: 274-8.

Stewart F, 2013. New Australian Experience: Improvement in Peripherally Inserted Central Catheter (PICC) Insertion technique using real time tracking and ECG for optimal PICC tip position (without need for CXR). Poster Presentation at the Association of Vascular Access Annual Scientific Meeting 2013.

Symington K, 2011. Sherlock 3CG Spokane Trial Results. Accessed 21 May 2014. Available online at http://sweetspot-venouscatheter.com/sherlock-results

References for economic submission

Adams T. The Clinical Efficacy of PICC Tip Confirmation using ECG Tip Locator Technology. Poster Presentation at the Association of Vascular Access Annual Scientific Meeting. 2013.

Angiodynamics Inc. The PROOF Study: The PICC Related Obstruction Of Flow Study. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of

Medicine (US). 2000-[cite 2007 July 17]. Available from: http://clinicaltrials.gov/show/NCT01921114

Bard CR. Assessment of the Precision of the Sherlock 3CG Tip Positioning System (STAT-PICC). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cite 2007 July 17]. Available from: http://clinicaltrials.gov/show/NCT01275430

Bard CR. Electrocardiogram (ECG) Guided Peripherally Inserted Central Catheter (PICC) Placement. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cite 2007 July 17]. Available from: http://clinicaltrials.gov/show/NCT00742053

The Bard SherLock 3CG Tip Confirmation System Education. Bard (2013): Unpublished.

CADTH. Electrocardiograms versus x-rays for guided placement of central venous catheter tips: a review of clinical and cost-effectiveness (Structured abstract). Health Technology Assessment Database [Internet]. 2012; (4). Available from: http://onlinelibrary.wiley.com/o/cochrane/clhta/articles/HTA-32012000699/frame.html.

Calvert N, Hind D, McWilliams R, Davidson A, Beverley CA, Thomas SM. Ultrasound for central venous cannulation: economic evaluation of cost-effectiveness. Anaesthesia. 2004; (11):1116-20 .

Centre Leon Berard. A Study to Assess Placement and Confirmation of Peripheral Inserted Central Catheters Tip Position Using a New Electrocardiographic Method (SHERLOCK 3CG). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000-[cite 2007 July 17]. Available from: http://clinicaltrials.gov/show/NCT01969981

Costantino TG, Parikh AK, Satz WA, Fojtik JP. Ultrasonography-guided peripheral intravenous access versus traditional approaches in patients with difficult intravenous access. Ann Emerg Med. 2005 Nov;46(5):456-61.

Cowl CT, Weinstock JV, Al-Jurf A, Ephgrave K, Murray JA, Dillon K. Complications and cost associated with parenteral nutrition delivered to hospitalized patients through either subclavian or peripherally-inserted central catheters. Clin Nutr.2000; 19(4): 237-43.

Davis J, Kokotis K. A new perspective for PICC line insertions: Cost effectiveness and outcomes associated with an independent PICC service. J Vasc Access. 2004;9(2):93-8.

Department of Health (2013) National Schedule of Reference Costs 2012-13 for NHS Trusts and Foundation Trusts [online dataset; accessed 22nd July 2014]

Girgenti C, Donnellan E. Successfully eliminating chest radiography by replacing it with dual vector technology and an algorithm for PICC placement. J Vasc Access. 2014;19(2):71-4.

Hahn ST, Pfammatter T, Cho KJ. Carbon dioxide gas as a venous contrast agent to guide upper-arm insertion of central venous catheters. Cardiovasc Intervent Radio. 1995;18(3):146-9.

Harako ME, Nguyen TH, Cohen AJ. Optimizing the patient positioning for PICC line tip determination. Emergen Radio. 2004; 10:186-9.

Hockley SJG, Hamilton V, Young RJ, Chapman MJ, Taylor J, Creed S, *et al*. Efficacy of the CathRite system to guide bedside placement of peripherally inserted central venous catheters in critically ill patients: a pilot study. Crit Care Resusc. 2007;9(3):251-5.

ISD Scotland. 2013. NHS Scotland radiology services costs 2013. Available from: http://www.isdscotland.org/Health-Topics/Finance/Costs/Detailed-Tables/Radiology.asp

Johnston A, Holder A, Bishop S, See T, Streater C. Evaluation of the Sherlock 3CG Tip Confirmation System on peripherally inserted central catheter malposition rates. Anaesthesia. 2014. DOI: 10.1111/anae.12785

Lamperti M, Bodenham AR, Pittiruti M, Blaivas M, Augoustides JG, Elbarbary M, *et al*. International evidence-based recommendations on ultrasound-guided vascular access. J. Intensive Care Med. 2012;38(7):1105-17.

Naylor CL. Reduction of malposition in peripherally inserted central catheters with tip location system. J Vasc Access. 2007;12(1):29-31.

National Institute for Health and Clinical Excellence. 2011. Medical technologies evaluation programme: methods guide. London: National Institute for Health and Clinical Excellence

NHS Information Centre. 2014. Reference NHS, Version 3.8, Mobile App. 2014. [cited 29th July 2014]. Available from: https://itunes.apple.com/gb/app/reference-nhs/id335643807?mt=8

NHS National Services Scotland. 2010. NHS Scotland radiology services costs 2013. Available from: http://www.isdscotland.org/Health-Topics/Finance/Costs/Detailed-Tables/Radiology.asp

Parikh A, Babcock L, Brumble L, Williams H and McComb B Successful Implementation of Electrocardiocardiographic-Guided PICC placement with a Nurse-Comprised PICC Team. Poster Presentation at Radiological Society of North America. 2012.

Pittiruti M, La Greca A, Scoppettuolo G. The electrocardiographic method for positioning the tip of central venous catheters. J Vasc Access. 2011; 12(4):280-91.

Pittiruti M, Scoppettuolo G, La Greca A, Emoli A, Brutti A, Ivano M, *et al*. The EKG method for positioning the tip of PICCs: Results from two preliminary studies. J Vasc Access. 2008;13(4):179-86.

PSSRU, 2013. Unit Costs of Health and Social Care 2013. Available from: http://www.pssru.ac.uk/

Schweickert WD, Herlitz J, Pohlman AS, Gehlbach BK, Hall JB, Kress JP. A randomized, controlled trial evaluating postinsertion neck ultrasound in

peripherally inserted central catheter procedures. Crit Care Med. 2009;37(4):1217-21.

Stewart F. New Australian Experience: Improvement in Peripherally Inserted Central Catheter (PICC) Insertion technique using real time tracking and ECG for optimal PICC tip position (without need for CXR). Poster Presentation at the Association of Vascular Access Annual Scientific Meeting 2013.

Walker G, Todd A. Nurse-led PICC insertion: is it cost effective? Br J Nurs. 2013 13;22(19):S9-15.

Yamada R, Morita T, Yashiro E, Otani H, Amano K, Tei Y, *et al*. Patient-reported usefulness of peripherally inserted central venous catheters in terminally ill cancer patients. J Pain Symptom Manage 2010;40(1):60-6.

11 Appendices

11.1 Appendix 1: Search strategy for clinical evidence (section 7.1.1)

The following information should be provided:

11.1.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

Response

11.1.2 The date on which the search was conducted.

Response

11.1.3 The date span of the search.

Response

11.1.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Response

11.1.5 Details of any additional searches, such as searches of company or professional organisation databases (include a description of each database).

Response

11.1.6 The inclusion and exclusion criteria.

Response

11.1.7 The data abstraction strategy.

Response

11.2 Appendix 2: Search strategy for adverse events (section 7.7.1)

The following information should be provided.

11.2.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

Response

11.2.2 The date on which the search was conducted.

Response

11.2.3 The date span of the search.

Response

11.2.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Response

11.2.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Response

11.2.6 The inclusion and exclusion criteria.

Response

11.2.7 The data abstraction strategy.

Response

11.3 Appendix 3: Search strategy for economic evidence (section 8.1.1)

The following information should be provided.

11.3.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- EconLIT
- NHS EED.

The following databases were searched:

- MEDLINE and MEDLINE In-Process (via OvidSP)
- EMBASE (via OvidSP)
- Econlit (via OvidSP)
- NHS Economic Evaluation Database (via Cochrane Library/Wiley Interscience)
- Health Technology Assessment Database (via Cochrane Library/Wiley Interscience)

- Health Economic Evaluations Database (via EBSCOhost)
- CEA (Cost-Effectiveness Analysis) Registry (via https://research.tufts-nemc.org/cear4/Home.aspx)
- ClinicalTrials.gov (via https://clinicaltrials.gov/ct2/home)
- International Clinical Trials Registry Platform (ICTRP) (via http://apps.who.int/trialsearch/)
- metaRegister of Controlled Trials (mRCT) (via http://www.controlled-trials.com/mrct/)
- Conference Proceedings Citation Index- Science (CPCI-S) - 1990-present (via Web of Science)

Details of additional sources used are given in section 10.3.5.

11.3.2 The date on which the search was conducted.

For search dates, see details of search strategies given in section 10.3.4 below.

11.3.3 The date span of the search.

The search was limited to studies published from 2000 to date.

11.3.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

The database search strategies are detailed below (sources A.1 to A.11).

A.1: Source: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present

Interface / URL: OvidSP

Search date: 03/07/14

Retrieved records: 234

Search strategy:

1 Catheterization/ 46020

2 Catheterization, Central Venous/ 11823

3 exp Catheterization, Peripheral/ 8496

4 Cardiac Catheterization/ 39425

5 exp Catheters/ 18714

6 (catheter$ or cannula$ or canula$).ti,ab,kf. 187212

7 (CVC or CVCs or PICC or PICCs).ti,ab,kf. 3317

8 (PIC adj3 line$).ti,ab,kf. 30

9 (central adj3 line$).ti,ab,kf. 3626

10 (venous adj3 line$).ti,ab,kf.1608

11 or/1-10 243386

12 Electrocardiography/ 164466

13 (electrocardiogram$ or cardiogram$ or electrocardiograph$ or cardiograph$ or ecg or ecgs or ekg or ekgs).ti,ab,kf. 112087

14 Magnetics/ 21743

15 Magnets/ 780

16 exp Magnetic Fields/ 16101

17 magnetic phenomena/ or electromagnetic phenomena/ 5600

18 (magnet$ or electromagnet$).ti,ab,kf. 330044

19 (real-time$ or realtime$).ti,ab,kf. 140425

20 (malposition$ or mal-position$).ti,ab,kf. 4766

21 ((tip or tips) adj5 (confirm$ or verif$ or locat$ or place$ or placing or misplace$ or misplacing or position$ or guid$)).ti,ab,kf. 6022

22 (TCS or TCSs or TPS or TPSs).ti,ab,kf. 5494

23 sapiens$.ti,ab,kf. 3010

24 or/12-23 695779

25 sherlock$.ti,ab,kf. 266

26 powerpicc$.ti,ab,kf. 3

27 or/25-26 269

28 economics/ 26987

29 exp "costs and cost analysis"/ 181481

30 economics, dental/ 1855

31 exp "economics, hospital"/ 19528

32 economics, medical/ 8609

33 economics, nursing/ 3916

34 economics, pharmaceutical/ 2539

35 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. 470429

36 (expenditure$ not energy).ti,ab. 18694

37 value for money.ti,ab. 984

38 budget$.ti,ab. 19256

39 or/28-38 597354

40 ((energy or oxygen) adj cost).ti,ab. 2916

41 (metabolic adj cost).ti,ab. 842

42 ((energy or oxygen) adj expenditure).ti,ab. 17174

43 or/40-42 20187

44 39 not 43 592775

45 11 and 24 and 44 446

46 27 and 44 6

47 45 or 46 452

48 exp animals/ not humans/ 3954113

49 (news or comment or editorial).pt. 987033

50 47 not (48 or 49) 433

51 limit 50 to (english language and yr="2000 -Current") 235

52 remove duplicates from 51 234

A.2: Source: Embase 1974 to 2014 July 02

Interface / URL: OvidSP

Search date: 03/07/14

Retrieved records: 590

Search strategy:

1 catheterization/ 36009

2 central venous catheterization/ 6948

3 heart catheterization/ 47605

4 exp catheter/ 100048

5 exp catheter complication/ 13685

6 (catheter$ or cannula$ or canula$).ti,ab,kw. 248785

7 (CVC or CVCs or PICC or PICCs).ti,ab,kw. 5186

8 (PIC adj3 line$).ti,ab,kw. 35

9 (central adj3 line$).ti,ab,kw. 5504

10 (venous adj3 line$).ti,ab,kw. 2302

11 or/1-10 322633

12 cardiography/ or electrocardiography/ or electrocardiography monitoring/ 132907

13 cardiograph/ or electrocardiograph/ 224

14 (electrocardiogram$ or cardiogram$ or electrocardiograph$ or cardiograph$ or ecg or ecgs or ekg or ekgs).ti,ab,kw. 142088

15 electronic sensor/ 1361

16 "magnetic and electromagnetic equipment"/ 1876

17 exp magnetism/ 56069

18 (magnet$ or electromagnet$).ti,ab,kw. 376092

19 (real-time$ or realtime$).ti,ab,kw. 186357

20 positioning device/ 90

21 (malposition$ or mal-position$).ti,ab,kw. 5929

22 ((tip or tips) adj5 (confirm$ or verif$ or locat$ or place$ or placing or misplace$ or misplacing or position$ or guid$)).ti,ab,kw. 7741

23 (TCS or TCSs or TPS or TPSs).ti,ab,kw. 7302

24 sapiens$.ti,ab,kw,dv. 3582

25 or/12-24 806354

26 sherlock$.ti,ab,kw,dv. 307

27 powerpicc$.ti,ab,kw,dv. 12

28 or/26-27 319

29 health-economics/ 33666

30 exp economic-evaluation/ 212723

31 exp health-care-cost/ 205727

32 exp pharmacoeconomics/ 167000

33 (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. 612751

34 (expenditure$ not energy).ti,ab. 24184

35 (value adj2 money).ti,ab. 1397

36 budget$.ti,ab. 24505

37 or/29-36 908792

38 (metabolic adj cost).ti,ab. 904

39 ((energy or oxygen) adj cost).ti,ab. 3166

40 ((energy or oxygen) adj expenditure).ti,ab. 20341

41 or/38-40 23592

42 37 not 41 903659

43 11 and 25 and 42 852

44 28 and 42 12

45 43 or 44 862

46 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ 4958662

47 editorial.pt. 451437

48 45 not (46 or 47) 827

49 limit 48 to (english language and yr="2000 -Current") 597

50 remove duplicates from 49 590

A.3: Source: Econlit 1886 to May 2014

Interface / URL: OvidSP

Search date: 04/07/14

Retrieved records: 4

Search strategy:

1 (catheter$ or cannula$).af. (30)

2 (CVC or CVCs or PICC or PICCs).af. (25)

3 (PIC adj3 line$).af. (1)

4 (central adj3 line$).af. (45)

5 (venous adj3 line$).af. (0)

6 or/1-5 (101)

7 (magnet$ or electromagnet$).af. (330)

8 (real-time$ or realtime$).af. (2092)

9 (malposition$ or mal-position$).af. (0)

10 ((tip or tips) adj5 (confirm$ or verif$ or locat$ or place$ or placing or misplace$ or misplacing or position$ or guid$)).af. (10)

11 (TCS or TCSs or TPS or TPSs).af. (75)

12 sapiens$.af. (35)

13 or/7-12 (2539)

14 sherlock$.ti,ab. (8)

15 powerpicc$.ti,ab. (0)

16 or/14-15 (8)

17 6 and 13 (1)

18 or/16-17 (9)

19 limit 18 to (yr="2000 -Current" and english) (4)

A.4: Source: Health Technology Assessment (HTA) Database - Issue 2 of 4, Apr 2014

Interface / URL: Cochrane Library/Wiley Interscience

Search date: 03/07/14

Retrieved records: 14

Search strategy:

#1 [mh ^Catheterization] 1478

#2 [mh ^"Catheterization, Central Venous"] 773

#3 [mh "Catheterization, Peripheral"] 717

#4 [mh ^"Cardiac Catheterization"] 982

#5 [mh Catheters] 1138

#6 (catheter* or cannula* or canula*) 16074

#7 (CVC or CVCs or PICC or PICCs) 394

#8 (PIC near/3 line*) 3

#9 (central near/3 line*) 299

#10 (venous near/3 line*) 212

#11 {or #1-#10} 16342

#12 [mh ^Electrocardiography] 6685

#13 (electrocardiogram* or cardiogram* or electrocardiograph* or cardiograph* or ecg or ecgs or ekg or ekgs) 14452

#14 [mh ^Magnetics] 308

#15 [mh ^Magnets] 10

#16 [mh "Magnetic Fields"] 353

#17 [mh ^"magnetic phenomena"] or [mh ^"electromagnetic phenomena"] 117

#18 (magnet* or electromagnet*) 13162

#19 (real-time* or realtime*) 2312

#20 (malposition* or mal-position*) 202

#21 ((tip or tips) near/5 (confirm* or verif* or locat* or place* or placing or misplace* or misplacing or position* or guid*)) 336

#22 (TCS or TCSs or TPS or TPSs) 214

#23 sapiens* 9

#24 {or #12-#23} 30107

#25 sherlock* 110

#26 powerpicc* 1

#27 #25 or #26 111

#28 #11 and #24 1480

#29 #27 or #28 1590

#30 #29 Publication Year from 2000 to 2014, in Technology Assessments 14

A.5: Source: NHS Economic Evaluation Database (NHS EED) - Issue 2 of 4, Apr 2014

Interface / URL: Cochrane Library/Wiley Interscience

Search date: 03/07/14

Retrieved records: 48

Search strategy:

#1 [mh ^Catheterization] 1478

#2 [mh ^"Catheterization, Central Venous"] 773

#3 [mh "Catheterization, Peripheral"] 717

#4 [mh ^"Cardiac Catheterization"] 982

#5 [mh Catheters] 1138

#6 (catheter* or cannula* or canula*) 16074

#7 (CVC or CVCs or PICC or PICCs) 394

#8 (PIC near/3 line*) 3

#9 (central near/3 line*) 299

#10 (venous near/3 line*) 212

#11 {or #1-#10} 16342

#12 [mh ^Electrocardiography] 6685

#13 (electrocardiogram* or cardiogram* or electrocardiograph* or cardiograph* or ecg or ecgs or ekg or ekgs) 14452

#14 [mh ^Magnetics] 308

#15 [mh ^Magnets] 10

#16 [mh "Magnetic Fields"] 353

#17 [mh ^"magnetic phenomena"] or [mh ^"electromagnetic phenomena"] 117

#18 (magnet* or electromagnet*) 13162

#19 (real-time* or realtime*) 2312

#20 (malposition* or mal-position*) 202

#21 ((tip or tips) near/5 (confirm* or verif* or locat* or place* or placing or misplace* or misplacing or position* or guid*)) 336

#22 (TCS or TCSs or TPS or TPSs) 214

#23 sapiens* 9

#24 {or #12-#23} 30107

#25 sherlock* 110

#26 powerpicc* 1

#27 #25 or #26 111

#28 #11 and #24 1480

#29 #27 or #28 1590

#30 #29 Publication Year from 2000 to 2014, in Technology Assessments 14

#31 #29 Publication Year from 2000 to 2014, in Economic Evaluations 48

A.6: Source: HEED: Health Economic Evaluations Database

Interface / URL: EBSCOhost

Search date: 03/07/14

Retrieved records: 18

Search strategy:

S19 S15 OR S16 OR S17 Limiters - Published Date: 20000101-20141231; Language: English 18

S18 S15 OR S16 OR S17 45

S17 TX(powerpicc*) 0

S16 TX(sherlock*) 7

S15 S6 AND S14 38

S14 S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 810

S13 TX(sapiens*) 0

S12 TX(TCS OR TCSs OR TPS OR TPSs) 1

S11 TX((tip OR tips) N5 (confirm* OR verif* OR locat* OR place* OR placing OR misplace* OR misplacing OR position* OR guid*)) 5

S10 TX(malposition* OR "mal-position*") 7

S9 TX("real-time*" OR realtime*) 56

S8 TX(magnet* OR electromagnet*) 454

S7 TX(electrocardiogram* OR cardiogram* OR electrocardiograph* OR cardiograph* OR ecg OR ecgs OR ekg OR ekgs) 301

S6 S1 OR S2 OR S3 OR S4 OR S5 805

S5 TX(venous N3 line*) 15

S4 TX(central N3 line*) 27

S3 TX(PIC N3 line*) 1

S2 TX(CVC OR CVCs OR PICC OR PICCs) 18

S1 TX(catheter* OR cannula* OR canula*) 797

A.7: Source: Conference Proceedings Citation Index- Science (CPCI-S) - 1990-present (via Web of Science)

Interface / URL: Web of Science

Search date: 03/07/14

Retrieved records: 55

Search strategy:

32 55 (#30 not #31) AND LANGUAGE: (English) Timespan=2000-2014

31 194,166 TI=("rat" or "rats" or "rodent" or "rodents" or "mouse" or "mice" or "murine" or "hamster" or "hamsters" or "animal" or "animals" or "dogs" or "dog" or "pig" or "pigs" or piglet* or "swine" or "swines" or "cats" or "bovine" or "cow" or "cows" or "cattle" or buffalo* or "sheep" or "ewe" or "ewes" or "lamb" or "lambs" or "horse" or "horses" or "equine" or "ovine" or "porcine" or "monkey" or "monkeys" or "rhesus macaque" or "rhesus macaques" or "rabbit" or "rabbits") NOT TS=(human*)

30 72 #29 OR #28

29 5 #27 AND #17

28 67 #27 AND #14 AND #6

27 351,049 #22 not #26

26 5,728 #25 OR #24 OR #23

25 2,613 TS=(("energy" or "oxygen") near/1 "expenditure")

24 120 TS=("metabolic" near/1 "cost")

23 3,093 TS=(("energy" or "oxygen") near/1 "cost")

22 354,435 #21 OR #20 OR #19 OR #18

21 15,143 TS=(budget*)

20 160 TS=("value for money")

19 3,320 TS=(expenditure* not "energy")

18 341,359 TS=(economic* or "cost" or "costs" or "costly" or "costing" or "price" or "prices" or "pricing" or pharmacoeconomic*)

17 56 #16 OR #15

16 0 TS=(powerpicc*)

15 56 TS=(sherlock*)

14 443,857 #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7

13 354 TS=(sapiens*)

12 2,174 TS=("TCS" or "TCSs" or "TPS" or "TPSs")

11 1,965 TS=(("tip" or "tips") near/5 (confirm* or verif* or locat* or place* or "placing" or misplace* or "misplacing" or position* or guid*))

10 292 TS=(malposition* or "mal-position*")

9 128,954 TS=("real-time*" or realtime*)

8 302,082 TS=(magnet* or electromagnet*)

7 13,504 TS=(electrocardiogram* or cardiogram* or electrocardiograph* or cardiograph* or "ecg" or "ecgs" or "ekg" or "ekgs")

6 16,701 #5 OR #4 OR #3 OR #2 OR #1

5 136 TS=("venous" near/3 line*)

4 977 TS=("central" near/3 line*)

3 58 TS=("PIC" near/3 line*)

2 660 TS=("CVC" or "CVCs" or "PICC" or "PICCs")

1 15,220 TS=(catheter* or cannula* or cannula*)

A.8: Source: ClinicalTrials.gov

Interface / URL: https://clinicaltrials.gov/ct2/home

Search date: 03/07/14 – 04/07/14

Retrieved records: 58

Search strategy:

Advanced interface used at: https://clinicaltrials.gov/ct2/search/advanced. Following searches run separately. Terms inserted using Expert Search option:

1. ((catheter OR catheterise OR catheterises OR catheterizes OR cannula OR cannulate OR cannulates OR cannulating OR cannulation OR canulates OR CVC OR CVCs OR PICC OR PICCs OR "PIC line" OR "PIC lines" OR "central line" OR "central lines" OR "venous line" OR "venous lines") AND (electrocardiogram OR cardiogram OR electrocardiograph OR cardiograph OR electrocardiograms OR cardiograms OR electrocardiographs OR

cardiographs OR electrocardiogramy OR cardiogramy OR electrocardiography OR cardiography OR ecg OR ecgs OR ekg OR ekgs OR magnet OR magnets OR magnetic OR magnetics OR magnetism OR electromagnet OR electromagnets OR electromagnetic OR electromagnetics OR electromagnetism OR "real-time" OR realtime OR malposition OR malpositions OR malpositioned OR malpositioning OR "mal-position" OR "mal-positions" OR "mal-positioned" OR "mal-positioning" OR tip OR tips OR TCS OR TCSs OR TPS OR TPSs OR sapiens OR sapiensr OR sapienstm) AND (economic OR economics OR economically OR cost OR costs OR costly OR costing OR price OR prices OR pricing OR pharmacoeconomic OR pharmacoeconomics OR pharmacoeconomically OR expenditure OR money OR budget OR budgets)) [ALL-FIELDS] AND ("01/01/2000" : "07/04/2014") [FIRST-RECEIVED-DATE] = 47

2. (sherlock OR sherlocktm OR sherlockr OR powerpicc OR powerpicctm OR powerpiccr) [ALL-FIELDS] = 11

A.9: Source: International Clinical Trials Registry Platform (ICTRP)

Interface / URL: http://apps.who.int/trialsearch/

Search date: 04/07/14

Retrieved records: 143

Search strategy:

Following searches run separately (using default search interface).

1. 16 records for 14 trials found for: catheter* AND electrocardiogram* OR cannula* AND electrocardiogram* OR canula* AND electrocardiogram* OR

CVC AND electrocardiogram* OR CVCs AND electrocardiogram* OR PICC AND electrocardiogram* OR PICCs AND electrocardiogram* OR PIC line* AND electrocardiogram* OR central line* AND electrocardiogram* OR venous line* AND electrocardiogram*

2. No results were found for: catheter* AND cardiogram* OR cannula* AND cardiogram* OR canula* AND cardiogram* OR CVC AND cardiogram* OR CVCs AND cardiogram* OR PICC AND cardiogram* OR PICCs AND cardiogram* OR PIC line* AND cardiogram* OR central line* AND cardiogram* OR venous line* AND cardiogram*

3. 10 records for 10 trials found for: catheter* AND electrocardiograph* OR cannula* AND electrocardiograph* OR canula* AND electrocardiograph* OR CVC AND electrocardiograph* OR CVCs AND electrocardiograph* OR PICC AND electrocardiograph* OR PICCs AND electrocardiograph* OR PIC line* AND electrocardiograph* OR central line* AND electrocardiograph* OR venous line* AND electrocardiograph*

4. No results were found for: catheter* AND cardiograph* OR cannula* AND cardiograph* OR canula* AND cardiograph* OR CVC AND cardiograph* OR CVCs AND cardiograph* OR PICC AND cardiograph* OR PICCs AND cardiograph* OR PIC line* AND cardiograph* OR central line* AND cardiograph* OR venous line* AND cardiograph*

5. 27 records for 25 trials found for: catheter* AND ecg* OR cannula* AND ecg* OR canula* AND ecg* OR CVC AND ecg* OR CVCs AND ecg* OR PICC AND ecg* OR PICCs AND ecg* OR PIC line* AND ecg* OR central line* AND ecg* OR venous line* AND ecg*

6. 1 trial found for: catheter* AND ekg* OR cannula* AND ekg* OR canula* AND ekg* OR CVC AND ekg* OR CVCs AND ekg* OR PICC AND ekg* OR PICCs AND ekg* OR PIC line* AND ekg* OR central line* AND ekg* OR venous line* AND ekg*

7. 35 records for 35 trials found for: catheter* AND magnet* OR cannula* AND magnet* OR canula* AND magnet* OR CVC AND magnet* OR CVCs AND magnet* OR PICC AND magnet* OR PICCs AND magnet* OR PIC line* AND magnet* OR central line* AND magnet* OR venous line* AND magnet*

8. No results were found for: catheter* AND electromagnet* OR cannula* AND electromagnet* OR canula* AND electromagnet* OR CVC AND electromagnet* OR CVCs AND electromagnet* OR PICC AND electromagnet* OR PICCs AND electromagnet* OR PIC line* AND electromagnet* OR central line* AND electromagnet* OR venous line* AND electromagnet*

7. 20 records for 20 trials found for: catheter* AND real-time* OR cannula* AND real-time* OR canula* AND real-time* OR CVC AND real-time* OR CVCs AND real-time* OR PICC AND real-time* OR PICCs AND real-time* OR PIC line* AND real-time* OR central line* AND real-time* OR venous line* AND real-time*

8. No results were found for: catheter* AND realtime* OR cannula* AND realtime* OR canula* AND realtime* OR CVC AND realtime* OR CVCs AND realtime* OR PICC AND realtime* OR PICCs AND realtime* OR PIC line* AND realtime* OR central line* AND realtime* OR venous line* AND realtime*

9. 1 trial found for: catheter* AND malposition* OR cannula* AND malposition* OR canula* AND malposition* OR CVC AND malposition* OR CVCs AND malposition* OR PICC AND malposition* OR PICCs AND malposition* OR PIC line* AND malposition* OR central line* AND malposition* OR venous line* AND malposition*

10. 1 trial found for: catheter* AND mal-position* OR cannula* AND mal-position* OR canula* AND mal-position* OR CVC AND mal-position* OR CVCs AND mal-position* OR PICC AND mal-position* OR PICCs AND mal-position* OR PIC line* AND mal-position* OR central line* AND mal-position* OR venous line* AND mal-position*

11. 2 records for 2 trials found for: catheter* AND tips OR cannula* AND tips OR canula* AND tips OR CVC AND tips OR CVCs AND tips OR PICC AND tips OR PICCs AND tips OR PIC line* AND tips OR central line* AND tips OR venous line* AND tips

12. 16 records for 16 trials found for: catheter tip OR cannula tip OR canula tip OR cannulae tip OR canulae tip OR CVC tip OR CVCs tip OR PICC tip OR PICCs tip OR PIC line tip OR central line tip OR venous line tip OR catheters tip OR cannulas tip OR canulas tip OR PIC lines tip OR central lines tip OR venous lines tip

13. 5 records for 5 trials found for: 5 records for 5 trials found for: catheter* AND tip location* OR cannula* AND tip location* OR canula* AND tip location* OR CVC AND tip location* OR CVCs AND tip location* OR PICC AND tip location* OR PICCs AND tip location* OR PIC line* AND tip location* OR central line* AND tip location* OR venous line* AND tip location*

14. 2 records for 2 trials found for: catheter* AND tip placement* OR cannula* AND tip placement* OR canula* AND tip placement* OR CVC AND tip placement* OR CVCs AND tip placement* OR PICC AND tip placement* OR PICCs AND tip placement* OR PIC line* AND tip placement* OR central line* AND tip placement* OR venous line* AND tip placement*

15. 1 trial found for: catheter* AND tip AND cost* OR cannula* AND tip AND cost* OR canula* AND tip AND cost* OR CVC AND tip AND cost* OR CVCs AND tip AND cost* OR PICC AND tip AND cost* OR PICCs AND tip AND cost* OR PIC line* AND tip AND cost* OR central line* AND tip AND cost* OR venous line* AND tip AND cost*

16. No results were found for: catheter* AND tip* AND economic* OR cannula* AND tip* AND economic* OR canula* AND tip* AND economic* OR CVC AND tip* AND economic* OR CVCs AND tip* AND economic* OR PICC AND tip* AND economic* OR PICCs AND tip* AND economic* OR PIC line* AND tip* AND economic* OR central line* AND tip* AND economic* OR venous line* AND tip* AND economic*

17. No results were found for: catheter* AND TCS* OR cannula* AND TCS* OR canula* AND TCS* OR CVC AND TCS* OR CVCs AND TCS* OR PICC AND TCS* OR PICCs AND TCS* OR PIC line* AND TCS* OR central line* AND TCS* OR venous line* AND TCS*

18. 1 trial found for: catheter* AND TPS* OR cannula* AND TPS* OR canula* AND TPS* OR CVC AND TPS* OR CVCs AND TPS* OR PICC AND TPS*

OR PICCs AND TPS* OR PIC line* AND TPS* OR central line* AND TPS* OR venous line* AND TPS*

19. 9 records for 9 trials found for: sherlock* OR powerpicc*

A.10: Source: metaRegister of Controlled Trials (mRCT)

Interface / URL: http://www.controlled-trials.com/mrct/

Search date: 04/07/14

Retrieved records: 103

Search strategy:

All registers selected for search, apart from the NIH ClinicalTrials.gov Register (International) - subset of randomised trial records – searched directly via ClinicalTrials.gov (see above)

Following searches carried out separately:

catheter* AND cost* = 56

cannula* AND cost* = 6

canula* AND cost* = 0

CVC AND cost* = 5

CVC* AND cost* = 6

PICC* AND cost* = 4

"PIC line*" AND cost* = 0

"central line*" AND cost* = 3

"venous line*" AND cost* = 1

catheter* AND economic* = 15

cannula* AND economic* = 0

canula* AND economic* = 0

CVC* AND economic* = 3

PICC* AND economic* - 0

"PIC line*" AND economic* = 0

"central line*" AND economic* = 0

"venous line*" AND economic* = 1

catheter* AND price* = 1

cannula* AND price* = 0

canula* AND price* = 0

CVC* AND price* = 0

PICC* AND price* = 0

"PIC line*" AND price* = 0

"central line*" AND price* = 0

"venous line*" AND price* = 0

catheter* AND pharmacoeconomic* = 0

cannula* AND pharmacoeconomic* = 0

canula* AND pharmacoeconomic* = 0

CVC* AND pharmacoeconomic* = 0

PICC* AND pharmacoeconomic* = 0

"PIC line*" AND pharmacoeconomic* = 0

"central line*" AND pharmacoeconomic* = 0

"venous line*" AND pharmacoeconomic* = 0

catheter* AND expenditure* = 0

cannula* AND expenditure* = 0

canula* AND expenditure* = 0

CVC* AND expenditure* = 0

PICC* AND expenditure* = 0

"PIC line*" AND expenditure* = 0

"central line*" AND expenditure* = 0

"venous line*" AND expenditure* = 1

catheter* AND money* = 0

cannula* AND money* = 0

canula* AND money* = 0

CVC* AND money* = 0

PICC* AND money* = 0

"PIC line*" AND money* = 0

"central line*" AND money* = 0

"venous line*" AND money* = 0

catheter* AND budget* = 0

cannula* AND budget* = 1

canula* AND budget* = 0

CVC* AND budget* = 0

PICC* AND budget* = 0

"PIC line*" AND budget* = 0

"central line*" AND budget* = 0

"venous line*" AND budget* = 0

sherlock* OR powerpicc* = 0

A.11: Source: CEA (Cost-Effectiveness Analysis) Registry

Interface / URL: https://research.tufts-nemc.org/cear4/Home.aspx

Search date: 04/07/14

Retrieved records: 65

Search strategy:

Following searches carried out separately. Only results with a publication date of 2000 or later were downloaded:

Catheter = 41

Catheters = 7

Catheterise = 0

Catheterises = 0

Catheterisation = 0

Catheterisations = 0

Catheterised = 0

Catheterising = 0

Catheterize = 1

Catheterizes = 0

Catheterization = 11

Catheterizations = 1

Catheterized = 1

Catheterizing = 0

Cannula = 1

Cannulas = 0

Cannulae = 0

Cannulate = 1

Cannulated = 1

Cannualtes = 0

Cannulating = 0

Cannulation = 0

Canula = 0

Canulas = 0

Canulae = 0

Canulate = 0

Canulated = 0

Canualtes = 0

Canulating = 0

Canulation = 0

CVC = 0 (2 records returned – excluded as duplicates)

CVCs = 0 (1 record returned – excluded as duplicate)

PICC = 0

PICCs = 0

PIC line = 0

PIC lines = 0

central line = 0

central lines =0

venous line = 0

venous lines = 0

sherlock = 0

powerpicc = 0

11.3.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Additional methods used to identify ongoing and recently completed research included searching the websites of key conferences to identify conference abstracts for the last 3 years, searching the websites of relevant organisations, searching Google, and communication with BARD. Details are given below (sources A.12 – A.27).

Conference abstract search

Websites of the following conferences were searched to identify conference abstracts for the last 3 years. The conferences were identified through discussion between the research team. If abstracts were not found freely available online and could not be provided by the conference organiser, no further search was carried out.

A.12: Source: Association for Vascular Access (AVA) Annual Meeting

Interface / URL: see below

Search date: 10/07/14; 18/07/14

Retrieved records: 12

Search strategy:

2014: meeting to be held in September 2014.

2013: poster abstracts available at:
http://www.eventscribe.com/2013/posters/ava/home.asp?linkid=282068&navitemid=1146

Search function used. Searches on following terms carried out:

sherlock

powerpicc

sapiens

electrocard

cardiogram

cardiograph

ecg

ekg

magnet

malposition

mal-position

tip location

tip confirmation

tip position

Results were screened for potential relevance. 5 records were retrieved for consideration

2012 / 2011. Unable to locate poster abstracts online – contacted AVA to query 07/07/14. AVA confirmed that abstracts from 2012 and 2011 are not available online anywhere, and not available to be sent for viewing.

2012: Only program schedule available to search – includes abstracts for oral presentations and titles of posters.

https://www.avainfo.org/website/download.asp?id=281442

Ctrl-F searches on following terms carried out:

sherlock

powerpicc

sapiens

electrocard

cardiogram

cardiograph

ecg

ekg

magnet

malposition

mal-position

tip location

tip confirmation

tip position

Results were screened for potential relevance. 3 records were retrieved for consideration

2011: Only program schedule available to search – includes title information on oral abstracts for oral presentations, no information on posters.

https://www.avainfo.org/website/download.asp?id=280450

Ctrl-F searches on following terms carried out:

sherlock

powerpicc

sapiens

electrocard

cardiogram

cardiograph

ecg

ekg

magnet

malposition

mal-position

tip location

tip confirmation

tip position

Results were screened for potential relevance. 4 records were retrieved for consideration

A.13: Source: World Congress of Vascular Access (WoCoVA)

Interface / URL: see below

Search date: 08/07/14

Retrieved records: 5

Search strategy:

2014: 3rd. Berlin (June)

Searched via: http://www.vascular-access.info/article/wocova-2014-abstracts

Ctrl F searches carried out across the following pdf file to identify relevant studies: Download JVA_2014_3_193-239_JVA-D-14-

00120_ABSTRACTS_WoCoVA.pdf. Searches carried out for the following terms.

sherlock

powerpicc

sapiens

electrocard

cardiogram

cardiograph

ecg

ekg

magnet

malposition

mal-position

tip location

tip confirmation

tip position

Results were screened for potential relevance. 4 records were retrieved for consideration.

2012: 2nd. Amsterdam.

Searched via: http://www.vascular-access.info/article/abstracts-from-wocova-2nd-world-congress-on-vascular-access--amsterdam-the-netherlands--june-27-29-2012

Ctrl F searches carried out across the following pdf file to identify relevant studies: Download JVA_ABS_WOCoVA.pdf. Searches carried out for the following terms.

sherlock

powerpicc

sapiens

electrocard

cardiogram

cardiograph

ecg

ekg

magnet

malposition

mal-position

tip location

tip confirmation

tip position

Results were screened for potential relevance. 1 record was retrieved for consideration

A.14: Source: National Infusion and Vascular Access Society (NIVAS) Annual Conference

Interface / URL: See below

Search date: 10/07/14

Retrieved records: 1

Search strategy:

4th conference: 2013. Pdfs for speaker presentations located here: http://www.nivas.org.uk/conference – but only available to members.

3rd conference: 2012. Pdfs for speaker presentations located here: http://www.nivas.org.uk/conference/view/3rd-annual-nivas-conference – but only available to members. Scanned titles – 1 identified as potentially relevant. Title downloaded for further consideration.

2nd conference: 2011. Pdfs for speaker presentations located here: http://www.nivas.org.uk/conference/view/2nd-annual-nivas-conference – but only available to members. Scanned titles – 0 identified as potentially relevant.

NIVAS contacted to see if abstracts for poster or oral presentations are available to view online anywhere 10/07/14. No reply as of 18/07/14. Sent

follow-up e-mail 18/07/14. No reply as of 22/07/14. Sent follow-up e-mail 22/07/14. No reply as of 22/07/14.

A.15: Source: ISPOR (International Society for Pharmacoeconomics and Outcomes Research) Annual Congress

Interface / URL:
http://www.ispor.org/RESEARCH_STUDY_DIGEST/research_index.asp

Search date: 10/07/14

Retrieved records: 94

Search strategy:

Searched via the ISPOR Scientific Presentations Database:
http://www.ispor.org/RESEARCH_STUDY_DIGEST/research_index.asp

Following keyword searches carried out. Results from conferences held between 2011 and 2014 downloaded for further consideration.

catheter- abstract field selected = 83

cannula – abstract field selected = 2 (3 returned, 1 excluded as duplicate)

canula – abstract field selected = 0

CVC – abstract field selected = 1 (4 returned, 3 excluded as duplicates)

PICC – abstract field selected = 1

PIC line – abstract field selected = 0

central line – abstract field selected = 1 (3 returned, 2 excluded as duplicates)

venous line – abstract field selected =2

sherlock – abstract field selected = 0

powerpicc – abstract field selected = 0

catheter - title field selected = 4 (49 returned, 45 excluded as duplicates)

cannula – title field selected = 0 (1 returned, excluded as duplicate)

canula – title field selected = 0

CVC – title field selected = 0

PICC – title field selected = 0

PIC line – title field selected = 0

central line – title field selected = 0

venous line – title field selected = 0

sherlock – title field selected = 0

powerpicc – title field selected = 0

Website search: Organisations was identified from the list of those contacted for expert advice detailed in the draft scope document (NICE medical technology draft scope: SherLock 3CG Tip Confirmation System for placement of peripherally inserted central catheters). Pragmatic searches were carried out on the device name. Only results not already retrieved elsewhere were downloaded.

A.16: Source: Association of Surgeons in Primary Care

Interface / URL: http://www.aspc-uk.net/

Search date: 10/07/14

Retrieved records: 0

Search strategy:

Homepage site search function used. Following terms searched on separately. Returned results assessed for relevance.

sherlock

powerpicc

sapiens

A.17: Source: British Cardiovascular Intervention Society

Interface / URL: http://www.bcis.org.uk/pages/default.asp

Search date: 10/07/14

Retrieved records: 0

Search strategy:

Homepage search function used. Following terms searched on separately. Returned results assessed for relevance.

sherlock

powerpicc

sapiens

A.18: Source: British Cardiovascular Society

Interface / URL: http://www.bcs.com/pages/default.asp

Search date: 10/07/14

Retrieved records: 0

Search strategy:

Homepage search function used. Following terms searched on separately. Returned results assessed for relevance.

sherlock

powerpicc

sapiens

A.19: Source: Intensive Care Society

Interface / URL: http://www.ics.ac.uk/

Search date: 18/07/14

Retrieved records:

Search strategy:

Homepage search function used. Following terms searched on separately. Returned results assessed for relevance.

sherlock

powerpicc

sapiens

A.20: Source: The Royal College of Anaesthetists

Interface / URL: http://www.rcoa.ac.uk/

Search date: 18/07/14

Retrieved records: 0

Search strategy:

Homepage search function used. Following terms searched on separately. Returned results assessed for relevance.

sherlock

powerpicc

sapiens

A.21: Source: Royal College of Nursing

Interface / URL: http://www.rcn.org.uk/

Search date: 18/07/14

Retrieved records: 0

Search strategy:

Advanced search function used at: http://bureau-query.funnelback.co.uk/search/search.cgi?collection=rcn-meta&form=advanced.

Following search run using the 'Any of these terms' option. Returned results assessed for relevance.

sherlock powerpicc sapiens

A.22: Source: Royal College of Physicians

Interface / URL: https://www.rcplondon.ac.uk/

Search date: 18/07/14

Retrieved records: 0

Search strategy:

Homepage search function used. Following terms searched on separately. Returned results assessed for relevance.

sherlock

powerpicc

sapiens

A.23: Source: British Association of Critical Care Nurses

Interface / URL: http://www.baccn.org.uk/

Search date: 18/07/14

Retrieved records: 0

Search strategy:

Searched using the BACCN search at: http://baccn.org.uk.master.com/texis/master/search/mysite.html. Following terms searched on separately. Returned results assessed for relevance.

sherlock

powerpicc

sapiens

A.24: Source: Royal College of Radiologists

Interface / URL: http://www.rcr.ac.uk/

Search date: 18/07/14

Retrieved records:

Search strategy:

Homepage search function used. Following terms searched on separately. Returned results assessed for relevance.

sherlock

powerpicc

sapiens

A.25: Source: National Infusion and Vascular Access Society

Interface / URL: http://www.nivas.org.uk/

Search date: 18/07/14

Retrieved records: 0

Search strategy:

No site search function found. Searched using Google. In main search box searched: site:.nivas.org.uk with the following terms, separately e.g. site:.nivas.org.uk sherlock

site:.nivas.org.uk powerpicc

sherlock = 0

powerpicc = 0

sapiens = 0

electrocardiograph = 0

electrocardiography = 0

electrocardiogram = 0

electrocardiogramy = 0

cardiograph = 0

cardiography = 0

cardiogram = 0

cardiogramy = 0

ecg = 0

ekg = 0

magnet = 0

magnets = 0

magnetic = 0

magnetics = 0

magnetism = 0

electromagnet = 0

electromagnets = 0

electromagnetic = 0

electromagnetics = 0

electromagnetism = 0

malposition = 0

mal-position = 0

malpositioned = 0

mal-positioned = 0

malpositioning = 0

mal-positioning = 0

"tip location" = 0

"tip confirmation" = 0

"tip position" = 0

A.26: Source: Google

Interface / URL: https://www.google.com/

Search date: 18/07/14

Retrieved records: 0

Search strategy:

A focused, pragmatic search was conducted to identify relevant research. The 5 searches below were run separately.

For each search, the first 50 ‘most relevant’ returned results (five pages) were scanned for potentially relevant research studies. Relevance ranking was determined by the Google algorithm. Choice of items to view and selection for further consideration was based searcher judgement. Records were only retrieved if they had not already been found previously via another source.

sherlock catheter cost filetype:pdf

sherlock catheter costs filetype:pdf

sherlock catheter economic filetype:pdf

sherlock catheter economics filetype:pdf

sherlock catheter economical filetype:pdf

No additional records were retrieved.

A.27: Source: Communication within Bard

Date: 19/06/14

Retrieved records: 7

Discussions were undertaken within BARD to identify any known studies relevant to the cost-effectiveness review. None were identified.

All relevant studies sourced to date for the clinical effectiveness review were sourced. 7 records were included for consideration.

11.4 Appendix 4: Resource identification, measurement and valuation (section 9.3.2)

The following information should be provided.

11.4.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- NHS EED
- EconLIT.

The following databases were searched:

- MEDLINE and MEDLINE In-Process (via OvidSP)
- EMBASE (via OvidSP)
- Econlit (via OvidSP)
- NHS Economic Evaluation Database (via Cochrane Library/Wiley Interscience)
- Health Technology Assessment Database (via Cochrane Library/Wiley Interscience)
- Health Economic Evaluations Database (via EBSCOhost)

11.4.2 The date on which the search was conducted.

For search dates, see details of search strategies given in section 10.4.4 below.

11.4.3 The date span of the search.

No date restriction was applied to the search. Databases were searched from inception to date.

11.4.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

The database search strategies are detailed below (sources A.1 to A.6).

A.1: Source: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present

Interface / URL: OvidSP

Search date: 09/07/14

Retrieved records: 555

Search strategy:

1 Catheterization, Central Venous/ and peripheral$.ti,ab,kf. 1257

2 exp Catheterization, Peripheral/ and central$.ti,ab,kf. 1003

3 Central Venous Catheters/ and peripheral$.ti,ab,kf. 37

4 (peripheral$ adj5 central$ adj5 (catheter$ or cannula$ or canula$)).ti,ab,kf. 1037

5 (PICC or PICCs).ti,ab,kf. 627

6 (peripheral$ adj5 (CVC or CVCs)).ti,ab,kf. 76

7 (PIC adj3 line$).ti,ab,kf. 30

8 (peripheral$ adj5 central adj5 line$).ti,ab,kf. 246

9 (peripheral$ adj5 venous adj5 line$).ti,ab,kf. 92

10 or/1-9 2583

11 (malposition$ or mal-position$).ti,ab,kf. 4780

12 (place$ or placing or replace$ or replacing or misplace$ or misplacing or position$ or reposition$ or insert$ or reinsert$ or mov$ or remov$).ti,ab,kf. 2188847

13 or/11-12 2190894

14 Time Factors/ 1006790

15 (time or times or timed or timing or timings or duration$).ti,ab,kf. 2749395

16 (minute or minutes or min or mins).ti,ab,kf. 740306

17 or/14-16 3833718

18 10 and 13 and 17 669

19 exp animals/ not humans/ 3964780

20 (news or comment or editorial or letter).pt. 1496892

21 18 not (19 or 20) 642

22 limit 21 to english language 573

23 remove duplicates from 22 555

A.2: Source: Embase 1974 to 2014 July 08

Interface / URL: OvidSP

Search date: 09/07/14

Retrieved records: 574

Search strategy:

1 peripherally inserted central venous catheter/ 1062

2 central venous catheterization/ and peripheral$.ti,ab,kw. 665

3 catheterization/ and peripheral$.ti,ab,kw. 1472

4 central venous catheter/ and peripheral$.ti,ab,kw. 1191

5 (peripheral$ adj5 central$ adj5 (catheter$ or cannula$ or canula$)).ti,ab,kw. 1645

6 (PICC or PICCs).ti,ab,kw. 1325

7 (peripheral$ adj5 (CVC or CVCs)).ti,ab,kw. 130

8 (PIC adj3 line$).ti,ab,kw. 35

9 (peripheral$ adj5 central adj5 line$).ti,ab,kw. 364

10 (peripheral$ adj5 venous adj5 line$).ti,ab,kw. 133

11 or/1-10 4787

12 positioning device/ 91

13 (malposition$ or mal-position$).ti,ab,kw. 5947

14 (place$ or placing or replace$ or replacing or misplace$ or misplacing or position$ or reposition$ or insert$ or reinsert$ or mov$ or remov$).ti,ab,kw. 2594193

15 or/12-14 2596625

16 time/ 367892

17 (time or times or timed or timing or timings or duration$).ti,ab,kw. 3409905

18 (minute or minutes or min or mins).ti,ab,kw. 923104

19 or/16-18 4179398

20 11 and 15 and 19 1176

21 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ 4960910

22 (editorial or conference$ or letter).pt. 3541634

23 20 not (21 or 22) 677

24 limit 23 to english language 582

25 remove duplicates from 24 574

A.3: Source: Econlit 1886 to June 2014

Interface / URL: OvidSP

Search date: 09/07/14

Retrieved records:

Search strategy:

1 (peripheral$ and (catheter$ or cannula$ or canula$)).af. 0

2 (PICC or PICCs).af. 1

3 (PIC adj3 line$).af. 1

4 (peripheral$ adj5 central adj5 line$).af. 1

5 (peripheral$ adj5 venous adj5 line$).af. 0

6 or/1-5 3

A.4: Source: NHS Economic Evaluation Database (NHS EED) - Issue 2 of 4, April 2014

Interface / URL: Cochrane Library / Wiley Interscience

Search date: 10/07/14

Retrieved records: 20

Search strategy:

#1 [mh ^"Catheterization, Central Venous"] and peripheral* 151

#2 [mh "Catheterization, Peripheral"] and central* 661

#3 [mh ^"Central Venous Catheters"] and peripheral* 7

#4 (peripheral* near/5 central* near/5 (catheter* or cannula* or canula*)) 198

#5 (PICC or PICCs) 87

#6 (peripheral* near/5 (CVC or CVCs)) 22

#7 (PIC near/3 line*) 3

#8 (peripheral* near/5 central near/5 line*) 28

#9 (peripheral* near/5 venous near/5 line*) 20

#10 {or #1-#9} in Economic Evaluations 20

A.5: Source: Health Technology Assessment Database (HTA) - Issue 2 of 4, April 2014

Interface / URL: Cochrane Library / Wiley Interscience

Search date: 10/07/14

Retrieved records: 9

Search strategy:

#1	[mh ^"Catheterization, Central Venous"] and peripheral*	151
#2	[mh "Catheterization, Peripheral"] and central*	661
#3	[mh ^"Central Venous Catheters"] and peripheral*	7
#4	(peripheral* near/5 central* near/5 (catheter* or cannula* or canula*))	198
#5	(PICC or PICCs)	87
#6	(peripheral* near/5 (CVC or CVCs))	22
#7	(PIC near/3 line*)	3
#8	(peripheral* near/5 central near/5 line*)	28
#9	(peripheral* near/5 venous near/5 line*)	20
#10	{or #1-#9} in Technology Assessments	9

A.6: Source: HEED: Health Economic Evaluations Database

Interface / URL: EBSCOHost

Search date: 10/07/14

Retrieved records:

Search strategy:

S7	S1 OR S2 OR S3 OR S4 OR S5 OR S6	20
S6	TX(peripheral* N5 venous N5 line*)	2
S5	TX(peripheral* N5 central N5 line*)	2
S4	TX(PIC N3 line*)	1
S3	TX(peripheral* N5 (CVC OR CVCs))	2
S2	TX(PICC OR PICCs)	11
S1	TX(peripheral* N5 central* N5 (catheter* OR cannula* OR canula*))	14

11.4.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

No additional searches were carried out.

11.4.6 The inclusion and exclusion criteria.

The inclusion and exclusion criteria are listed in section 9.3.3.

11.4.7 The data abstraction strategy.

The data extraction is shown in Table C5b.

12 Related procedures for evidence submission

12.1 Cost models

An electronic executable version of the cost model should be submitted to NICE with the full submission.

NICE accepts executable cost models using standard software – that is, Excel, TreeAge Pro, R or WinBUGs. If you plan to submit a model in a non-standard package, NICE should be informed in advance. NICE, in association with the External Assessment Centre, will investigate whether the requested software is acceptable, and establish if you need to provide NICE and the External Assessment Centre with temporary licences for the non-standard software for the duration of the assessment. NICE reserves the right to reject cost models in non-standard software. A fully executable electronic copy of the model must be submitted to NICE with full access to the programming code. Care should be taken to ensure that the submitted versions of the model programme and the written content of the evidence submission match.

NICE may distribute the executable version of the cost model to a consultee if they request it. If a request is received, NICE will release the model as long as it does not contain information that was designated confidential by the model owner, or the confidential material can be redacted by the model owner without producing severe limitations on the functionality of the model. The consultee will be advised that the model is protected by intellectual property rights, and can be used only for the purposes of commenting on the model's reliability and informing comments on the medical technology consultation document.

Sponsors must ensure that all relevant material pertinent to the decision problem has been disclosed to NICE at the time of submission. NICE may request additional information not submitted in the original submission of evidence. Any other information will be accepted at NICE's discretion.

When making a full submission, sponsors should check that:

- an electronic copy of the submission has been given to NICE with all confidential information highlighted and underlined
- a copy of the instructions for use, regulatory documentation and quality systems certificate have been submitted
- an executable electronic copy of the cost model has been submitted
- the checklist of confidential information provided by NICE has been completed and submitted.

- A PDF version of all studies (or other appropriate format for unpublished data, for example, a structured abstract) included in the submission have been submitted

12.2 Disclosure of information

To ensure that the assessment process is as transparent as possible, NICE considers it highly desirable that evidence pivotal to the Medical Technologies Advisory Committee's decisions should be publicly available at the point of issuing the medical technology consultation document and medical technology guidance.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence').

When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly, and to provide reasons why they are confidential and the timescale within which they will remain confidential. The checklist of confidential information should be completed: if it is not provided, NICE will assume that there is no confidential information in the submission. It is the responsibility of the manufacturer or sponsor to ensure that the confidential information checklist is kept up to date.

It is the responsibility of the sponsor to ensure that any confidential information in their evidence submission is clearly underlined and highlighted

correctly. NICE is assured that information marked ‘academic in confidence’ can be presented and discussed during the public part of the Medical Technologies Advisory Committee meeting. NICE is confident that such public presentation does not affect the subsequent publication of the information, which is the prerequisite allowing for the marking of information as ‘academic in confidence’.

Please therefore underline all confidential information, and highlight information that is submitted under ‘commercial in confidence’ in blue and information submitted under ‘academic in confidence’ in yellow.

NICE will ask sponsors to reconsider restrictions on the release of data if there appears to be no obvious reason for the restrictions, or if such restrictions would make it difficult or impossible for NICE to show the evidential basis for its guidance. Information that has been put into the public domain, anywhere in the world, cannot be marked as confidential.

Confidential information submitted will be made available for review by the External Assessment Centre and the Medical Technologies Advisory Committee. NICE will at all times seek to protect the confidentiality of the information submitted, but nothing will restrict the disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

The Freedom of Information Act 2000, which came into force on 1 January 2005, enables any person to obtain information from public authorities such as NICE. The Act obliges NICE to respond to requests about the recorded information it holds, and it gives people a right of access to that information. This obligation extends to submissions made to NICE. Information that is designated as ‘commercial in confidence’ may be exempt under the Act. On receipt of a request for information, the NICE secretariat will make every effort to contact the designated company representative to confirm the status of any information previously deemed ‘commercial in confidence’ before making any decision on disclosure.

12.3 Equality

NICE is committed to promoting equality and eliminating unlawful discrimination, including paying particular attention to groups protected by equalities legislation. The scoping process is designed to identify groups who are relevant to the evaluation of the technology, and to reflect the diversity of the population. NICE consults on whether there are any issues relevant to equalities within the scope of the evaluation, or if there is information that could be included in the evidence presented to the Medical Technologies Advisory Committee to enable them to take account of equalities issues when developing guidance.

Evidence submitters are asked to consider whether the chosen decision problem could be impacted by NICE's responsibility in this respect, including when considering subgroups and access to recommendations that use a clinical or biological criterion.

For further information, please see the NICE website (www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp).