External Assessment Centre report

The purpose of the External Assessment Centre (EAC) report is to review and critically evaluate the sponsor's clinical and economic evidence and may include additional analysis of the submitted evidence or new clinical and/or economic evidence.

Title: The SecurAcath device for securing percutaneous catheters

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Date completed: 05/09/2016

Declared interests of the authors

Description of any pecuniary relationship with sponsors, both personal and of the EAC. Please refer to NICE's Code of Practice for declaring and dealing with conflicts of interests.
http://www.nice.org.uk/niceMedia/pdf/Guidanceondeclarationsofinterest.pdf

None

Acknowledgements

The authors would like to thank the following expert advisers who were appointed by NICE and provided advice about the dressings used at intravascular access sites to complement the clinical and economic evidence:

- Lisa Dougherty, Nurse Consultant, Intravenous Therapy, Nursing, Rehabilitation & Quality Assurance, The Royal Marsden NHS Foundation Trust
- Meinir Hughes, Intravenous Access Nurse Specialist, Velindre Cancer Centre
- Dympna McParlan, Infusional Services Coordinator, Belfast Health and Social Care Trust
- Jackie Nicholson, Consultant Nurse in Vascular Access, National Infusion and Vascular Access Society
- Liz Simcock, Clinical Nurse Specialist, Royal College of Nursing

Rider on responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

Contents

1 Summary

Scope of the sponsor's submission

This report assesses the submission to NICE by the manufacturer (Interrad Medical, inc) supporting the use of SecurAcath for the securement of catheters in people who require an intravascular catheter for central venous access. Four subgroups were defined in the scope: people who receive a peripherally inserted central venous catheter (PICC), people who receive a centrally inserted central venous catheter (CICC), people with co-morbidities, children and young people, and people with a medium to long dwell time. The sponsor did not specifically refer to these subgroups in their submission.

For the intervention, the company included evidence related to all versions of SecurAcath. From the information provided by the manufacturer, the EAC concluded that the design differences between the different versions could potentially have an impact on pain during removal and time taken to remove the device but not to the remaining clinical outcomes.

The sponsor submitted clinical and economic evidence related to SecurAcath and 1 of the comparators listed in the scope. The sponsor mainly included studies with poorly defined populations. Although these fell within the broad scope of this assessment report, it is difficult to assess the suitability of the submitted studies to support the assumption included in the sponsor's cost analysis that the technology is likely to be predominantly used in older, critically ill patients, who are likely to have a number of co-morbidities and in patients following major trauma, or those with conditions requiring long-term ongoing therapy such as cancer. In these individuals, catheter often need to remain in place for long periods of time. With the exception of one RCT study (Janssens 2016) there is a lack of comparative data for the intervention. A small number of studies included descriptive comparisons of SecurAcath with historical cohorts using mostly unidentified comparators.

The cost analysis submitted by the sponsor assessed the impact of SecurAcath and its two main comparators in the patient population as

specified by the scope. However, the EAC identified issues related to the model structure and specific assumptions used in the model.

Summary of clinical evidence submitted by the sponsor

The EAC reviewed all of the sponsor-submitted evidence. Clinical evidence was provided for the intended intervention and 1 of the comparators specified in the scope. The sponsor provided clinical outcome evidence based on 20 publications, 4 of these were either commentaries or narrative reviews and 16 were primary studies (the majority published as conference abstracts). Four of the primary studies were excluded by the EAC as they either investigated the intervention in combination with other interventions or they had a small sample size based on our exclusion criteria. All narrative reviews and commentaries were excluded by the EAC. One unpublished (Anonymous 2015) and 11 published studies met the scope and were accepted by the EAC. One of the submitted conference abstracts (Janssens 2016a) was subsequently updated with an unpublished full-text manuscript (Janssens 2016b) after communication by the EAC with the corresponding author.

With the exception of 1 RCT (Janssens 2016b) the rest of the studies are observational cohorts conducted retrospectively or prospectively as part of audits prior to or after the implementation of SecurAcath for clinical use. Only the RCT directly compared SecurAcath with 1 of the comparators (StatLock). Eight studies compared SecurAcath with historical controls, however, in the majority of studies the comparator is not specified. No single study compared the intervention with all the comparators. The studies were carried out on adult inpatient populations. Only 3 studies included a paediatric population.

Summary critique of clinical evidence submitted by the sponsor

The sponsor included the majority of relevant evidence on SecurAcath. However, the sponsor did not perform a full methodological quality assessment of the evidence. In their submission, the sponsor argued that

regardless of the design methodology used, and whilst the data presented may not have been submitted for peer reviewed publication, all observational prospective clinical evaluations resulted in clinicians adopting the device and incorporating it into their routine clinical practice. The EAC notes, however, that the majority of the sponsor's submitted evidence consisted of conference abstracts, some published as early as 2012. These abstracts never resulted in full-text publications, potentially reflecting poor methodological quality and also the possibility of publication bias. Hence the sponsor's interpretation of the available clinical evidence does not provide a fair assessment of the studies submitted.

Of the 16 primary studies provided by the sponsor, 12 fitted the required scope in terms of population and outcome measures. The sponsor mainly included studies with poorly defined populations. Although these fell within the broad scope of this assessment report, it is difficult to assess the suitability of the submitted studies to support the assumption included in sponsor's cost analysis that the technology is likely to be predominantly used in patient populations with specific characteristic such as older patients with co-morbidities. In addition, it is not possible to assess the effectiveness and safety of the technology in the subgroups specified in the scope.

Based on the EAC's methodological quality assessment, the unpublished RCT was of medium to high quality, however, the primary outcome of a difference in dressing change times is outside the scope. It is unclear if the study was sufficiently powered to detect differences for the secondary outcomes such as migration that are of interest and included in the economic model. The study is effectively focused on its primary endpoint and the authors address the need for separate research into migration, dislodgement and catheter-related blood stream infections (CRBSIs).

Summary of economic evidence submitted by the sponsor

The sponsor submitted the results of a search strategy aimed at finding economic evidence relevant to the scope. The sponsor included 3 papers in their final review. However, after conducting its own literature review the EAC excluded these studies because they did not match the population specified in the scope. The EAC concluded that there is no economic evidence - costing studies or economic evaluations – that is directly relevant to the scope.

The sponsor submitted a very simple decision analysis that involved multiplying the probability of an event by an average cost and summing across events. The events were a lack of complications, migration, malposition, occlusion, CRSBI and CRT. The models compared SecurAcath with an adhesive device (StatLock) for securement of PICC lines (25-day dwell time) and SecurAcath with sutures for the securement of CVC lines (3-day dwell time). The submission estimates a saving of £41 with the use of SecurAcath compared with an adhesive device. The submission estimates a saving of £1006 with the use of SecurAcath compared with sutures. These results are robust to single-way and multi-way deterministic sensitivity analyses. Despite the small sample sizes of studies used to calculate model inputs, no probabilistic sensitivity analysis was undertaken.

Summary critique of economic evidence submitted by the sponsor

The EAC was reasonably satisfied with the structure of the decision analysis, because of the limited clinical literature that is relevant to the scope. The EAC did not believe that the treatment comparisons made were exhaustive enough to fit the scope. The EAC considered the assumptions on fixed dwell times to be acceptable, particularly because they are conservative with respect to how cost-saving SecurAcath can be. The EAC decided that the clinical events included in the model required amendment – in particular, malposition should be replaced with dislodgement. In general, the choice of values for parameter inputs into the model was not justified in a transparent fashion. The EAC considered the deterministic sensitivity analysis to be too selective and so

insufficient in scope. The EAC believes that given the small amount of relevant clinical literature (of low quality) at least some probabilistic sensitivity analyses should be undertaken to measure parameter uncertainty.

The EAC found the model shell used by the sponsor difficult to follow and so rebuilt the model in a separate Excel workbook. The EAC decided to keep the general structure of the submission, but make adaptations to the following features: comparator arms, choice of modelled clinical events, dwell times, deterministic sensitivity analysis. The EAC conducted a probabilistic sensitivity analysis for key scenarios.

External Assessment Centre commentary on the robustness of evidence submitted by the sponsor

There is a lack of direct comparative data for the intervention and its comparators. The most relevant evidence to the decision problem is the unpublished RCT results. Janssens (2016b) showed that [redacted]

The EAC's meta-analysis supports the findings of the RCT. With the exception of dislodgment, the 95% confidence intervals (CIs) for migration, total catheter-related infections and CRBSIs are similar between SecurAcath and StatLock. The majority of the observational studies report higher pain scores during device removal in comparison with device placement and in-situ. The most relevant study for UK practice reporting pain scores (Hughes

2014) states that device removal caused the most dissatisfaction among staff and patients were complaining of pain or discomfort.

Comparative evidence and the EAC's meta-analysis of non-comparative evidence suggests that SecurAcath and StatLock are superior to sutures for catheter migration, dislodgment, total catheter-related infections and CRBSIs. However, it should be noted that this evidence is from study populations requiring PICC lines for which currently sutures are not standard of practice.

As a result of the above, the EAC concludes that there is insufficient evidence to suggest that SecurAcath is clinically superior in effectiveness and adverse events to StatLock. There is some evidence to suggest that SecurAcath is non-inferior in effectiveness and side effects to StatLock.

There is some evidence to suggest that both SecurAcath and StatLock are superior to sutures, however, this evidence is from a population requiring PICC lines which is not relevant to clinical practice (as sutures are not typically used to secure PICCs).

There is insufficient information to compare the effectiveness and safety of SecurAcath with its comparators in terms of the subgroups specified in the scope.

Summary of any additional work carried out by the External Assessment Centre

For the clinical evidence, the EAC designed and performed an independent systematic review to ensure that all available evidence had been considered. In addition to literature related to the intervention the EAC expanded the search to include evidence related to the comparators as specified in the scope. In addition, the EAC reviewed all the studies included by the sponsor.

The searches resulted in the retrieval of additional relevant evidence. Specifically, 2 studies (Sansivero 2011, McParlan 2016) on SecurAcath and 6

studies with the comparators were identified. In addition, the EAC contacted the authors of the RCT published currently as a conference abstract (Janssens 2016a) and obtained an academic in confidence copy of the full text (Janssens 2016b) unpublished report (total number of EAC identified studies = 9). The EAC used subsequently 8 of the retrieved studies (the McParlan 2016 retrieved by the EAC was in addition submitted by the manufacturer) and 8 of the studies accepted from the sponsor's submission to perform its own meta-analysis to provide pooled estimates for clinical outcomes between SecurAcath and its comparators (total number of studies included in the meta-analysis = 16). The results of the meta-analysis also contributed to the revised economic model.

The EAC critically appraised all studies included in the sponsor's submission and the ones retrieved by its own systematic review.

2 Background

2.1 Overview and critique of sponsor's description of clinical context

2.1.1. Critique of sponsor's description of background condition

The sponsor provided a brief overview of the range of indications and the prevalence of central venous catheter usage in the UK. Although the sponsor provided a list of the possible indications for central venous catheterisation, no detailed information was provided on the procedure or the population, and there were no objective definitions of the outcomes under considerations. The outcomes and definitions are particularly important as they can affect the measurements reported by the studies and ultimately introduce bias to the results. The EAC has provided a more comprehensive and up to date description of the condition, population and outcomes in the sections below.

2.1.2. EAC's overview of the procedure, population and outcomes (complications)

Procedure

A central venous catheter (CVC), is a long, thin, flexible tube used to provide intravenous access to the proximal third of the superior vena cava (SVC), the right atrium of the heart, or the inferior vena cava. Central venous access can be achieved using various puncture sites but the most common are the internal jugular vein (IJV), the subclavian vein (SV), the femoral vein (FV), and the upper limb veins (the latter using peripherally inserted central catheters, PICCs). The choice of access route depends on multiple factors including the reason for CVC insertion, the anticipated duration of access, the intact venous sites available and the skills of the operator (NICE TA49).

There are various different types of CVC but in all cases, the tip of the catheter floats freely within the bloodstream in a large vein and parallel to the vein wall. Compared with less invasive conventional peripheral intravenous catheters (where veins are typically accessed in the hand or arm) and midline catheters (accessed via the antecubital or other upper arm vein) in which the catheter tips do not reach central veins, with CVCs the blood flow within the catheter is maximised, and physical and chemical damage to the internal walls of the vein are minimised (Cheung, 2009). A CVC can also remain in situ for longer than a peripheral intravenous catheter, which gives medicines into a vein near the skin surface. CVCs can differ in length, internal diameter, and number of access ports. Typically, the material they are made of is silicon or polyurethane. The Royal Marsden Manual for Clinical Nursing Procedures (Dougherty et al. 2015) categorises CVCs into the 4 following types[1]:

- Short term percutaneous (non-tunnelled) catheters: CVCs that are placed into a large vein near the neck, chest, or groin (the jugular, subclavian or femoral veins respectively). The catheter is fixed in place at the site of insertion. Ease of insertion and removal makes this more useful for short term access when peripheral venous access is impractical or in acute, urgent situations. Non-tunnelled catheters are indicated for short-term use (up to 7 – 10 days).
- Skin-tunnelled catheters: CVCs that are passed under the skin from the insertion site to a separate exit site. Passing the catheter under the skin helps to prevent infection and provides stability. Tunnelled catheters are recommended for patients in whom long-term (>30 days) central venous access is necessary (Pratt et al., 2001), for example if people require repeated administration of chemotherapy, parenteral feeding and blood products. Skin-tunnelled CVCs are often referred to as Hickman lines.

[1] Central venous catheters include both centrally inserted CVCs and peripherally inserted CVCs. NICE TA49 also states that PICCs or ports can be considered types of CVCs. However, the literature often uses the term CVCs to solely describe centrally inserted CVCs. CVCs inserted via the jugular, subclavian or femoral veins (including short term percutaneous [non-tunnelled] catheters and skin tunnelled catheters) will be referred to in this document as centrally inserted central catheters (CICCs) to distinguish them from PICCs.

- PICC: CVCs inserted into a peripheral vein in the arm (via the basilic or cephalic veins) rather than a vein in the neck or chest. The use of PICCs is decided on the basis of indication and treatment duration. PICCs may be used for short term access (7 to 10 days) but are more typically used in people requiring several weeks or months of intravenous access. They are used equally in inpatient and outpatient settings.
- Implanted ports: CVCs placed entirely under the skin which are used for long term therapies. Ports are beneficial for their portability, relatively few mechanical complications compared to their length of use, and have minimal risk of infection.

Bishop et al. (2007) also describes apheresis/dialysis catheters (tunnelled and non-tunnelled) as a category of CVC. These are large bore CVCs for short or long term use with high blood flow rates. The procedure for insertion or removal is the same as with tunnelled and non-tunnelled CVCs via internal jugular or femoral routes.

Before CVC insertion, a patient should undergo physical assessment, vein assessment, and the history of previous CVCs should be recorded. Pre-existing haemorrhagic, thrombotic or infective problems must be effectively managed before catheter insertion. Anticoagulants are not typically administered unless there is a pre-existing condition related to thrombosis. Rigorous skin cleansing with a chlorhexidine gluconate 2% in alcohol or aqueous solution should be carried out prior to catheter insertion. Catheters are normally inserted under local anaesthesia, with or without sedation.

Ultrasound guided insertion is typically used for all CVC routes. The use of ultrasound is particularly recommended for the insertion of PICC when the peripheral veins are not visible or palpable. The appropriate vein is located using an ultrasound device and a hollow needle is advanced through the skin until blood is aspirated. The line is then inserted using the Seldinger technique: a blunt guidewire is passed through the needle, then the needle is

removed. The CVC itself is then passed over the guidewire, which is then removed.

Once in position, the CVC may be held in place by specialised adhesive devices (such as StatLock), subcutaneous securement devices (SecurAcath), sutures, surgical tape or steri-strips. Use of a securement device helps to prevent the catheter from being unintentionally dislodged which may lead to complications requiring premature removal. For skin-tunnelled and non-tunnelled CVCs, sutures are typically used in UK practice to secure the line. In skin tunnelled catheters, sutures are removed after the skin's fibroblastic response (skin granulation) is adequate to secure the catheter in place (around 2-4 weeks). For PICCs, the catheter is typically held in place by an adhesive dressing (such as StatLock) which is covered by a sterile dressing. Sutures or staples may be used in people who are at higher risk of catheter dislodgement (such as young children).

Catheter tip placement should be checked prior to use. Optimum tip position is in the lower third of the SVC or the cavoatrial junction or within the inferior vena cava above the level of the diaphragm (Gorski et al. 2016, Dougherty 2010, Dougherty et al. 2015). Typically, plain radiographs are used to confirm catheter position within the chest and to detect pneumothorax, haemothorax, or effusions after CVC placement Gibson and Bodenham (2013). Ultrasound may be used to aid insertion of a CVC, but is of limited value for confirming tip position in the SVC (because the SVC lies further inside the body it cannot be visualised adequately with ultrasound). ECG technology may also be used to confirm position.

Dressings should be changed weekly if there is no sign of bleeding or infection. Dressings and any adhesive securement devices are removed and discarded and the insertion site is then cleaned thoroughly with chlorhexidine gluconate 2% in alcohol or aqueous solution. Adhesive securement devices will also be removed and discarded (unless manufacturer instructions for use state otherwise). Unless there is an indication of device malfunction or insertion site infection, subcutaneous securement devices (such as sutures)

do not need to be removed. The catheter may be held in place manually while cleaning is carried out, or surgical tape may be used. The catheter is flushed with saline solution after each access or on a weekly basis to maintain catheter patency. There is insufficient evidence to recommend antimicrobial lock solutions (Heparin 10 units/ml or 0.9% sodium chloride) therefore standardised solutions should be determined for each population organisation wide (Gorski et al. 2016, Royal College of Nursing 2016). Fresh adhesive securement devices are applied (as per the instructions for use specified by the manufacturer) and the insertion site is then redressed.

Length of dwell for catheters is dependent on the needs of the patient. There is variation in the literature regarding the categorisation of indwell times. For example, Bishop et al. (2007) defines short term catheterisation as <10 days in situ, and long term as >30 days in situ. Chopra et al. (2015) categorise duration of PICC insertions as ≤5 days, 6 to 14 days, 15 to 30 days, and ≥31 days). For dwell times in parenteral nutrition, Singer et al (2009) define medium term dwell as < 3 months and long term as > 3 months.

Unless complications requiring removal arise, CVCs are removed at the end of treatment. Removal of a skin-tunnelled catheter requires local anaesthetic and minor surgical cut-down to remove the cuff if the catheter has been in situ for more than approximately 3 weeks. The patient should lie down to avoid air embolus. Simple traction can remove the catheter and cuff in catheters which have been in place for less than 3 weeks. Ports require surgical removal in theatre or equivalent. PICCs and short term, non-tunnelled catheters can be removed at the patient's bedside and pressure applied. CVC tips should be sent for microscopy and culture if clinically indicated.

CVC removal before completion of the intended treatment, which may occur as a result of complications such as dislodgment, infection, phlebitis or thrombosis is categorised as unplanned removal. The decision to remove or salvage the catheter depends on the clinical condition of a patient, continued need for the CVC, any pathogen involved and response to treatment. In the case of catheter migration, whether a catheter is reinserted or a new catheter

is put in depends on how far the catheter has migrated. If a minor migration has occurred, the line can be salvaged. A malpositioned CVC is managed depending on the location of the CVC, the continued need for infusion therapy and the patient's acuity. Infusion through a malpositioned CVC should be withheld until proper tip position has been established. A catheter which has migrated externally should not be re-advanced prior to re-stabilisation. If the CVC becomes dislodged, for example when the tip moves further out than the SCV, there is a higher risk of thromboembolism and appropriate management may require CVC exchange or removal and insertion at a new site (Gorski et al. 2016). Catheter related blood stream infections (CRBSIs) often require catheter removal for effective treatment. However, in some patients, who have a continued need for an intravenous catheter, and in whom there are limited options for future lines, catheter salvage may be attempted (Snaterse et al. 2010, Gorski et al. 2016). The decision to salvage or remove a catheter should be made following discussion with the microbiologist and after consideration of the patient's clinical status and position on the treatment pathway (Bishop et al. 2007).

NICE TA49 states that CVCs are inserted in a wide range of clinical settings by a diverse group of clinicians including radiologists, anaesthetists, nephrologists, oncologists, surgeons, general physicians and paediatricians. Bishop et al. (2007) states that it is essential that only experienced personnel insert CVCs to minimise infections and other complications. In the USA and in the UK, nurse specialists (usually band 6 or 7 in the NHS) typically undertake CVC procedures. The range of settings in which CVCs are inserted includes operating theatres, emergency rooms, nephrology, oncology and other wards, radiology departments, intensive therapy units (ITUs) and high dependency units (HDUs). CVC insertion procedures are carried out in a hospital under surgical asepsis. PICCs and short term non-tunnelled CVCs may be inserted at the patient bedside. Once secured, CVCs can be used in the inpatient setting, outpatient setting or at home.

Population

CVCs are used in a heterogeneous range of indications where venous access is required for either long-term or a short-term care. Indications for CVCs include the following (adapted from Smith et al. [2013]):

- Access for drugs and nutrition
  - Infusion of irritant drugs—for example, chemotherapy
  - Total parenteral nutrition
  - Poor peripheral access
  - Long term administration of drugs, such as antibiotics
- Access for extracorporeal blood circuits
  - Renal replacement therapy
  - Plasma exchange
  - Extracorporeal membrane oxygenation
- Monitoring or interventions
  - Central venous pressure
  - Central venous blood oxygen saturation
  - Pulmonary artery pressure
  - Temporary transvenous pacing
  - Targeted temperature management
  - Repeated blood sampling

CVCs may be required for patients undergoing treatment requiring long term intravenous fluids or medications, cancer treatment, dialysis, coronary or other major surgery, and for those admitted to ITUs, HDUs or accident and emergency departments.

The exact number of annual CVC procedures carried out within the last 20 years was not found in the literature. Smith et al. (2013) and Gibson and Bodenham (2013) refer to a study that found an estimated 200,000 central venous catheters were inserted in the UK in 1994 (Waghorn, 1994). The authors note that the more recent number is likely to be higher.

Hospital episode statistics (HES) data indicate that there were 258,956 critical care episodes in 2014-15. About half of critical care records (51.1 %, 132,295 records) finished one or two calendar days after they started. After a consultation with experts, NICE MTG25 estimates that 95% of critical care episodes require CVC. Therefore, the annual number of critical care episodes requiring CVC may range approximately between 125,680 and 246,008.

CVCs are also widely used in the treatment of chronic conditions, such as cancer. The National Audit Office (2015) suggested that 130,000 cancer patients received chemotherapy in 2013-2014 in all settings (hospital admissions, outpatient attendances and community care). Typically, peripheral intravenous catheters are used, but PICC lines may be used in patients with poor vasculature. Patients with bowel diseases may also require CVC insertion due to the nature of their disease and feeding requirements. Patient preference and tumour/ disease grading may also be considered when decided on vascular access device.

Outcomes (complications) associated with CVCs

CVC complications can be related to insertion, indwelling, or extraction and may be immediate (typically relating to insertion or extraction) or delayed (typically related to indwelling) (Jabeen et al. 2014). Delayed complications which can be associated with unsecured or poorly secured catheters include catheter migration or dislodgement, infection, thrombosis, and phlebitis. The literature suggests CVC use may have complication rates of 1–26% (Nolan and Smith 2013).

Complications can be caused by pre-existing conditions and comorbidities in the patient. For example, if a patient is thrombocytopenic, RCN standards recommend “prompt immediate treatment to arrest bleeding /minimise blood loss. Treatment will depend on cause and site of bleeding” (Royal College of Nursing 2016). In patients with disseminated intravascular coagulation (associated with forms of leukaemia, for example) there should be vigorous correction of any abnormality of coagulation, for example with orally or

intravenously administered phytomenadione. Haemophiliac patients will require appropriate factor replacement as will patients with other coagulopathies. Infection at the time of catheter insertion, for example if a patient is methicillin-resistant staphylococcus aureus (MRSA) positive or has septicaemia, may contraindicate placement of a CVC (Bishop et al. 2007).

Catheter migration is defined as accidental movement greater than 0.5 cm without loss of function, even if the catheter tip is no longer in a central position, whereas accidental removal or movement that resulted in the loss of function is defined as catheter dislodgment (Yamamoto et al. 2002). One randomised controlled trial (RCT) involving 170 adults found PICC migration rates of 11% (9 of 85 people) for sutures and 6% (5 of 85 people) for StatLock. (Yamamoto et al. 2002). Migration did not result in loss of function. The same study found a PICC dislodgement incidence rate of 4.1 (sutures) and 3.6 (StatLock) per 1000 catheter days. Dislodgement resulted in the PICC ceasing to function. CVC migration and dislodgement in turn can lead to adverse outcomes both in financial terms and in relation to the clinical management and outcomes of patients (Frey and Schears, 2001; Yamamoto et al. 2002). An incorrectly positioned CVC increases risk of thrombosis and patency impairment. Risk factors may include poorly secured CVCs, or arm movement, body habitus, and patient manipulation (Gorski et al. 2016). Stressors include friction due to clothes or bed covers, manipulation by clinicians and forced removal by patients (Ullman, 2015). The Association of Anaesthetists of Great Britain and Ireland (AAGBI, 2016) states that management of misplaced CVCs includes “using the device if it is safe to do so; manipulating the position under X-ray guidance; or replacement, using fluoroscopic guidance or other imaging as required” and that if the catheter tip is outside the SVC or upper right atrium the catheter should be repositioned, replaced or removed.

Laboratory-confirmed catheter related blood stream infection (CRBSI) is one of the most frequent and serious complications associated with CVCs. CRBSI accounts for 10% to 20% of hospital-acquired infections in the UK and is

associated with both increased ICU length of stay and mortality (Gahlot et al. 2014). Many studies have estimated the incidence of CRBSI, generally reporting a range between 1 and 3.1 per 1000 patient days, primarily within the adult intensive care unit (ICU) setting (Pronovost et al. 2006; Schwebel et al .2012), however, rates can be reduced by handwashing and antisepsis (Han et al. 2010). One of the primary causes of CRBSI is inadequate aseptic technique (Loveday et al. 2013) in the care of wounds and surgical incisions. CRBSI is generally caused either by skin microorganisms at the insertion site, which contaminate the catheter during insertion and migrate along the cutaneous catheter track after insertion, or microorganisms from the hands of healthcare workers that contaminate and colonise the catheter hub during care interventions. Treatment should adhere to local guidance and may include CVC removal (NHS England). Local infection may also occur; a diagnosis of cellulitis established on the basis of skin tenderness, erythema, oedema, and purulent exudate that resolves with antibiotic treatment and/or catheter removal (Yamamoto et al. 2002).

A thrombosis is a blood clot that can present at a tip of a CVC or surround the CVC. Thrombosis related to CVCs has a reported incidence of 3–32% (Frykolm et al. 2014), reflecting variations in definition and imaging, and frequent asymptomatic cases. Any intravenous catheter has the potential to cause venous thrombosis, however the incidence depends upon the catheter type and location, criteria for diagnosis, and population studied (Rooden et al. 2005). Risk factors for catheter-induced upper extremity venous thrombosis include catheter-related factors (such as catheter malposition), the presence of prothrombotic states (congenital or acquired), hormonal therapy, and infusion of irritating substances. Patient characteristics play an important role, for example ICU and cancer patients (Chopra et al. 2013) are at high risk for deep vein thrombosis and therefore have a higher chance of catheter-related thrombosis. PICCs appear to be associated with a greater risk for venous thrombosis overall (superficial and deep thrombosis) compared with centrally-inserted CVCs (CICCs), including those attached to a port, particularly in those who are critically ill or who have malignancy (Pikwer et al. 2012). The

incidence is also affected by the size of the catheter with larger-bore catheters having a higher risk (Zochios et al. 2014). The most common site of deep vein thrombosis for centrally placed catheters is the internal jugular vein (Bishop et al. 2007). For PICC catheters, the brachial, axillary, or subclavian veins may be involved. Suspected central venous thrombosis is confirmed by duplex ultrasound or venography (Yamamoto et al. 2002). Symptomatic thrombosis is usually treated with full anticoagulation. Removal of a functioning CVC depends on the clinical situation and ease of re-insertion (AAGBI, 2016). Catheter occlusion may occur due to thrombus, fibrin sheath, or precipitation within the catheter. Occlusion is recognised by inability to aspirate or flush the CVC. It is typically managed by a local protocol. A 'linogram' may identify a kinked catheter, aberrant tip position, or a fibrin sheath with reflux of contrast. Thrombolytics can be used to clear the lumen. In the case of precipitants, strong acid or alkali has been used to unblock devices (AAGBI, 2016).

Phlebitis (inflammation of a vein) tends to occur in patients with PICCs and may be mechanical or infective in origin. Mechanical phlebitis may occur as a result of "particulate matter and damage to the vein during forceful insertion or excessive movement of the PICC" (Todd, 1998). Vascular erosion by CVCs occurs when the catheter breaches the blood vessel wall, which can result in extravasation of total parenteral nutrition into the pleural cavity or mediastinum. Diagnosis and management are often delayed, leading to increased morbidity and mortality. Mechanical phlebitis can be prevented by securing the CVC. RCN guidance states that "Each organisation should have guidelines regarding the definition, prevention and management of phlebitis" and that "Removal of the device should be in line with the phlebitis scale in use and local policy and procedures (Royal College of Nursing 2016, INS 2016 [Gorski et al. 2016])".

Air embolism may be fatal and occur at any time from CVC insertion to removal. The incidence may be as high as 0.8% (Nayeemuddin et al. 2013). Prevention requires careful insertion/removal techniques, secure fixation and

safe handling when accessing the catheter (AAGBI, 2016). Presentation ranges from subtle neurological, respiratory or cardiovascular signs to shock, loss of consciousness and cardiac arrest. If suspected, damaged catheters should be clamped, pressure and wet dressings applied, and occlusive dressings used.

As well as factors including population, type of CVC, site of CVC insertion, and appropriate CVC insertion and management (Abolfotouh et al 2014), risk of CVC-related complication may be related to length of CVC dwell time (Greenberg et al. [2015], Mermel [2011]).

CVC dislodgment and bloodstream infections (and resulting complications) may be related to the movement of the catheter at the skin entry site, a problem that can be addressed with improved catheter securement methods (O'Grady et al. 2011).

2.1.3. EAC's overview of the intervention and comparators

SecurAcath

The SecurAcath is a subcutaneous catheter securement device. The device uses a small anchor that is placed just beneath the skin at the catheter insertion site. The anchor is attached to a base that is used to grip the catheter shaft to prevent inadvertent movement. The SecurAcath is designed for round-shaft catheters.

SecurAcath is a single use securement device indicated for short or long term securement of percutaneous indwelling catheters to the access site by means of a subcutaneous anchor at the insertion site. Once in place it secures the catheter for the duration of therapy. It is not currently indicated for conventional peripheral intravenous catheters.

SecurAcath was CE marked in February 2010, under Directive 93/42/EEC for Medical Devices.

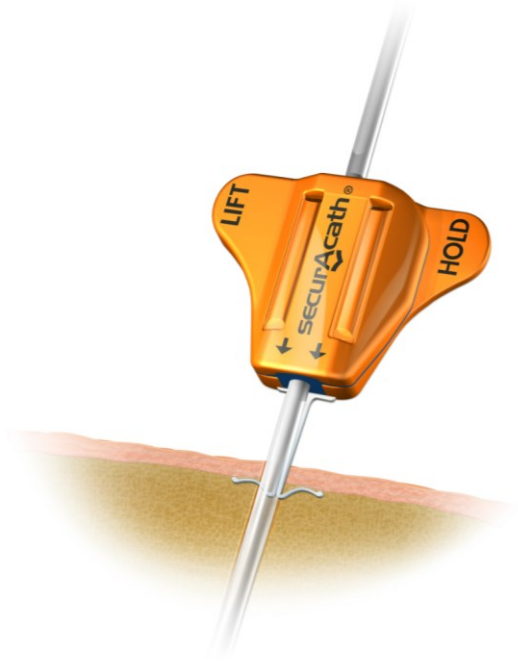


Figure 1 SecurAcath device inserted into skin

The device is contraindicated whenever:

- Skin integrity is deemed unfavourable by the operator, for example friable skin due to chronic steroid use, presence of cellulitis or rashes at the desired site of catheter insertion.
- Local tissue factors will prevent proper device stabilisation and/or access.
- The presence of device-related infection, bacteraemia, or septicaemia is known or suspected.
- The patient's body size is insufficient to accommodate the size of the implanted device.
- The patient is known or is suspected to be allergic to materials contained in the device.
- The prospective insertion site has previously received irradiation.

There are 6 versions of SecurAcath. These are used with 3, 4, 5, 6, 7, 8 French (Fr) size[2] CVCs. All sizes have the same functionality. The anchor base and anchor sizes are the same for each version, only the channel diameter changes.

A SecurAcath device must be selected to match the catheter diameter. If catheter is labelled with a half Fr size, the closest smaller size SecurAcath should be used.

The device is used once a catheter has been placed following the standard procedure. The SecurAcath requires a minimum of 3 cm of catheter shaft exposed above the skin surface and the manufacturer recommends that a dermatotomy of approximately 3 mm is made parallel to the shaft of the catheter.

To use the device, the anchor base is folded down until the anchor tips come together. The catheter is then lifted until it is perpendicular to the skin. The folded anchor base is held perpendicular to the catheter line and light traction is applied to the skin to help dilate the insertion site. The anchor tips are then inserted into the catheter insertion site. The anchor is then advanced as closely as possible to the catheter shaft and the anchor base is released to open flat, ensuring that the anchors are fully open under the skin. The anchor is then secured open by placing a cover over the anchor base. Once the device is secured it lays flat on the skin. The site should then be dressed as per hospital protocol. Unlike adhesive securement devices, SecurAcath does not need to be changed at the same time as the dressing.

The device is removed at the same time that the catheter requires removal. This is done by removing the cover from the anchor base. The catheter is then removed. The anchor base can then be cut lengthways and each half removed separately or the anchor base can be folded and the anchors removed. The manufacturer states that a swift, deliberate tug may be needed

[2] French size: unit of measurement for the outer diameter of a catheter.

for anchor removal in either method. Local anaesthesia may be used at the site prior to removal to reduce pain.

Comparators

Adhesive securement devices aim to increase attachment to the skin, thus minimising catheter movement and reducing complications such as phlebitis, dislodgement, infiltration and vessel occlusion. The StatLock adhesive securement device (Bard Access Systems) is commonly used within the NHS for catheter stabilisation. The StatLock is a single use adhesive anchor device that uses a 'post and door' design, the doors locking the suture wings of the CVC to a foam-based anchor pad which adheres firmly to the patient's skin and is removed using alcohol. The device must be changed at least every 7 days or along with dressing changes. The StatLock stabilisation device is compatible with medical tubes and catheters. The device is contraindicated in people with known tape or adhesive allergies or a known sensitivity to benzoin. Similarly, the Grip-Lok device (Zefon International) includes an adhesive base layer that attaches to the patient's skin. The catheter or catheter/connector combination is pressed onto an adhesive pad attached to an upper surface of the base layer. A Velcro closure layer is then folded over the catheter and attaches to the upper surface of the base layer. CVCs may also be secured using surgical tape. Adhesive securement devices are most typically used with PICCs.

Sutures are surgical stiches used to hold together wounds or to secure devices. Sutures are typically used in short term percutaneous (non-tunnelled) catheters and in skin-tunnelled catheters. They are not typically used in PICCs, but may be used in neonates or people likely to forcibly remove the line.

2.1.4. Overview of relevant clinical guidelines

No specific NICE guidance about CVCs or CVC line securement was found.

The Royal College of Nursing (RCN) is currently reviewing and updating its guidelines for infusion therapy (anticipated publication in 2016). The 2010

RCN guidelines (Dougherty et al. [2010], no longer available on the RCN website) state as follows:

- Devices should be stabilised in a manner that does not interfere with assessment and monitoring of the access site, that does not impede delivery of the prescribed therapy, and that is acceptable to the patient.
- Products employed to stabilise the catheter should include sterile tapes, transparent moisture-permeable dressings, sutures, manufactured catheter securement devices and sterile surgical strips. Whenever feasible, the use of a manufactured catheter securement device, e.g. StatLock is preferable. [2016 RCN standard states: “Products employed to stabilise peripheral cannulae, midlines or central venous catheters include transparent semi-permeable membrane (TSM) dressing, sutures, manufactured catheter securement devices, and sterile surgical strips” with no mention of specific manufactured securement devices].
- When a catheter securement device is used for stabilisation, placement should be in accordance with manufacturers’ guidelines.
- To accurately confirm catheter dislodgement and catheter tip position a chest X-ray should be performed with an anteroposterior and lateral view.
- A catheter which has migrated externally should not be re-advanced prior to re-stabilisation.
- Sutures should not be routinely used for stabilisation of midlines, PICCs or non-tunnelled central vascular access devices due to their potential for contributing to the risk of infection (CDC, 2002; Maki, 2002; Heckler, 2005; Dougherty, 2006; Gabriel, 2008).
- External catheters should be secured with tape, sutures and an intact dressing (Hadaway, 1998).
- Use of tape and/or transparent dressing, plastic shields or adhesive anchoring devices (for example ‘StatLock™’) will reduce the risk of catheter dislodgment (Hanchett, 1999).

The first 5 recommendations are similar in new guidance from the RCN. The last 3 recommendations do not appear in the draft guidance, and it is unclear whether they will appear in the final version.

The 2016 RCN report considers including the use of the term “engineered stabilisation devices” (ESDs) to secure vascular access devices, as mentioned in Gorski et al. (2016). ESD is a term used to describe securement devices specifically manufactured to stabilise and secure vascular access devices and include adhesive and subcutaneous ESDs (Royal College of Nursing 2016).

The Royal Marsden Manual for Clinical Nursing Procedures (Dougherty et al 2015) and the American Infusion Nurses Society (INS) standards (Gorski et al. 2016) are also commonly used in practice.

The Royal Marsden Manual for Clinical Nursing Procedures (Dougherty et al 2015) includes the following guidelines on vascular access device securement:

- Devices are secured to prevent movement, which reduces the risk of phlebitis, infiltration, infection and migration. This can be achieved by suturing, taping or the use of securing devices [the SecurAcath device image is given as an example].
- The stabilisation device should be used in a manner that does not interfere with the assessment and monitoring of the access site.
- Tapes or securing devices should be changed at the same time as dressing changes if loose or contaminated or due to be changed. Tapes or securing devices should be reapplied if necessary.
- Short term percutaneous non-tunnelled CVCs may be sutured into place but this is no longer recommended due to the risk of infection and the need to reduce use of sharps. The use of other securement devices is recommended such as a StatLock.

- In skin tunnelled catheters, exit site sutures should be retained until fibrotic response is adequate to secure the catheter, usually within 2-3 weeks.
- PICCs should be secured with a securing device such as a StatLock or a SecurAcath.

The Infusion Nurses Society (USA) publishes the Infusion Therapy Standards of Practice (Gorski et al. 2016). These guidelines are commonly used in the NHS as gold standard guidelines. The latest revision released in January 2016 includes the following guidelines:

- Never advance any external portion of the CVC that has been in contact with the skin into the insertion site. No antiseptic agent or technique applied to skin or the external catheter will render skin or the catheter to be sterile.
- Consider use of an "engineered stabilization device" (ESD) as inadequate stabilisation and securement can cause unintentional dislodgement and complications requiring premature VAD removal.
- ESDs promote consistent practice among all clinicians, reduce VAD motion that can lead to complications, reduce interruption of needed infusion therapy, and may decrease cost of care.
- Avoid use of tape or sutures as they are not effective alternatives to an ESD.

The 2016 Standards include a new category called Subcutaneous Engineered Stabilization Devices (ESDs). The standards state that these "have been successful in stabilizing PICCs and CVADs [central venous access devices], patient outcomes and patient and inserter satisfaction have been favorable; however, additional studies with other CVADs are needed."

British Committee for Standards in Haematology guidance (Bishop et al. 2007) outlines the following information and guidance for securing CVCs:

- Securing devices, for example StatLock, are preferable to stitches, and lines should not be sewn into or around the vein.
- For patients with a tunnelled catheter, the upper suture over the insertion site into the vein should be removed at 7–10 days and the lower one at the exit point should be removed after 3 weeks. Recent evidence supports the use of securing devices, including tapes, adhesives or staples, particularly with non-tunnelled CVCs and PICC.
- Securing devices have also been shown to reduce infection rates when compared with sutures.

Epic-3 guidelines (issued by the Healthcare Infection Society, Loveday et al. 2014) include the following recommendations:

- Use a tunnelled or implanted central venous access device with a subcutaneous port for patients in whom long-term vascular access is required.
- Use a peripherally inserted central catheter for patients in whom medium term intermittent access is required.
- Use maximal sterile barrier precautions for the insertion of central venous access devices.
- Transparent, semi-permeable polyurethane dressings should be changed every 7 days, or sooner, if they are no longer intact or if moisture collects under the dressing.
- Do not routinely replace central venous access devices to prevent catheter-related infection.

The Association of Anaesthetists of Great Britain and Ireland (AAGBI) guidelines on Safe vascular access (AAGBI 2016) includes the following recommendations:

- Secure fixation is important to minimise withdrawal, which may be identified by the loss of a venous waveform from the proximal lumen of the catheter. Correct placement of the catheter tip will

help prevent venous erosion and ensure an adequate length of catheter within the vein.

- Assessment of tip position includes: post-insertion chest X-ray, real-time fluoroscopy, and ECG guidance.
- Management of misplaced catheters within central veins includes: using the device if it is safe to do so; manipulating the position under X-ray guidance; or replacement, using fluoroscopic guidance or other imaging as required.

The British Association of Perinatal Medicine recommends that PICCs should be secured with a sterile transparent dressing that allows visualisation of the site of entry and that "[t]he final fixation method for a central catheter should minimise skin injury and potential for catheter migration or loss".

European Council Directive 2010/32/EU (the Sharps Directive) recommends against the use of medical sharps altogether, including sutures, where there is a practicable alternative.

The NICE Clinical Guidelines on infection control (CG139) provides guidance on preventing infection for adults and children with vascular access devices in primary and community care settings. The guideline recommends that the skin at and around the catheter insertion site should be cleaned with 2% chlorhexidine gluconate in 70% alcohol and allowed to air dry during dressing changes. The insertion site should be covered by a sterile transparent semipermeable membrane dressing which should be changed every 7 days or sooner if the dressing is no longer intact or moisture collects under it.

CG139 notes that systemic anticoagulants should not be used routinely to prevent CRBSI. Systemic antimicrobial prophylaxis should not be used routinely to prevent catheter colonisation or CRBSI, either before insertion or during the use of a central venous catheter.

NICE Technology Appraisal Guidance (TA49) discusses the necessity of ultrasound for CVC insertion. The guidance recommends that 2-D imaging

ultrasound guidance should be considered in most clinical situations where CVC insertion is necessary, whether the situation is elective or an emergency.

Local NHS guidelines for CVC insertion, management and removal include the following:

- Great Ormond Street Hospital for Children NHS Foundation Trust recommends that "[long term] PICCs are usually secured by suturing the catheter to the child's skin above the antecubital region or with a securement device e.g. StatLock" to minimise the risk of accidental dislodgement.
- London Cancer care guidelines recommend that non-tunnelled CVCs are always fixed with StatLock devices, and that tunnelled CVCs are fixed firmly to the patient's skin using tape or a "dedicated device" such as the Skin Fix adhesive patch. PICCs should always be secured using steri-strips, StatLock and transparent dressing. Port CVCs are secured with sutures. For apheresis CVCs, the same process applies as for tunnelled or non-tunnelled CVCs.
- Bradford and Airedale NHS guidelines recommends that StatLocks are "the securement method of choice for PICC catheters and Skin Tunnelled Catheters for the first three weeks whilst the anchor wing is in situ. Its placement should be in accordance with the manufacturer's guidelines". "StatLock devices should be replaced every seven days, if their integrity is compromised or where they are contaminated (e.g. with blood)."
- Doncaster and Bassetlaw Hospitals NHS Foundation Trust recommends that CVCs are secured with an "appropriate securement device. For example; stat-lock for PICC, [and] sutures or stat-lock for jugular or subclavian lines, and sutures for Hickman lines."

2.1.5. Issues relating to current practice

Dressings and adhesive devices for CVCs must be changed weekly or as necessary (for example if the dressing is soiled). The time during which the dressing and securement device are removed presents a period of increased likelihood that the catheter will accidentally migrate or dislodge. During this time, the catheter is typically stabilised by hand. The risk of dislodgement during this time can be related to the skill and experience of the operator.

Adhesives may cause medical adhesive-related skin injury. The probability of this complication increases significantly in patients with altered skin integrity or diseases that lead to fragile skin, such as epidermolysis bullosa and graft versus host disease.

Local NHS protocols may vary in terms of recommendations for securement. Some protocols recommend different methods of securement by CVC type, for example StatLock for use in PICCs and sutures in skin-tunnelled CVCs. Other guidance may recommend that tunnelled CVCs are secured by adhesive patches.

The population that requires CVC is heterogeneous, which may produce variation in outcomes. For example, longer CVC dwell time may relate to increased risk of infection and dislodgement (as there are more opportunities for this to occur). The longer a skin-tunnelled CVC is in situ, the more difficult to remove it will be (this may result in lower patient satisfaction if there is difficulty removing the device). Patient satisfaction scores depend largely on correct CVC placement, which in turn is related to operator experience and training.

2.1.6. Potential changes to the pathway by introducing SecurAcath

SecurAcath may be used in adults and children needing non-tunnelled, PICC and apheresis/dialysis CVCs. Use in skin-tunnelled CVCs may be less likely as natural skin granulation after 2-4 weeks holds the catheter in place without

need for a securement device. In addition, the majority of skin-tunnelled CVCs have diameters larger than 8 Fr (in both children and adults). Because the maximum size CVC that SecurAcath can be used with is 8 Fr, this may also limit the use in this type of catheter. SecurAcath would be used in place of existing methods of catheter securement such as tape, sutures, or adhesive securement devices such as StatLock to prevent catheter migration and dislodgement. As with existing methods, SecurAcath is used in conjunction with an appropriate dressing to prevent catheter-related infection. SecurAcath can remain in place for the duration of the catheter placement and does not require changing when dressings are changed.

2.2 Overview of sponsor's description of ongoing studies

No ongoing studies were submitted by the sponsor. The EAC did not identify any ongoing studies.

2.3 Critique of sponsor's definition of the decision problem

Population

The population described by the sponsor was patients who require an intravascular catheter for central venous access. This definition is in accordance with the population identified in the scope. Because of the broadness of the definition, the population included in the clinical evidence submitted by the sponsor is considered relevant to the scope. However, as the majority of the evidence is submitted as abstracts, no details are provided about population characteristics and it is therefore not possible to assess whether they reflect the characteristics of the patient population in England eligible for CVCs.

From the 20 studies included in the sponsor's clinical evidence submission 4 (Dougherty 2013, Hughes 2014, McParlan 2016, Sandeluss 2013) were

conducted in the UK and as a result they may reflect the characteristics of an NHS population.

The majority of the studies were conducted in adults apart from 3 (Peveler 2013, Pittiruti 2015, Stone 2013) studies investigating a paediatric population.

Intervention

The sponsor describes the intervention as a single use securement device used to hold percutaneous catheters in place. It consists of two components, a base and cover. The base contains two small, blunt, flexible securement feet which are placed beneath the skin; the cover snaps onto the base outside the body to hold the catheter shaft in place. It is designed to remain in situ throughout the period of catheter placement and does not need replacing. The EAC queried the existence of different versions of the device and the possible impact these differences may have in clinical outcomes. According to the sponsor, the device has had some design iterations since it was originally CE marked in 2010. The first version was only available in 2 sizes (5 Fr and 7 Fr). It was never launched for sale or use in UK. The second version was available to the UK, and was launched in 2011. It had some modifications in shape and added sizes (3, 4, 5, 6, 7, and 8 Fr). The lift tab was moved to the back corner of the cover to make cover removal more intuitive and user-friendly. This difference in shape aimed to facilitate cover removal. The current version, which was launched in the UK in October 2015, had the HOLD tab added to the opposite back corner to give users a place to grip the device when removing the cover. It also featured a larger LIFT tab to improve user-friendliness of cover removal. All of the design modifications are covered under the current CE certificate which was renewed in July 2015. The sponsor claims that none of these changes impacted upon the intended use or principles of operation. From the provided information the EAC concluded that the design differences could potentially have an impact on pain during removal and time taken to remove the device but not to the rest of the outcomes.

The EAC believes that the sponsor has satisfied the regulatory requirements and all relevant documents have been made available in the submission. A detailed description of the intervention is provided in section 2.1.3.

Comparator(s)

The sponsor did not provide any background information on the comparators as defined by the scope. One of the included studies (Janssens 2016a) was an RCT using StatLock as the comparator, and 7 other studies (Anonymous 2015, Balance 2012/2013, Djurcic-Jovan 2016, McParlan 2016, Pittiruti 2015, Sandeluss 2013, Stone 2013,) were cohort studies that referenced StatLock or unidentified comparators as historical controls. Although not included in their submission, the sponsor refers to the RCT by Yamamoto et al. 2002 in section 7.9.1 for comparison of the dislodgement rate between SecurAcath, StatLock and sutures. The EAC asked the sponsor whether they ran a full systematic review to retrieve evidence for the comparators, or whether this publication was selected based on clinical expertise. The sponsor confirmed that the use of the study was solely based on expert advice. A detailed description of the comparators as specified in the scope is provided in section 2.1.3.

Outcomes

The outcomes listed in the scope, and their reporting in the included studies, are listed in Table 5 and Table 6. The sponsor's submission included studies covering all the outcomes described in the scope with the exception of quality of life. The sponsor did not provide detailed information and objective definitions of the outcomes under consideration. The outcomes and definitions are particularly important as they can affect the measurements reported by the studies and ultimately introduce bias to the results. The EAC has provided a more comprehensive and up to date description of the clinical outcomes in section 2.1.2.

Cost analysis

The sponsor's submission compares SecurAcath with StatLock for the securement of PICC and with sutures for the securement of CICC (referred to in the submission as CVCs) lines. The scope specifies the following comparators: adhesive devices, sutures, steristrips, adhesive tape. The scope does not differentiate between CICC and PICC lines regarding appropriate comparators. Consequently, the EAC regarded the sponsor's submission as inadequate with respect to the comparators included within the cost analysis.

Subgroups

The following subgroups were specified in the final scope.

- People who receive a PICC
- People who receive a CVC (referred to in this document as CICC)
- People with co-morbidities
- Children and young people
- People with a medium to long dwell time

There is no detailed description of these subgroups in the sponsor's submission. More detailed information for the PICC, CICC and medium to long dwell time subgroups are given in section 2.1.2.

Special considerations, including issues related to equality

In the scope 3 groups with protected characteristics (Equality Act, 2010) were identified:

- The technology may be used by adults or children, but is most commonly used in older patients with chronic conditions who may be classed as disabled if their condition has a significant and long-standing adverse effect on activities of daily living.

- The technology may also be used regularly in people with cancer, who are protected under the Act from the point of diagnosis.

- The technology is not suitable for people with an allergy to nickel.

Although the assumption included in the sponsor's cost analysis that the technology is likely to be predominantly used in older, critically ill patients, who are likely to have a number of co-morbidities and in patients following major trauma, or those with conditions requiring long-term ongoing therapy such as cancer, these subgroups are not specifically addressed in their submission. No new equality issues have been raised by the sponsor.

The majority of skin-tunnelled CVCs have diameters larger than 8 Fr (in both children and adults). Because the maximum size CVC that SecurAcath can be used with is 8 Fr, this may also limit its use with this type of catheter in this patient population. These are likely to be patients requiring haemodialysis which is a protected characteristic according to the Equality Act, 2010.

3 Clinical evidence

3.1 Critique of the sponsor's search strategy

The sponsor did not provide details of the full search strategies used. The EAC subsequently requested the sponsor to provide these, however, they were never made available and the EAC was unable to replicate them.

The following databases are listed in the original submission: OVID Medline, Embase, Google, Google Scholar and ClinicalTrials.gov, Cochrane Central Register of Controlled Trials, EBSCO CINAHL and PubMed. Upon further clarification requested from the manufacturer, it was confirmed that only Cochrane Central Register of Controlled Trials, EBSCO CINAHL and PubMed databases were searched by the sponsor.

Similarly, the original submission mentions the following keywords: 'securement', 'stabilisation', 'central venous catheter', 'peripherally inserted catheter', 'PICC', 'StatLock', 'replacement', 'migration', 'SecurAcath'. In subsequent communications the following terms were also mentioned by the sponsor: 'securement device' and 'novel securement'. The following are cited in the submission as "headings": 'PICC migration', 'replacement', 'PICC stabilisation', 'Central venous catheter securement'. These are not recognised MeSH or EMTREE terms. The EAC requested from the manufacturer further information on the use of keywords and MeSH terms for their submission. According to the manufacturer, the MESH terms migration/replacement were not used and that their search strategy was mainly focused on securement with multiple variables for migration/replacement used.

The EAC queried the sponsor's selection of date limits for their search strategies, which only included publications from 2010 onwards. The sponsor clarified that SecurAcath was not available prior to 2010 and the search period was limited to studies from 2010 to 2016 to take into account the date

of FDA clearance.[3] The EAC considered the date limits chosen by the sponsor with regards to the intervention to be adequate.

The EAC, however, considers that the search terms used for the sponsor's submission do not have enough sensitivity to capture the relevant literature, and more keywords could have been used to describe the intervention and the comparators. The EAC, therefore, developed and ran a new search of OVID Medline, Embase and Cochrane Central using a broader range of keywords and MeSH and EMTREE terms (Appendix 1). This search retrieved 2296 studies of which 2 studies relating to SecurAcath (McParlan 2016, Sansivero 2011) and 6 studies relating to StatLock (Fang 2011, McMahon 2002, Teichgräber 2011, Venturini 2011, Yamamoto 2002, Zerla 2015) were included.

There is no PRISMA flow diagram provided by the sponsor ("due to scarcity of available data") and no mention of how unpublished studies (posters and abstracts) were considered for inclusion.

Finally, for searches of unpublished and professional organisation databases, the sponsor provided the following general description of their methodology.

'Additional searches included the company database (repository of published and unpublished data) i.e. inclusive of posters presented at vascular access conferences. Additional search of Association Vascular Access Journal, Infusion Nursing Society, British Journal Nursing.'

However, full details as to which databases were searched for ongoing clinical trials, or which professional meetings and online publications were regularly monitored to gather the abstracts and scientific meeting presentations, were not provided.

[3] http://www.businesswire.com/news/home/20100712006585/en/Interrad-Medical-Receives-FDA-Clearance-SecurAcath-Universal

3.2 Critique of the sponsor's study selection

The sponsor used the criteria outlined in Table 1 to select relevant clinical outcomes studies. Only inclusion criteria were used. According to the sponsor there is no other technology comparable to SecurAcath available to date, and consequently all publications including either the name of the technology or accurate descriptors were included. The EAC queried the use of the general term 'Securement' to characterise the intervention. According to the sponsor, the rationale for choosing this general term and not the intervention as defined in the scope was that SecurAcath is mainly described as a securement device and that securement of the catheter is the function it provides.

Table 1: Sponsor's selection criteria for published clinical outcomes studies

Inclusion criteria:	
Population	Patients who require an intravascular catheter for central venous access
Interventions	Securement
Comparator	Nothing listed by the sponsor
Outcomes	Successful deployment and removal of device without complication. Successful securement. General comment review publications of securement devices, technologies, PICC migration and reduction in this complication.
Study design	Observational, prospective observational, multi- centre. Editorial comment, review of available technology
Language restrictions	None
Search dates	2010-2016
Exclusion criteria	
Population	First published studies in USA and Europe no direct comparison to described technology within the scope
Interventions	
Comparator	

Outcomes	
Study design	
Language restrictions	
Search dates	

3.3 Included and excluded studies

The sponsor's submission included 20 studies reporting clinical outcomes with SecurAcath, including 7 (Cordovani 2013, Hughes 2014, Egan 2012, Egan 2013, Oliver 2016, Alpenberg 2016, Higginson 2015) full-text publications (table B3 of the submission), 12 conference abstracts (Table B4 of the submission) and 1 (Anonymous 2015) unpublished report (Table B4 of the submission). Of the full-text studies 4 (Alpenberg 2016, Egan 2012, Higginson 2015 and Oliver 2016) were commentaries and reviews, and 3 were primary studies. The sponsor considered all studies relevant to the scope and none were excluded from their submission. See Table 2 below for details of all the sponsor's included studies. The Balance 2012/2013 are summarised as 1 study as they were the same study.

Table 2: List of included studies identified by the sponsor

Included/Excluded by sponsor and EAC	Primary study reference	Population	Intervention	Comparator
Included by the sponsor Excluded by the EAC	Ballance 2012/2013	Patients requiring PICCs	SecurAcath	Sutures
Included by the sponsor and the EAC	Cordovani 2013 NCT00903539	Adults requiring CICCs	SecurAcath	None
Included by the	Djurcic-Jovan	Complex	SecurAcath	Unclear

sponsor and the EAC	2016	continuing care patients requiring PICCs		comparator
Included by the sponsor and the EAC	Dougherty 2013	Inpatients and outpatients requiring PICCs	SecurAcath	None
Included by the sponsor and the EAC	Egan 2013	Adults including medical and surgical inpatients, patients in ICU or transplant unit, and outpatients requiring PICCs	SecurAcath	None
Included by the sponsor and the EAC	Hughes 2014	Adults, oncology requiring PICCs	SecurAcath	None
Included by the sponsor and the EAC	Hill 2014	Inpatients requiring PICCs	SecurAcath	None
Included by the sponsor Excluded by the EAC*	Janssens 2016a	Adults requiring PICCs	SecurAcath	StatLock
Included by the sponsor and the EAC	McParlan 2016	Haematoncology patients requiring PICCs	SecurAcath	StatLock
Included by the sponsor and the EAC	Anonymous 2015	Patients requiring PICCs	SecurAcath	Unclear comparator
Included by the	Peveler 2013	Children with	SecurAcath	None

sponsor Excluded by the EAC		fragile skin requiring PICCs		
Included by the sponsor Excluded by the EAC	Pittiruti 2015	Adults and children requiring PICCs and tunnelled CVCs	SecurAcath and glue	StatLock
Included by the sponsor Excluded by the EAC	Sandeluss 2013	Haematology and oncology patients requiring PICCs	SecurAcath and secondary stabilisation device	Unclear comparator
Included by the sponsor and the EAC	Stone 2013	Children with previous skin issues or skin irritation/allergic reaction to standard dressing products requiring PICCs	SecurAcath	Unclear comparator
Included by the sponsor and the EAC	Zerla 2016	Adult oncology patients requiring 2016	SecurAcath	None
*The EAC obtained an unpublished full-text (Janssens 2016b) with updated results leading to the exclusion of Janssens (2016a)				

The EAC reviewed all the primary studies identified by the sponsor. All studies that did not fit the EAC's inclusion/exclusion criteria (Table 4), were excluded from further review. For a summary of the EAC's included studies, including those also accepted by the sponsor, please section 3.9, Table 5.

The following narrative reviews and commentaries identified in the sponsor's submission were excluded by the EAC: Alpenberg 2016, Egan 2012, Higginson 2015 and Oliver 2016. These were excluded because they were either commentaries or narrative reviews. This type of publication expresses expert opinion and is not considered relevant evidence for the assessment report.

Details of the primary studies excluded by the EAC are given below.

Ballance 2012/2013

Ballance (2012) and Balance 2013 investigated PICCs secured with SecurAcath in patients with a dwell time of 0 to 29 days (N=10). The author reported 100% acute procedure success rate and no instances of malfunctions or device-related adverse events. Pain scores were measured on a 0-10 scale: scores were 0 in all patients at insertion, in situ and at removal. Patient satisfaction was 'neutral or satisfied' in 100% of patients.

Critical appraisal

This was a small cohort study reporting pilot data on 10 patients with SecurAcath. Based on our inclusion criteria for a sample size >10 patients this study was excluded from further consideration.

Peveler 2013

Peveler (2013) investigated PICCs secured with SecurAcath in paediatric patients (N=2) with fragile skin. These were patients who are unable to tolerate adhesives used in traditional central line dressings. The overall dwell times were 57 and 61 days respectively. The author reported that the subcutaneous anchoring device proved to significantly extend the life of the catheter in patients with fragile skin.

Critical appraisal

This was a small case series study reporting pilot data on 2 patients with SecurAcath. Based on our inclusion criteria for a sample size >10 patients this study was excluded from further consideration.

Pittiruti 2015

Pittiruti (2015) investigated PICC and tunnelled CICC placements secured with SecurAcath in two separate cohorts: adults with dwell time >2 months (N=48) and elderly, adult and paediatric patients with median dwell time of 2 weeks (N=47). The first (cohort A) included 4-5Fr catheters (all PICCs) while cohort B used 4-7 Fr catheters (29 PICCs and 18 CICCs). The study records adverse events related to SecurAcath and the addition of glue to secure the device and control bleeding. In cohort A: catheter migration and unplanned removal rates were 0%. Author reports no pain at insertion but 'some degree of pain' at removal in 5 patients of whom 2 had local inflammation. 1 patient suffered skin irritation (glue was not used). The device was described as effective in 100% of cases. In cohort B: there were 2 cases of difficulty at insertion and unplanned removal occurred in 2 patients (4.7%) both of whom were elderly and had dementia. Five patients had pain at removal of whom 2 had local inflammation. The device was described as effective in 100% of paediatric and collaborative adult cases, but it was <100% effective in patients with dementia. The author concludes that SecurAcath is 98% effective at preventing dislodgements, complications were minimal and that placement/removal should be done by expert clinicians, with local anaesthetic in selected cases.

Critical appraisal

This study comprises 2 prospective evaluations of distinct cohorts and although the demographics are very different the author does not attempt to compare the cohorts. The insertion and maintenance protocols are clearly defined which should aid repeatability. In both cohorts, glue was used in around half of the patients but it is not reported whether or not this influenced pain outcome. Cohort B is heterogeneous and it is unclear which patients

suffered difficulty at insertion. The term ‘expert clinicians’ is not defined, and it is not clear which cases would benefit from local anaesthetic. The data on pain scores does not include a measurement scale (e.g. visual analogue scale [VAS]) and so has limited generalisability. As both cohorts used SecurAcath in addition to glue as the intervention, this study was excluded from further consideration.

Sandeluss 2013

Sandeluss et al. (2013) investigated PICCs secured with SecurAcath in haematology and oncology patients with a dwell time of >4 weeks (N=100). The device was originally piloted without a secondary stabilisation device (n=22) and this was used as a comparator for some outcomes. Following the pilot, in addition to SecurAcath, a secondary stabilisation device was used because the pilot showed that although the SecurAcath appeared to prevent migration of the PICC during dressing changes, if the PICC was accidentally pulled vigorously, it would stretch and slip through the SecurAcath. The objectives were to assess migration rates, patient experience (benefits and discomfort) and clinical implications of SecurAcath. The catheter migration rate decreased from 7% in the pilot to 2% in the study cohort. 88% of patients found SecurAcath ‘tolerable’ and ‘would have it again’. Pain scores were measured on a 0-10 scale (Mild=1-3, Moderate=4-6, Severe=7-10): at <2 weeks after insertion pain scores were mild or no pain in 87%; at >2 weeks pain scores were mild or no pain in 96%; and at removal pain scores were mild or no pain in 60% and severe in 29%. Authors report qualitative data about patient and clinician experience of SecurAcath: patients said pain related to SecurAcath is preferable to having to replace the PICC. Authors conclude that further work is needed to improve insertion and maintenance techniques, a staff survey will be carried out, and they will continue to use SecurAcath.

Critical appraisal

This is a retrospective audit published as a poster presentation. Data collection methods (phone and face-to-face interviews) resulted in some missing data, which is not explained. The authors do not clearly define 'migration'. Comparisons to the pilot cohort are at risk of bias because the securement protocol had changed in the study cohort (secondary stabilisation device added). There is very little demographic data on the pilot cohort. There is no information about how qualitative data are selected so conclusions are at risk of bias. The pain scores are well defined and the use of visual analogue scale enables generalisability. This study was excluded because patients had a secondary stabilisation device in addition to SecurAcath.

3.4 Overview of methodologies of all included studies

The EAC reviewed the methodologies of the 16 sponsor- identified studies, outlined below.

- With the exception of 1 RCT by Janssens (2016a) the rest of the studies are observational cohorts conducted retrospectively or prospectively as part of audits prior to or after the implementation of SecurAcath for clinical use. Two multi-centre studies were included (Cordovani 2013, Egan 2013), the rest were single centre.

- The majority of the studies evaluated the intervention specified in the scope. The unpublished audit by Anonymous 2015 investigated SecurAcath with the use of an antithrombotic PICC catheter (Arrow Chlorag+ard).

- Only 1 study (Janssens 2016a) directly compared SecurAcath with 1 of the comparators (StatLock). Seven studies compared SecurAcath with historical controls ((Balance 2012/2013, Djurcic-Jovan 2016, McParlan 2016, Anonymous 2015, Pittiruti 2015, Sandeluss 2013, Stone 2013,)), however, for the majority the comparator is not specified. The EAC contacted the authors of these studies to request further clarifications

on the comparators; the results are listed in the methodology column of Table 5 in section 3.9. No single study compared the intervention with all the comparators.

- The studies were performed mostly on adult inpatients. Three studies included a paediatric population (Stone 2013, Peveler 2013, Pittiruti 2015), however, the study by Peveler 2013 only included 2 patients.

- With the exception of Janssens (2016a), the rest of the studies did not report sample size calculations or confidence intervals.

- With the exception of 3 full text publications (Cordovani 2013, Egan 2013, Hughes 2014) the rest of the included studies were conference abstracts or posters. The study by Cordovani (2013) was published as a letter to the editor.

- Only Egan (2013) and Janssens (2016a) provided adequate baseline characteristics of the study populations, including sex and age, vein used, and indication for PICC insertion. The assumption included in the sponsor's cost analysis that the technology is likely to be predominantly used in older, critically ill patients, who are likely to have a number of co-morbidities and in patients following major trauma, or those with conditions requiring long-term ongoing therapy such as cancer. However, given the poor reporting of patient baseline characteristics it is difficult to assess the suitability of the submitted studies to support this assumption.

3.5 Overview and critique of the sponsor's critical appraisal

The sponsor conducted a critical appraisal of the 3 full text studies (Hughes 2014, Egan 2013, Cordovani 2013) and the abstract by Janssens (2016a) included in their submission. Checklists for cohort studies or RCTs were used depending on the study design.

The critical appraisal of the Janssens (2016a) study provided relevant information mainly on the randomisation and blinding of treatment allocation. The sponsor, however, did not comment on other aspects of study design that may introduce bias, such as follow-up, training of the operators, catheter installation and maintenance protocols, definitions of clinical outcomes and statistical methods. The EAC noted that the specific criteria used for methodological quality assessment scoring of the studies included in the clinical evidence submission for both the RCT and the observational studies were not included in the submission. The EAC also noted variability in the criteria used to assess a study as negative for bias. This again reflects the lack of tailored criteria for scoring the checklist items and the variability of study design and outcomes included in the studies.

When asked to clarify the use of the quality assessment criteria the sponsor stated that due to the observational design of the majority of studies included in their submission, no substantive quality assessment was undertaken. The sponsor in their submission argued that because the majority of the submitted data are observation studies, or product evaluations, a critical appraisal is difficult to perform. In addition, the sponsor states that regardless of the design methodology used, and whilst the data presented may not have been submitted for peer reviewed publication, all observational prospective clinical evaluations resulted in clinicians adopting the device and incorporating it into their routine clinical practice. The EAC notes however that the majority of the sponsor's submitted evidence consisted of conference abstracts, some published as early as 2012. These abstracts were not developed into full-text publications, potentially reflecting poor methodological quality but also raising the possibility of publication bias. When questioned, the sponsor stated that in the vascular access arena most studies never translate into full text publication. The EAC, however, notes the presence of full text publications for some of the SecurAcath comparators such as StatLock and sutures.

3.6 Results

The sponsor summarised and presented the results for the 16 published and unpublished clinical outcome studies included in the submission (Table B9). After excluding Janssens 2016a after obtaining the unpublished draft of Janssens 2016b, the EAC accepted 10 of the sponsor's primary studies as eligible for inclusion in the assessment report. The results from the 10 primary studies (Cordovani 2013, Djurcic-Jovan 2016, Dougherty 2013, Egan 2013, Hill 2014, Hughes 2014, McParlan 2016, Anonymous 2015, Stone 2013, Zerla 2016) included by the sponsor and accepted by the EAC are provided in Table 6 in section 3.9. The rest of the studies included in section 3.9 by the EAC were not identified by the sponsor.

Only the unpublished RCT study by Janssens (2016a) included a direct comparator (StatLock) as defined in the scope. The remaining studies had either no comparators (Cordovani 2013, Dougherty 2013, Egan 2013, Hill 2014, Hughes 2014, Peveler 2013, Zerla 2016) or compared SecurAcath performance against a historical cohort (Anonymous 2015, Balance 2012/2013, Djurcic-Jovan 2016, McParlan 2016, Pittiruti 2015, Sandeluss 2013, Stone 2013,).

3.7 Description of the adverse events reported by the sponsor

The sponsor searched the MHRA and FDA-MAUDE databases using the term 'SecurAcath' with a search period of 2010 to 2016. Their MHRA search found no results while the MAUDE search retrieved one item. The sponsor's inclusion/exclusion criteria (section 10.1.6) indicate that all data relating to 'SecurAcath' would be included. However, the EAC ran the same search in MAUDE and MHRA and found an additional 9 reports on adverse events in the MAUDE database relating to SecurAcath. Most of the events were categorised as device malfunctions. These are listed in Table 3.

The sponsor did not search any databases other than MHRA and MAUDE. However, the clinical evidence search was not limited by outcome and the sponsor states that no studies were excluded (7.3.2).

Table 3: Adverse events reports in the MAUDE database relating to SecurAcath

FDA-MAUDE search (03-Aug-2016)				
	Brand Name and link to report	**Date Report Received (MM/DD/YYYY)**		**Event type**
1	SECURACATH	03/11/2014	*Included in sponsor submission (section 7.7.3) – difficulty removing long-term SecurAcath*	*Other*
2	SECURACATH	12/06/2013	Catheter fractured, used with SecurAcath	Malfunction
3	SECURACATH	12/03/2013	Same event as 1 but more details (patient pain, nurse experience)	No answer provided
4	SECURACATH	10/07/2013	Incorrectly installed SecurAcath device caused catheter rupture	Malfunction
5	SECURACATH	10/07/2013	Same event as 4 but rupture cause is 'unknown'	Malfunction
6	SECURACATH	05/17/2013	Subsequent similar event to 7	Malfunction
7	SECUREACATH	04/09/2013	Ruptured catheter, unclear cause	Malfunction
8	SECURACATH	02/01/2013	Catheter migration due to incorrectly installed SecurAcath device ('operator error')	Malfunction

9	SECURACATH	12/11/2012	Pain caused by removal of SecurAcath device	Malfunction
10	SECURACATH UNIVERSAL	11/05/2010	Cover came off during dressing change	Malfunction

3.8 Description and critique of evidence synthesis and meta-analysis carried out by the sponsor

According to the sponsor a meta-analysis or systematic review was not possible due to scarce literature.

3.9 Additional work carried out by the External Assessment Centre in relation to clinical evidence

For the clinical evidence, the EAC designed and performed an independent systematic review to ensure that all available evidence had been considered. In addition to literature related to the intervention, the EAC expanded the search to include evidence related to the comparators as specified in the scope. The authors of Janssens (2016a) were contacted and an unpublished full-text draft of the results was made available to the EAC. In addition, the EAC reviewed all the studies included by the sponsor. The EAC used the retrieved studies and the studies accepted from the sponsor's submission to perform its own meta-analysis to provide pooled estimates for clinical outcomes between SecurAcath and its comparators. The results of the meta-analysis also contributed to the revised economic model. The EAC critically appraised all studies included in the sponsor's submission and those retrieved in its own systematic review. The sections below describe in detail the additional work carried out by the EAC.

3.9.1 Overview of clinical evidence

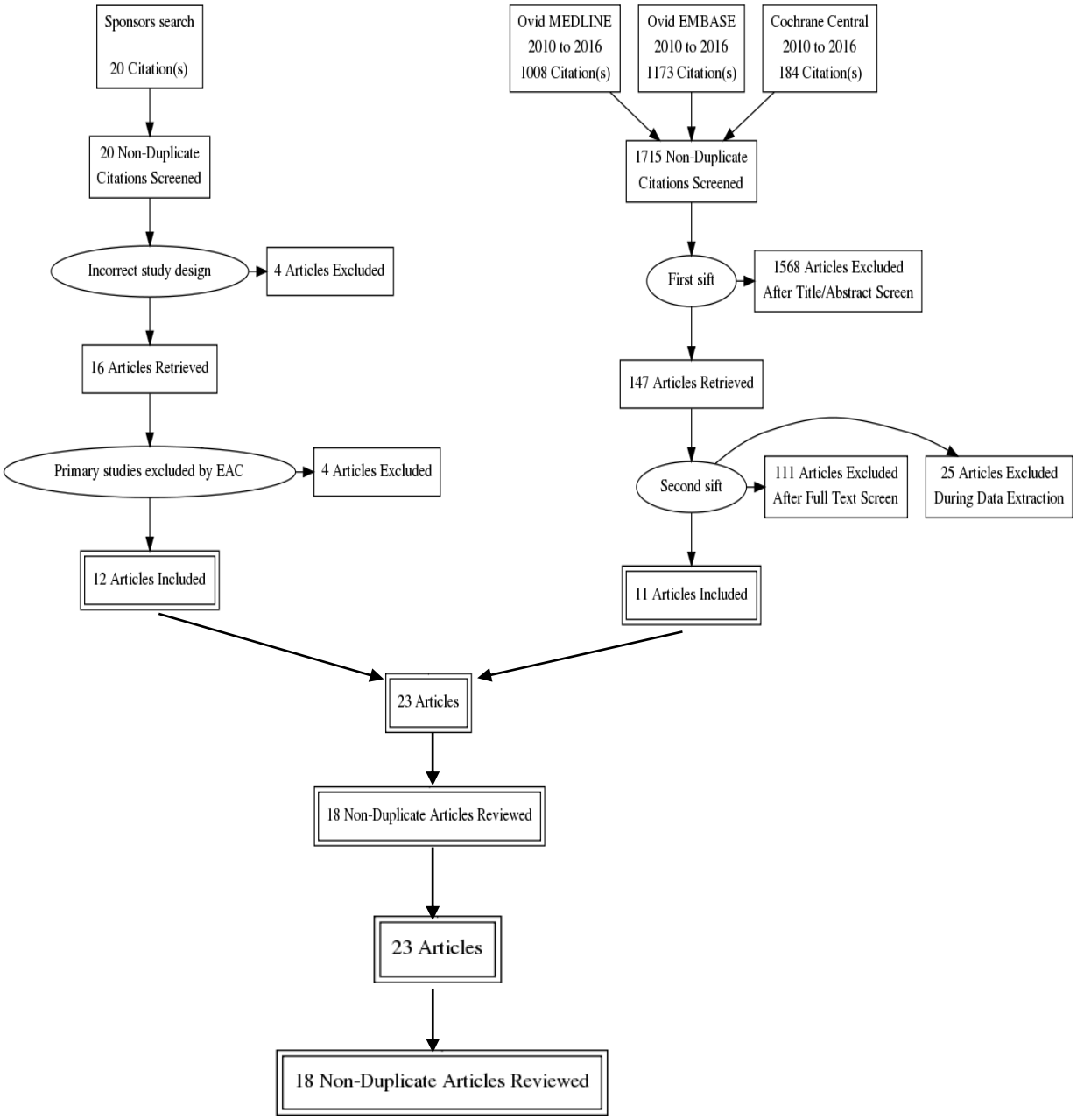
The EAC selected the studies based on the criteria identified in the scope (Table 4). The findings of all the EAC-accepted papers for clinical outcomes studies are presented in Table 5 and Table 6.

Table 4: Selection criteria used by the EAC to identify relevant published studies.

Inclusion criteria	
Population	People who require an intravascular catheter for central venous access
Intervention	The SecurAcath securement device
Comparator	- Adhesive catheter securement devices, such as StatLock or Grip-Lok, or other adhesives (such as steristrips) - Sutures
Outcomes	The outcome measures to consider include: • Rates of catheter migration and dislodgement • Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis • Number of unplanned catheter removals and re-insertions • Time taken to secure catheter • Patient and clinician satisfaction scores • Pain while in situ and on insertion and removal • Quality of life measures • Device-related adverse events eg. catheter malfunction, thrombosis and vessel erosion

Study design	Clinical outcome primary studies Systematic reviews and meta-analysis
Language restrictions	• English language only • Foreign language papers with English abstracts could be included
Search dates	2000 – Current (evidence related to the comparators) 2010 – Current (evidence related to the intervention)
Exclusion criteria	
Population	When studies reflected overlapping populations, the study with the largest population or more up-to-date data were included.
Interventions	SecurAcath used in combination with other securement devices or CICCs catheters that are not standard of care
Comparator	None
Outcomes	Any clinical outcome not specified in the scope
Language	Not English
Study design	Case reports, narrative reviews, letters to the editor, commentaries

Figure 2: PRISMA flow diagram showing the sponsor and EAC's search results



Cordovani 2013

(CICC)

Cordovani and Cooper (2013) investigated (ClinicalTrials.gov Identifier: NCT00903539) adult patients who had CICC placement (mean dwell time of 3.1 days) secured with SecurAcath (N=74); there was no comparator. The primary outcome was device securement success which was reported in 72 patients (97%). Mean catheter securement time was 62.5 seconds. Discomfort scores were measured on a 1-10 scale and mean scores were 1.6 at removal and 0.9 in situ. Of patients with previous experience of a sutured catheter, 14 of 15 found SecurAcath 'as or more comfortable'. 6 out of 8 healthcare professionals found maintenance 'somewhat' or 'much easier' than sutured securement. The authors conclude SecurAcath is a safe and reliable securement device.

Critical appraisal

The study is published as a letter to the editor; as a result, there was limited information available to assess methodological quality. It is a medium-sized multi-centre prospective cohort study without a comparator. Patient characteristics are not reported so it is not possible to assess the population heterogeneity and the effect it may have on internal and external validity. No information is provided on CICC placement and maintenance or regarding the number and training of operators. The 3 different hospitals had different protocols for CICC maintenance which could create unwanted bias. Mean catheter indwelling time was only 3.1 days which limits the suitability of this study to the question of long-term catheterisation. Sample size calculations and CIs are not reported.

Djurcic-Jovan 2016

(PICC)

Djurcic-Jovan et al. (2016) compared PICCs secured with and without SecurAcath in a longitudinal study in a single cohort of patients requiring complex continuing care (N=54). The catheter dwell time was ≥31 days. The primary outcome measure was unplanned catheter reinsertion. Qualitative data were measured retrospectively. Without SecurAcath there were 60 unplanned catheter reinsertions compared to 3 unplanned reinsertions with SecurAcath. Catheter migration rate was 0%. The authors report substantial time savings for nurses and physicians following the introduction of SecurAcath. In terms of qualitative outcomes, catheter stability during maintenance was rated 'very good' or 'good' in 95% of cases; catheter migration was rated 'very good' or 'good' in 88%; ease of dressing was rated 'very good' or 'good' in 95%; and overall use of the device was rated 'very good' or 'good' in 95%.

Critical appraisal

This is a single-centre, Canadian based retrospective observational comparative study published as a poster. It includes a single-cohort and two interventions. 'Migration' of the catheter tip was confirmed by x-ray and the authors present an algorithm for dealing with migrations. There is a radical difference in the primary outcome but the longitudinal nature of the study raises the possibility of bias. There is no information on patient characteristics or data about how the cohort changed over time such as adverse events or comorbidities. There is no information on the insertion/maintenance protocol. The study is primarily about managing PICC migrations and does not focus on SecurAcath.

Dougherty 2013

(PICC)

Dougherty (2013) evaluated PICCs secured with SecurAcath in a one month period (N=30). Qualitative data was gathered from nurses and patients. There was a reduction in malposition and catheter damage and no skin reactions were seen. Nurses reported increased confidence in maintenance but also reported some difficulty removing the device. Patients reported pain at insertion ('if incorrectly placed and the anchor was too superficial') and pain at removal.

Critical appraisal

This is a small, UK-based single-centre prospective evaluation with no comparator, published as a poster. The population is not defined and dwell time is not reported. Although there is no comparator the author describes the use of StatLock 'for over 10 years' but does not give any data on malpositions, catheter damage or maintenance. Data on pain is qualitative and therefore cannot be used for future comparison or generalised. The author mentions a maintenance protocol ('referral letter to district') but there is no detail or information on compliance. The author's attendance at the conference was sponsored by the manufacturer.

Egan 2013/Sansivero 2011

(PICC)

Egan et al. (2013)[4] investigated SecurAcath used in PICC placement in adults with a mean dwell time of 22.6 days. The patient population (n=68) included medical and surgical inpatients, patients in ICU or the transplant unit, and outpatients; there was no comparator in this study. The primary endpoint was device securement success, defined by the absence of device-related

[4] The study by Sansivero 2011 is the same as the Egan 2013 and it is included in the report only for the reporting of the additional outcome of numbers of catheter-related infections for a smaller number of patients (n=50).

malfunctions and adverse events. Secondary endpoints included securement time, patient comfort and ease of maintenance. Securement-related malfunctions were seen in 6 patients (8.8%) with 20 (22.1%) adverse events reported. Mean securement time was 31 seconds. Pain scores were measured on a 0-10 scale, and immediately after device removal the mean pain score was 1.5. In situ mean pain score was 0.7, and 91.2% of patients were either neutral, satisfied or very satisfied. Use of SecurAcath did not influence placement or maintenance techniques. The authors conclude that SecurAcath performs favourably compared to historical data on StatLock reported by Yamamoto et al. 2002 (migration and dislodgement rates of 6% and 12% for StatLock vs. 2.9% and 0% for SecurAcath).

Critical appraisal

This medium sized multi-centre prospective cohort study does not include a direct comparator and the internal validity of the results could be compromised by a heterogeneous population of varying comorbidities, settings and ages. The 3 different hospitals had different protocols for PICC maintenance which could create unwanted bias. The authors note improvement in securement times as the study progressed. However, the authors clearly define ‘dislodgement’ and ‘migration’, in line with Yamamoto et al. (2002), which helps support historical and future comparisons. Sample size calculations and CIs are not reported.

Hill 2014

(PICC)

Hill (2014) carried out a pilot evaluation of SecurAcath for PICC placements (N=60). There was no comparator for this study. The author reported 0% malposition rate and accidental dislodgement in 3.33% (2 patients, both delirious). The author describes dressing changes as being performed by ‘general unit staff, not IV team staff’: SecurAcath gave staff increased

confidence, reduced anxieties and increased efficiencies. The author describes successful use in patients with skin integrity issues, where the device was used without adhesive dressing. The author concludes that patients were satisfied overall.

Critical appraisal

This is a small, Canadian based single-centre prospective pilot evaluation without a comparator, published as a poster presentation. The author does not clearly describe insertion/maintenance protocols and does not provide any information on patient characteristics. 'Malposition' is not clearly defined and dwell time is not reported. Although skin integrity, adhesive dressings and patient satisfaction are all mentioned, there is no quantitative data to analyse. It is difficult to draw any firm conclusions due to the lack of information presented.

Hughes 2014

(PICC)

Hughes (2014) prospectively evaluated PICC placements secured by SecurAcath in adult patients (N=31); there was no comparator. In 45% of cases the mean dwell time was >30 days. The study aimed to establish the device's efficacy and benefits. The author reports 100% successful placement with 11% placed with 'difficulty' and 19% with 'slight difficulty'. Staff reported difficulty with removal 'fairly frequently'. One patient experienced catheter migration of 1cm. Pain scores were measured on a 0-10 scale: at placement pain scores were 0 in all patients, in situ 5 patients' scores were >5, and at removal over half of patients' scores were >3. Three patients had PICC removed due to severe or unresolved pain. The author reports a PICC-related infection rate of 12% (n=31) which was reduced to 2% in a subsequent cohort (n=100).

Critical appraisal

This is a medium sized, single-centre UK based prospective study with no direct comparator. PICCs were placed by 3 individuals (1 placed 79% of PICCs) following one placement policy, which suggests good internal validity. Pain scores are reported for placement, in situ and removal, but the absolute numbers are not recorded consistently. However, the use of a visual analogue score aids future comparisons. The evaluation describes 31 patients but the infection section discusses 100 PICCs subsequently placed with SecurAcath: it is unclear whether or not other outcomes data have been omitted for the subsequent cohort. Sample size calculations and CIs are not reported.

(Anonymous [Misericordia]) 2015

(PICC)

The Parenteral Therapy Team at the Misericordia Community hospital in Canada, evaluated data on PICCs placed without subcutaneous anchor (n=164) during 2013 and PICCs placed with SecurAcath (n=542) during 2014; average dwell time was 29 days. In addition to the SecurAcath the report also evaluated the use of a PICC catheter designed to reduce the number of patients with catheter-related thrombosis (CRT). Six different operators took part in the evaluation. The primary outcomes were CRT, PICC occlusions, catheter malposition, local infection and CRBSI. In the SecurAcath cohort there were no confirmed CRBSIs. From 2013 to 2014 CRT decreased from 3.75% to 3.69%; PICC occlusions increased from 14.35% to 16.97%; malpositions decreased from 10.98% to 1.66%. The authors conclude that without SecurAcath an estimated 60 patients (of 542) would have required catheter replacements.

Critical appraisal

This is an unpublished audit report that includes retrospective comparative data though internal validity is compromised by the longitudinal nature of the comparison (historical control). Patient characteristics are not reported, so it is

not possible to assess the population heterogeneity and the effect it may have on internal and external validity. The comparator is not explicitly mentioned. The study lists several different catheter types (CRT rates were more markedly reduced in a catheter-specific sub-cohort), including those with and without anticoagulant prophylaxis. However, there are no multivariate or propensity matched analyses to account for potential confounding. There is no information on maintenance or securement protocols or the training of staff involved in placing PICCs. Sample size calculations and CIs are not reported.

Zerla 2016

(PICC)

Zerla et al. (2016) investigated adult oncology patients requiring chemotherapy with a PICC in place for more than 2 months, secured with SecurAcath (N=30). The authors regularly collected data on catheter securement, maintenance and complications. The median dwell time was 145 days. Skin integrity issues were seen in 32.17% of patients. Pain scores were measured on a 0-10 scale: at placement pain scores were ≤2 in 90% of patients, in situ ≤2 in 98.7%, and at removal ≤2 in 66.7%. Authors report median maintenance time of 10 minutes for SecurAcath which was compared to a historical cohort which had a median of 20 minutes maintenance time for an adhesive device. No devices were dislodged. The authors conclude that, after effective training, SecurAcath is comfortable for the patient, reduces catheter movements, and is safely indicated in oncology patients with long-term catheterisation and ambulatory maintenance.

Critical appraisal

This single-centre prospective study has no comparator and is probably too small to derive any meaningful data for future comparison. It is published as a poster presentation and a conference abstract; as a result there was limited information available to assess methodological quality. The authors report some baseline characteristics (such as BMI) and the cohort is homogenous.

The study uses the visual analogue scale for pain scores, which is generalisable to future studies. The only outcomes measured are skin integrity and pain scores: it is unclear if other adverse events were unrecorded or omitted. The authors do not report maintenance or securement protocols. Sample size calculations and CIs are not reported.

Stone 2013

(PICC)

Stone et al. (2013) describe PICC placements in paediatric patients with previous skin issues or skin irritation/allergic reaction to standard dressing products, secured with SecurAcath (N=42). The authors compared outcomes to historic data on 17 migrations occurring in the same centre (undefined cohort). In the study cohort, rates of migration, complications, and unplanned catheter removal were all 0%. The authors conclude that further research is required to optimise protocol for dressings in patients with skin integrity issues.

Critical appraisal

This is a prospective single-centre study without a comparator, published as a poster presentation; as a result, there was limited information available to assess methodological quality. It is unclear whether or not the reported improvements in skin patch testing had an influence on the reported migration rates. The authors do not report the dwell time and do not define migration which makes future comparisons difficult.

Janssens 2016b

(PICC)

Janssens et al. (2016b) compared SecurAcath to StatLock in PICCs [redacted]

[redacted]

Critical appraisal

[redacted]

McParlan 2016

(PICC)

McParlan et al. (2016) compared PICCs secured with SecurAcath and StatLock in in a longitudinal study in haematoncology patients. [redacted]

Critical appraisal

[redacted]

Fang 2011

(PICC)

Fang et al. (2011) compared StatLock, tape securement and sutures in PICC placements (N=120). Patients were randomised 1:1:1 and followed throughout

their catheterisation. Average dwell times were 20.1 days for sutures, 18.9 days for tape securement and 21.5 days for StatLock. Outcomes measured were: catheter migration without function loss, catheter dislodgment, catheter-related complications (cellulitis and phlebitis), skin injuries and patient satisfaction. Rates of catheter migration without function loss were higher in the tape group (57.5% vs. 12.5% (suture) vs. 7.5% (StatLock); p<0.001). Dislodgement rates were also higher in the tape group (15% vs. 0% (suture and StatLock); p=0.034). Furthermore, phlebitis rates were higher in the tape group (25% vs. 7.5% (suture; p=0.034) vs. 5% (StatLock; p=0.012). Cellulitis was higher in the suture group (20%) vs. StatLock (2.5%; p=0.034). Skin injury was also higher in the suture group (22.5% vs. 5% (tape; p=0.023) vs. 0% (StatLock; p=0.005). Irritation/pain at securement site was statistically significantly higher in the suture group (52.5%) than in than in the other groups. Patient satisfaction was statistically significantly higher in the StatLock group (90%) than in the other groups. The authors concluded that StatLock is a viable alternative as a securement device: securement effectiveness is as good as suturing and StatLock also reduces complications and skin irritation.

Critical appraisal

This is a single-centre, prospective, randomised controlled trial, set in China and available as an English abstract. There is no mention of a randomisation or concealment protocol. Information on patient characteristics is unavailable and it is unclear whether or not multivariate or propensity matched analyses were undertaken. ANOVA would have made more sense when comparing the 3 groups but the analyses presented give a clear outcome.

McMahon 2002

(PICC)

McMahon (2002) compared PICCs in inpatients secured with sutures and StatLock. A total of 1212 lines were placed, of which 486 lines were secured with sutures during 1999 and 726 lines were placed subsequently with

StatLock during 2001. Outcome measures included rates of unplanned removals due to migration. In lines placed without StatLock there was an unplanned removal rate of 6% (28 of 486), while in the StatLock group the rate was 1.5% (11 of 726). In the conclusion the authors state that they 'do not endorse or renounce any particular product'.

Critical appraisal

This is a single-centre, US based retrospective comparative cohort study. The cohorts are not investigated concurrently so the main outcome is at risk of bias. The cohorts comprise all patients from separate 6-month periods. The authors do not report patient demographic information or catheter dwell time. However, the large sample size increases generalisability. The authors do not provide information on dwell times or insertion/maintenance protocols. However, they mention education and training support for staff which indicates some degree of internal validity. The study has a focus mainly on aspects of PICC placement other than securement, but the relevant outcome (premature removal due to migration) is well defined: 'pulled completely' or 'partial migration out of the superior vena cava'.

Teichgräber 2011

(CICC)

Teichgräber et al. (2011) compared StatLock with suture securement in tunnelled CICC placements for haemodialysis patients (N=72) requiring a catheter prior to arteriovenous fistula creation. Patients were randomised 1:1 and were followed for a mean dwell time of 42 days. The outcomes measured were success and complication rates of catheter placement. There was a 100% placement success rate in both groups. The complication rate in the StatLock group was 8.3% (3) vs. 13.9% (5) for the suture group, which was statistically significant difference. A Kaplan-Meier analysis showed StatLock to have a slight advantage in catheter survival time but it is unclear whether the difference was statistically significant. The authors mention 5 cases requiring

catheter explantation (3 thromboses and 2 catheter displacements) but do not specify the group in which these occurred. There were no catheter-related infections. That authors conclude that StatLock is superior to suture fixation of tunnelled catheters.

Critical appraisal

This is a single-centre, German based prospective unblinded randomised controlled trial. The cohort described is homogenous, comprising only patients in chronic renal failure requiring haemodialysis. Patients received 14.5 Fr catheters of 3 different lengths. The authors do not provide any information on how patients were selected or inclusion/exclusion criteria, which raises the possibility of selection bias. The authors provide a high level of detail on their insertion protocol.

Venturini 2011

(CICC)

Venturini et al. (2011) evaluated CICCs secured with StatLock in haematology patients; median dwell time was 24 days. Patients did not receive prophylactic antibiotics or anticoagulants. A total of 211 short-term CICCs and 5162 catheter days were studied. Outcomes measured were rate of successful catheter placement, dislodgement rate and catheter-related infections. Successful catheter placement occurred in 98% of patients, with premature dislodgement in 1.4% and extravasation in 2%. Exit site catheter-related infection occurred in 7% while there were 3.5 catheter related infections per 1000 days. The authors conclude that StatLock can replace traditionally sutured securement of CICCs.

Critical appraisal

This is a single-centre, Italian based, prospective observation cohort study with no comparator, published as a conference abstract. The cohort includes haematology patients but no further information is provided on patient

characteristics. The authors do not provide information on insertion/maintenance protocols, nor on whether or not the infection rates influenced (or were influenced by) dislodgement or extravasation. In the conclusion the authors state that StatLock reduced complication rates compared to suture fixation, but they do not present any data on the latter group.

Yamamoto 2002

(PICC)

Yamamoto et al. (2002) compared StatLock and suture securement in PICC placement (N=170). Patients were randomised 1:1 with a mean dwell time of 33 days in the StatLock group and 35 days in the suture group. Patients were examined daily or were followed up by phone every other day. The primary endpoint was catheter-related complications. Outcomes data were also available for unplanned removals, migration and catheter-related infection rates. Total PICC complication rates were 71.7% and 49.4% for the suture and StatLock groups, respectively (p=NS). There were no statistically significant differences between the groups for unplanned removals or migration rates. However, confirmed and suspected infection rates were statistically significantly higher in the suture group (12% vs. 2% for StatLock, p=0.032). The authors conclude that StatLock reduces infection rates and needlestick injuries and 'performs as well or better' in preventing dislodgement/migration.

Critical appraisal

This is a single-centre, US based, prospective randomised controlled trial. The concealment protocol is clearly described. Patient characteristics and comorbidity information are clearly presented, with no statistically significant differences between the groups. The authors clearly define migration (movement ≤0.5cm without loss of function) and dislodgement (accidental removal and/or loss of function). Diagnoses of CRBSI, cellulitis and phlebitis

are all also clearly defined. The large number of clinicians involved (25 operators for the suture group, 28 for StatLock) increases the generalisability of the results. The authors discuss the likelihood of under-reporting of adverse events. They report that the study was underpowered, which may indicate that the non-significant outcomes represent type 2 errors. Although the authors conclude that StatLock reduced needlestick injuries, there was only 1 incident in the suture group.

Zerla 2015

(PICC and midline)

Zerla et al. (2015) evaluated midline catheters and PICCs in adult oncology patients secured with StatLock (N=1341). Mean dwell time was 101 days and patients received either PICCs or midline catheters. The main outcome measure was complications, including infections, thromboses and unplanned removals. The authors reported 75 unplanned removals (5.5%): 11 infections (0.8%), 29 thromboses (2.1%) and the remaining 35 removals were reported as ‘mechanical’ (2.6%).

Critical appraisal

This is a single-centre, Italian based retrospective observational cohort study, using data from 2010 to 2013, with no comparator for the securement device. The insertion and maintenance protocol is clearly defined. Information on patient characteristics is limited to catheter indication (primary chemotherapy and total parenteral nutrition). The main focus of the study is not StatLock and although every patient received StatLock it is difficult to draw any firm conclusions. Authors do not clearly define infection – there is not enough information to show whether or not infection, thrombosis and removal rates were influenced by one another.

Table 5: Summary of key points from all studies accepted by the EAC (n=18).

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Cordovani (2013) NCT00903539 Included by the sponsor	Prospective cohort study, multi-centre Canada. Mean dwell time = 3.1 days	74 adults requiring a 7Fr CVC in the internal jugular vein CICCs 7Fr size	SecurAcath No comparator	Catheter dislodgement Patient satisfaction Pain scores Device-related adverse events	Medium One of 3 published full-texts found in the literature, however, this was published as letter to the editor. The study design is prospective with a medium size population, however, no detail provided about population characteristics (cannot tell if population produces a bias). There was no comparator. The dwell time reported appears to be short term, whereas, the literature tends to report medium to long term dwell times. Therefore, results from this study may be less comparable. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Djurcic-Jovan 2016 Included by the sponsor	Single-centre retrospective comparative cohort (Canada) Dwell time not reported (>31 days?)	Complex continuing care patients (n=54) PICCs	SecurAcath StatLock	Unplanned catheter removals	Low The study compares SecurAcath and its main competitor (StatLock) but the outcomes are unclear. The study is published as a poster presentation.
Dougherty 2013 Included by the sponsor	Single-centre prospective evaluation (UK) Dwell time not reported	Inpatients and outpatients (n=30) PICCs	SecurAcath No comparator	Clinician and patient satisfaction Pain scores	Low This is a non-comparative study reporting only qualitative data. The sample size is very small. The study is published as a poster presentation.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Egan (2013) Included by the sponsor	Prospective cohort study, multi-centre, United States. Mean dwell time = 22.6 days	68 adults including medical and surgical inpatients, patients in ICU or transplant unit, and outpatients. PICCs 5Fr size	SecurAcath No comparator	Dislodgement Migration Unplanned catheter removals CRBSI Patient satisfaction Pain scores	Medium. This study is prospective and has a medium sample size. There was no within study comparator. It provides data on a number of relevant outcomes. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Hill 2014 Included by the sponsor	Single-centre prospective evaluation (Canada) Dwell time not reported	Inpatients (n=60) PICCs	SecurAcath No comparator	Dislodgement Clinician and patient satisfaction	Low This is a non-comparative study reporting a limited number and unclear set of outcomes. The study is published as a poster presentation. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Hughes (2014) Included by the sponsor	Prospective cohort study, single centre UK. Mean dwell time not specified.	31 adults diagnosed with cancer PICCs 4Fr (96%) and 5Fr (4%) size	SecurAcath No within study comparator	Dislodgement Migration Catheter-related infection Clinician and patient satisfaction Pain scores	Medium This is a UK study, therefore, results are potentially more applicable in NHS settings. There was no within study comparator, however some results are compared with previous practice (securement involving wound closure strips and an adhesive securement device). The mean dwell time is unspecified, however, a figure in the publication indicates that most patients had an indwelling catheter > 30 days Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Janssens (2016b) NCT02311127 Included by the EAC and the sponsor	Randomised, controlled trial, single centre, Belgium. [redacted]	105 adults 1:1 randomised PICCs 4-6Fr size	SecurAcath StatLock	Dislodgement Migration Catheter-related infection Unplanned catheter removals Patient satisfaction Pain scores Device-related adverse events	Medium/High This is only full text RCT found in the literature, however it is an unpublished pre-peer review draft. [redacted] Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Anonymous (2015) Included by the sponsor	Audit report, single centre, Canada. Mean dwell time = 29 days	706 patients PICCs	SecurAcath (n=542) PICC with no subcutaneous anchor (n=164) (comparator is unclear)	Dislodgement Catheter-related infection Thrombosis Catheter-related adverse events	Low This is an unpublished audit report that includes retrospective comparative data. No methodology is described therefore study design is unclear. The comparator is not explicitly mentioned. Though, relative to other studies included, the population size is large, there is no description of its characteristics. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
McParlan 2016 Included by the sponsor and the EAC	[redacted]	Haematoncology patients [redacted] PICCs	SecurAcath (n= [redacted] StatLock [redacted]	[redacted]	Medium The study compares SecurAcath and its main competitor (StatLock) in a UK-based setting. [redacted] The study is published as a poster presentation. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Stone (2013) Included by the sponsor	Prospective cohort study, single centre, United States. Mean dwell time not specified.	42 children with previous skin issues or skin irritation/allergic reaction to standard dressing products PICCs	SecurAcath No within study comparator	Catheter migration and dislodgement Catheter-related infection Number of unplanned catheter removals and re-insertions Device related adverse events	Low This is a poster presentation therefore there is limited information to assess methodological quality. Dwell time was not reported and no definition of migration was provided, therefore it may be challenging to compare outcomes with other studies. An unclear comparison with historical data is made (it is unclear for example, which device was used and how many PICC insertions were carried out). The study was funded by the manufacturer. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Zerla 2016 Included by the sponsor	Prospective cohort study, single centre Italy. Median dwell time 145 days (presentation describes "observation days").	30 adults diagnosed with cancer PICCs 4-5Fr size	SecurAcath No within study comparator	Catheter dislodgement Pain scores	Low This is a PowerPoint presentation and abstract, therefore limited information is available to assess methodological quality. There was no within study comparator, however, some historical comparisons were made with historical data (securement using StatLock). However, the historical data are not appropriate as an accurate basis for comparison. For example, the authors compare 63 dislodgements in 1111 PICC insertions with StatLock (presumably), and compare this with a 0% dislodgement found in 30 patients with SecurAcath PICC securement. The only outcomes measured a priori appear to be skin integrity and pain scores: it is unclear if other adverse events were unrecorded or omitted Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Fang 2011 Included by the EAC	Single-centre prospective RCT (China) Average dwell times were 20.1 days for sutures, 18.9 days for tape securement and 21.5 days for StatLock.	Inpatients (n=120) PICCs 4Fr size	StatLock (n=40) Suture (n=40) Tape (n=40)	Catheter dislodgement and migration Catheter-related complications (thrombophlebitis) Number of unplanned catheter removals and re-insertions Patient satisfaction Pain scores Device-related adverse events	Medium The study compares SecurAcath's main competitor (StatLock) with two other securement methods (suturing and tape). It provides data on a number of relevant outcomes. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
McMahon 2002 Included by the EAC	Single-centre retrospective comparative cohort (US) Dwell time not reported	Inpatients (n=1212) PICCs 5Fr size	StatLock (n=726) Suture (n=486)	Catheter dislodgement	Low The study compares SecurAcath's main competitor (StatLock) with another securement method (suturing), but only one relevant outcome is reported. The two cohorts were not studied concurrently. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Sansivero 2011 Included by the EAC	Single-centre Mean dwell time was 19.08 days	50 adult patients PICCs 5Fr size	SecurAcath No within study comparator	Catheter-related infections	Low. This study has overlapping population with Egan 2013. There was no within study comparator. Study was included in the EAC's evidence synthesis.
Teichgräber 2011 Included by the EAC	Single-centre prospective RCT (Germany) Mean dwell time 42 days	Haemodialysis patients (n=72) CICC 14.5Fr size	StatLock (n=36) Suture (n=36)	Catheter dislodgement and migration Catheter related infections Number of unplanned catheter removals and re-insertions Thrombosis	Low The study compares SecurAcath main competitor (StatLock) with another securement method (suturing); the outcomes data are poorly defined and the sample size is small. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Venturini 2011 Included by the EAC	Single-centre prospective observational cohort (Italy) Median dwell time 24 days	Haematology patients (n=211) CICC	StatLock No comparator	Catheter dislodgement Catheter related infection Device-related adverse events	Low This is a non-comparative study which does not include SecurAcath. It is published as a conference abstract and many of the outcomes are not clearly defined. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Yamamoto 2002 Included by the EAC	Single-centre prospective RCT (US) Mean dwell time: 33 days in the StatLock group, 35 days in the suture group	Adult inpatients and out patients (n=170) PICCs	StatLock (n=85) Suture (n=85)	Catheter dislodgement and migration Unplanned removal Catheter-related infection including suspected and confirmed CRBSI Venous thrombosis Clinician satisfaction Device-related adverse events	Medium The study compares SecurAcath's main competitor (StatLock) with another securement method (suturing); it provides clear data for StatLock on a number of important variables. Study was included in the EAC's evidence synthesis.

Study	Study design (country) Follow up	Population	Intervention and/or comparators	Outcomes considered	Usefulness to decision problem
Zerla 2015 Included by the EAC	Single-centre, retrospective observational cohort (Italy) Mean dwell time 101 days	Adult oncology patients (n=1341) PICCs and midline catheters 4Fr size	StatLock No comparator	Catheter-related infection Number of unplanned catheter removals and re-insertions Venous thrombosis	Low This is a non-comparative study which does not include SecurAcath. Outcomes are not clearly defined and the main focus of the study is not securement. Study was included in the EAC's evidence synthesis.

Table 6: Clinical outcome results from Sponsor and EAC accepted studies (n=18)

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Cordovani (2013) NCT00903539 Included by the sponsor	2 patients experienced catheter dislodgement, attributed to improper coupling of the two device components	NA	NA	NA	Fourteen of the 15 patients with previous CVC or PICC experience considered SecurAcath to be as or more comfortable than a sutured catheter. Six of the 8 healthcare professionals	Discomfort analogue score (scale 1-10) during device use and at removal was 0.9 (1.6) and 1.6 (2.1), respectively.	There was no device-related adverse events	Mean 3.1 days	CVC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
					thought that maintenance of the device site was somewhat or much easier than with a sutured catheter, and all stated they would recommend this device to other professional colleagues.				

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Djurcic-Jovan 2016 Included by the sponsor	NA	NA	6.66% (3/45) SecurAcath 100% (60) comparator	NA	NA	NA	NA	31 days	PICC
Dougherty 2013 Included by the sponsor	NA	NA	NA	NA	Nurses more confident about dressing changes	Reported pain if anchor placement too superficial; pain at removal (not quantified)	NA	Not reported	PICC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Egan (2013) Included by the sponsor	Catheter migration = 2 patients within the securement device (2.9%) There was 1 catheter dislodgment	1 bloodstream infection	Unscheduled removal for any reason = 20.6% (14) of patients specific reasons: suspected or confirmed bloodstream infections (n = 4), patient removal of own catheter (n= 4), pain (n = 2), dislodgment (n = 1), catheter	0%	Overall satisfaction = 91.2% (52/57) patients responding were either neutral, satisfied, or very satisfied, and 84.2% (48) were either satisfied or very satisfied.	The mean pain score immediately after device removal in 57 patients was 1.5 - 2.5 (range, 0-10). Five people reported pain at anchor securement site (presumably		22.6±36.0 days (range, 0-228 days)	PICC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
			kinking (n = 1), a 7 Fr SecurAcath used in error with a 5 Fr catheter (n = 1), and SecurAcath lid lost during home dressing change (n = 1).			while it was in situ).			

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Hill 2014 Included by the sponsor	3.33% (2) accidental dislodgement, both delirious patients	NA	NA	NA	Overall satisfaction (patients) Increased staff satisfaction (confidence, efficiencies and reduced anxiety)	NA	NA	Dwell time not reported	PICC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Hughes (2014) Included by the sponsor	1 patient (3%) experienced catheter migration No (0%) cases of catheter dislodgement were reported	Catheter-related infection = 2%	NA	NA	83% of the patients were very satisfied with the device 70% were placed with ease, 19% with slight difficulty and 11% with difficulty Device removal caused the most dissatisfaction among staff. Difficulty with removal was experienced fairly frequently and patients were	No patients reported any pain during placement. 50% of the patients had a pain score > 3 24% of the patients had between 6-10	NA	In 45% of the cases dwell time was < 30 days	PICC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Janssens (2016b) NCT02311127 Included by the sponsor as abstract and as a full text by the EAC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	PICC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Anonymous (2015) Included by the sponsor	1.66% (4) SecurAcath, dislodgement10.98% (18) comparator, dislodgement	Catheter-related bloodstream infection (CRBSI) = 0%	NA	1.7% (4 of 229)	NA	NA	PICC occlusions = 16.97% (n=92)	Mean dwell time = 29 days	PICC
McParlan 2016 Included by the sponsor and the EAC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	PICC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Stone (2013) Included by the sponsor	0%	0%	0%	NA	NA	NA	0%	Mean dwell time not specified.	PICC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Zerla 2016 Included by the sponsor	0%	NA	NA	NA	NA	98.7% pain score ≤2 at maintenance [in situ] 90% pain score ≤2 at insertion 66.7% ≤2 pain score at removal (Numerical Pain Intensity Score)	NA	Median 145 days	PICC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Fang 2011 Included by the EAC	7.5% (3) StatLock, migration 12.5% (5) suture, migration 57.5% (23) tape 15% (6) tape, dislodgement .	Thrombophlebitis: 5% (2) StatLock 7.5% (3) suture 25% (10) tape	0% StatLock 0% suture 15% (6) tape	NA	Satisfaction was 90% for StatLock, statistically significantly higher than the other groups	52.5% (21) suture group had pain at secure site, statistically significantly more than the other groups	Skin injuries: 0% StatLock 22.5% (9) suture 5% (2) tape	Average dwell times were 20.1 days for sutures, 18.9 days for tape securement and 21.5 days for StatLock	PICC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
McMahon 2002 Included by the EAC	1.5% (11/726) StatLock 6% (28/486) comparator	NA	NA	NA	NA	NA	NA	Dwell time not reported	PICC
Sansivero 2011 Included by the EAC	NA	0%	NA	NA	NA	NA	NA	Mean 19.08 days	PICC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Teichgräber 2011 Included by the EAC	0% StatLock 5.5% (2) suture	0% (both groups)	0% StatLock 5.5% (2) suture	StatLock 5.5% (2 of 36) Suture 2.7% (1 of 36)	NA	NA	NA	Mean dwell time 42 days	CVC
Venturini 2011 Included by the EAC	1.4% (3) dislodgement	7% (14) exit site infections (3.5 per 1000 catheter days)	NA	NA	NA	NA	2% (4) extravasation	24 days (1 to 106)	CVC

Study	Rates of catheter migration and dislodgement	Rates of catheter-related infection, including catheter-related bloodstream infection (CRBSI), local infection/inflammation and thrombophlebitis	Number of unplanned catheter removals and re-insertions	Thrombosis	Patient and clinician satisfaction scores	Pain while in situ, on insertion and removal	Device-related adverse events	Dwell time (short term: ≤10 days medium term: 11-29 days long term: ≥30 days)	CVC or PICC
Yamamoto 2002 Included by the EAC	Migration without loss of function: 5.8% (5) StatLock 10.6% (9) suture Dislodgement: 11.7% (10) StatLock 14.1% (12) suture	Confirmed CRBSI: 1.2% (1) StatLock 9.4% (8) suture	24% (20) StatLock 36% (31) suture	StatLock 1.1% (1 of 85) Suture 1.1% (1 of 85)	Securement ease/satisfaction scores (operators): 7.0/7.1 StatLock 7.2/7.3 suture	NA	Total PICC complications: 49.4% (42) StatLock 71.7% (61) suture	33 ± 42 days StatLock 35 ± 38 days suture	PICC
Zerla 2015 Included by the EAC	NA	11 infections	75 removals	29 thromboses	NA.	NA	NA	Mean 101 days	PICC and Midline

3.9.2 Evidence synthesis and meta-analysis performed by the EAC

Clinical evidence and outcomes for meta-analysis

Of the 8 outcome categories included in the scope, a meta-analysis was deemed appropriate for 5 outcomes that were considered to be objective. These were:

- migration
- dislodgement
- catheter-related infection
- CRBSI
- unplanned removals/reinsertions

Eight studies (Cordovani 2013, Egan 2013, Hill 2014, Hughes 2014, McParlan 2016, Anonymous 2015, Stone 2013, Zerla 2016) included by the sponsor and 8 studies (Fang 2011, Janssens 2016b, McMahon 2002, Sansivero 2011, Teichgräber 2011, Venturini 2011, Yamamoto 2002, Zerla 2015) included by the EAC were included in the meta-analysis. The EAC concluded that despite the limitations associated with evidence submitted as conference abstracts these studies could contribute to the decision problem and provide data for synthesis in the EAC's meta-analysis by providing at least an indication of the difference in clinical outcomes between SecurAcath and its comparators.

Methods for meta-analysis

The included studies were reviewed and outcome data were extracted. Raw values were calculated based on available study data. Randomized controlled trials (RCTs) that compared SecurAcath with a comparator were considered as the best quality evidence available (N=1). Relative risks and 95% confidence intervals were calculated for each required RCT outcome using the Cox-Hinckley-Miettinen-Nurminen method for small samples (Miettinen 1985).

For all non-RCT studies that did not directly compare SecurAcath with StatLock, a pooled relative risk could not be calculated. The fixed effects

pooled proportions and 95% confidence interval were calculated for all studies by intervention and outcome separately.

The following outcome measures were considered for inclusion according to availability of data: catheter migration, catheter dislodgement, total catheter-related infection, catheter-related bloodstream infection (CRBSI), unplanned catheter removals and unplanned catheter reinsertions.

There were too few studies to explore publication bias. Similarly, subgroup analyses were not possible due to insufficient data. All analyses were conducted using Stata v 12.0.

Results

Table 7 gives the randomized controlled trial estimates for migration, dislodgement, total catheter infection and CRBSI. The estimates are rather imprecise due to the relatively small sample size. Further, the study was not published in the peer-reviewed literature and so its quality cannot be assured. However, these data represent the 'best' quality evidence available.

Table 7: Randomized controlled trial of SecurAcath versus comparator (StatLock)

Reference	Outcome	SecurAcath results n/N (percent)	StatLock results n/N (percent)	Individual relative risk SecurAcath/StatLock (95% CI)
Janssens 2016b	migration	[redacted]	[redacted]	[redacted]
Janssens 2016b	dislodgement	[redacted]	[redacted]	[redacted]
Janssens 2016b	total catheter infection	[redacted]	[redacted]	[redacted]
Janssens 2016b	CRBSI	[redacted]	[redacted]	[redacted]

Table 8 shows the study pooled estimates by intervention and outcome. As with estimates in Table 7, these estimates are imprecise as shown by the wide confidence intervals. The full data available are reported in Table 9 for reference.

Table 8: Pooled estimates with 95% confidence interval for proportions from all studies of SecurAcath and/or a comparator

Outcome	Intervention	No. of studies	Proportion (as percent)	95% CI (as percent)
Migration	SecurAcath	3	4.00%	1.48, 8.50%
	StatLock	4	4.72%	2.28, 8.50%
	Suture	2	11.20%	6.26, 18.08%
Dislodgement	SecurAcath	9	0.59%	0.30, 1.03%
	StatLock	7	4.07%	3.29, 4.97%

Outcome	Intervention	No. of studies	Proportion (as percent)	95% CI (as percent)
	Suture	3	8.70%	4.84, 14.16%
Total catheter infections	SecurAcath	5	0.77%	0.28, 1.66%
	StatLock	6	1.64%	1.10, 2.35%
	Suture	3	6.83%	3.46, 11.90%
CRBSI	SecurAcath	2	1.68%	0.20, 5.94%
	StatLock	2	1.47%	0.18, 5.21%
	Suture	na		
Unplanned removals	SecurAcath	3	15.53%	10.31, 22.06%
	StatLock	na		
	Suture	na		
Unplanned reinsertions	SecurAcath	1	0%	0, 8.41%*
	StatLock	na		
	Suture	na		

'na' denotes estimates are not available

* 95% confidence interval is one-sided

Table 9: Summary of outcome data for all studies

Included	References	No. migration	No. dislodgement	No. total catheter infection	No. CRBSI	No. unplanned removals	No. unplanned reinsertions	Total population
	SecurAcath							
Sponsor	Cordovani 2013		2					74
Sponsor	Egan 2013	2	1		1	14		68
Sponsor	Hill 2014		2					60
Sponsor	Hughes 2014	1	0	4				31
EAC	Janssens 2016b	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
Sponsor and EAC	McParlan 2016		[redacted]					[redacted]
Sponsor	Anonymous 2015		4	0				542
EAC	Sansivero 2011			0				50
Sponsor	Stone 2013		0	0			0	42
Sponsor	Zerla 2016		0			0		30
	StatLock							
EAC	Fang 2011	3	0	2				40

Included	References	No. migration	No. dislodgement	No. total catheter infection	No. CRBSI	No. unplanned removals	No. unplanned reinsertions	Total population
EAC	Janssens 2016b	[redacted]	[redacted]	[redacted]	[redacted]			[redacted]
EAC	McMahon 2002		11					726
Sponsor and EAC	McParlan 2016		[redacted]					[redacted]
EAC	Teichgräber 2011	0	0	0				36
EAC	Venturini 2011		3	14				211
EAC	Yamamoto 2002	5	10	1	1			85
EAC	Zerla 2015			11				1341
	Sutures							
EAC	Fang 2011	5	0	3				40
EAC	Teichgräber 2011		2	0				36
EAC	Yamamoto 2002	9	12	8				85

3.10 Conclusions on the clinical evidence

The EAC considers that the sponsor's systematic review was not comprehensive; however, the sponsor did identify the majority of the studies related to SecurAcath. From the 16 primary studies on clinical outcomes and 4 narrative reviews included by the sponsor, and after excluding overlapping cohorts, the EAC agreed with the inclusion of 10 primary studies, only 3 of which were full text publications. One of the abstracts representing the only RCT evidence on SecurAcath, was subsequently substituted by the unpublished full-text draft

Clinical evidence was provided on the intended intervention and 1 of the comparators specified in the scope and covered all of the outcomes listed in the scope with the exception of quality of life. The sponsor did not perform a full methodological quality assessment of the evidence. The sponsor argued that regardless of the design methodology used, and whilst the data presented may not have been submitted for peer reviewed publication, all observational prospective clinical evaluations resulted in the clinicians adopting the device and incorporating it into their routine clinical practice. The EAC notes however, although the majority of the sponsor's submitted evidence seems to be independent research not funded by the manufacturer, it consists mainly of conference abstracts, some published as early as 2012. These abstracts never resulted in full-text publications, potentially reflecting poor methodological quality and also the possibility of publication bias. Hence the sponsor's interpretation of the available clinical evidence does not provide a fair assessment of the strengths and weaknesses of the studies submitted.

The sponsor did not perform a meta-analysis of the submitted evidence. The EAC performed its own systematic review and a meta-analysis. The EAC's systematic review resulted in the inclusion of 18 clinical outcomes studies, of which 10 had been included by the sponsor. The additional studies retrieved by the EAC were evidence relating to SecurAcath (2 studies) and the

comparators (6 studies). The EAC concluded that despite the limitations associated with evidence provided as conference abstracts these studies could contribute to the decision problem and provide data for synthesis in the EAC's meta-analysis by providing at least an indication of the difference in clinical outcomes between SecurAcath and its comparators.

Based on the sponsor's submitted evidence and the EAC's additional systematic review and evidence synthesis the conclusion is that there is a lack of data on direct comparison of SecurAcath with the comparators listed in the scope. The most relevant evidence to the decision problem is the unpublished RCT results. Janssens (2016b) showed that [redacted]

The EAC's meta-analysis supports the findings of the RCT. With the exception of dislodgment, the 95% confidence intervals (CIs) for migration, total catheter-related infections and CRBSIs are similar between SecurAcath and StatLock. The majority of the observational studies report higher pain scores during device removal in comparison with device placement and in-situ. The most relevant study for UK practice reporting pain scores (Hughes 2014) states that device removal caused the most dissatisfaction among staff and patients were complaining of pain or discomfort.

Comparative evidence and the EAC's meta-analysis of non-comparative evidence suggests that both SecurAcath and StatLock are superior to sutures for migration, dislodgment, total catheter-related infections and CRBSIs.

However, it should be noted that this evidence relates to people requiring PICC lines for which currently sutures are not standard of practice.

The EAC concludes that there is insufficient evidence to determine that SecurAcath is clinically superior in effectiveness and adverse events to StatLock. There is some evidence that SecurAcath is non-inferior in effectiveness and side effects profiles to StatLock.

There is some evidence to suggest that both SecurAcath and StatLock are superior to sutures, however, this evidence is from a population requiring PICC lines, for which suturing is not relevant to clinical practice.

There is insufficient information to compare the effectiveness and safety of SecurAcath with its comparators in terms of the subgroups specified in the scope.

4 Economic evidence

4.1 Published economic evidence

Critique of the sponsor's search strategy

The sponsor submitted a search strategy intended to retrieve health economic and cost literature relevant to the scope. The sponsor searched 2 databases: PubMed and Embase. The search strategy, inclusive of Boolean operators, was described by the sponsor as follows: (PICC OR CVC) AND (economic# OR cost#) AND (securement device). No unpublished sources of information were included by the sponsor in this section.

The EAC reviewed the sponsor's search strategy and concluded that it was insufficient. First, the number of databases included was not satisfactory. For example, no HTA databases were included such as the Cochrane databases: Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment Database (HTA), NHS Economic Evaluation Database (NHS EED).

Second, the search strategy was too narrow. The scope included the comparators adhesives (such as steristrips) and sutures in addition to securement devices (StatLock or Grip-Lok). The search strategy is unlikely to find evidence relating to these comparators.

Third, the search terms used were too limited. Full terms should have been included as well as the abbreviations (PICC and CVC or CICC). Alternative terms for securement should have been included such as stabilisation.

Given these concerns, the EAC undertook a new search for economic evidence related to the technology and comparators. The databases searched were Medline, Embase and all Cochrane databases. The full search strategies can be found in Appendix 1. The EAC employed the same search strategy as was used for the clinical review, but with additional search terms related to health economics.

Critique of the sponsor's study selection

The Inclusion criteria applied by the sponsor included the following:

- Population: Patients who require an intravascular catheter for central venous access (PICC or CVC) and have had catheter securement devices in place
- Interventions: Catheter securement device; must be comparative
- Outcomes: costs (comparative)
- Study design: Cost comparison of at least 2 securement options (Cost-Effective Analysis, Meta-Analysis, Economic Analysis, Cost-Impact Analysis, Cost Consequences, Cost Minimization)

The sponsor applied the following exclusion criteria: not English language, no costs reported or no comparison of costs.

After reviewing the inclusion and exclusion criteria, the EAC determined that most of them were appropriate. However, the inclusion criterion limiting interventions to securement devices risked excluding securement with Steristrips, tape or sutures, which is not consistent with the scope.

The search undertaken by the EAC employed the same criteria but with a wider set of comparators to match the scope. An additional exclusion criterion was added: studies reporting on catheters placed in locations other than central venous access (e.g. peripheral intravenous catheters).

Included and excluded studies

The sponsor's initial search of PubMed and Embase yielded two articles. Following this the sponsor used the PubMed "related articles" feature. A total of 297 articles were retrieved and after screening three studies were included. The three studies are Bausone-Gazda et al. (2010), Reynolds et al. (2015) and Tuffaha et al. (2014).

After full text inspection it was decided by the EAC that none of these studies satisfied the sponsor's inclusion criteria or the population specified in the scope. Specifically, none had a population of patients requiring an intravascular catheter for central venous access. Bausone-Gazda et al. (2010) explicitly concerns securement of peripheral intravenous catheters. Tuffaha et al. (2014) concerns peripheral arterial catheters and does not mention central venous access or intravascular catheters. Although Reynolds et al. (2015) contains some discussion of central venous catheters, the key inclusion criterion was patients with scheduled elective surgery requiring an arterial catheter. The results of the EAC search are summarised in **Error! Reference source not found.**.

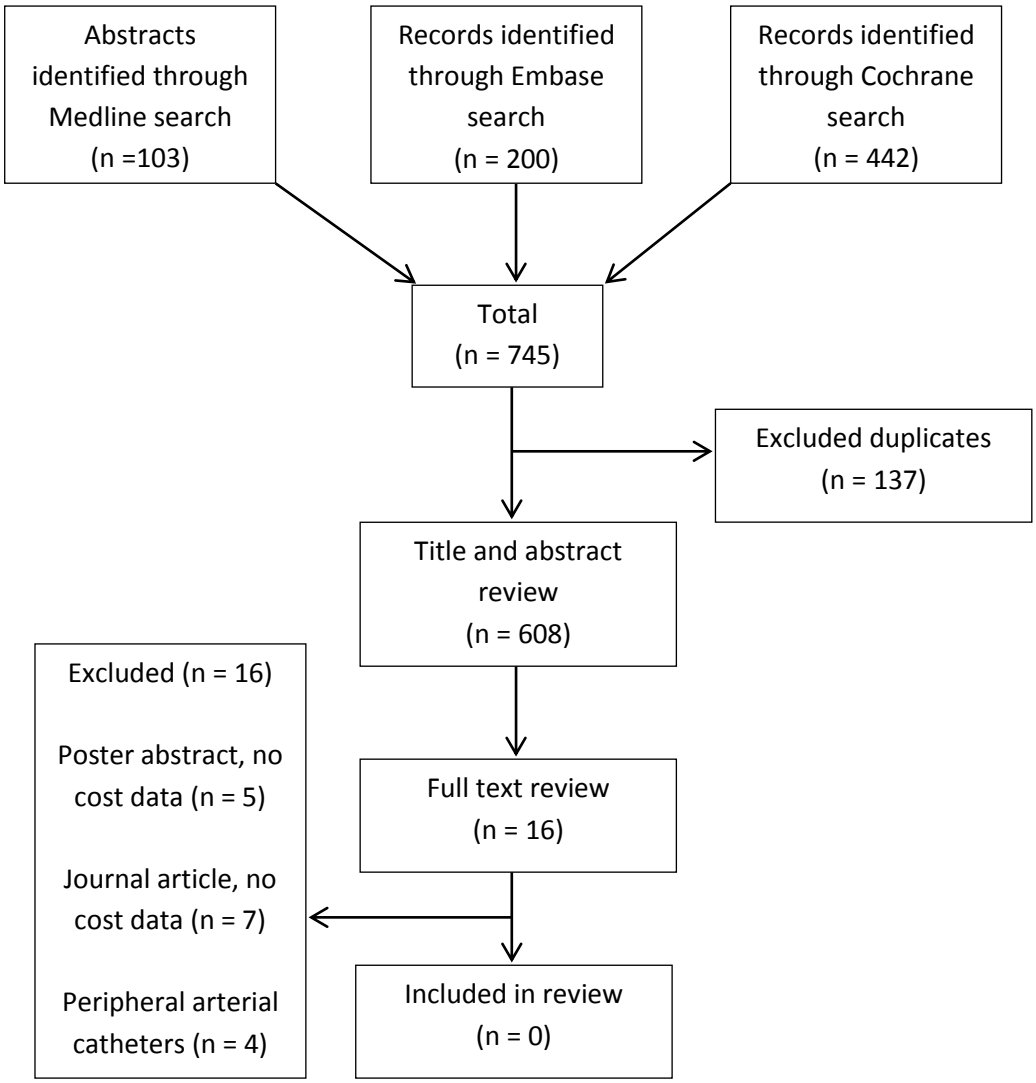


Figure 3: PRISMA flow diagram showing EAC search results

The EAC screened a total of 608 abstracts after removing duplicates. Sixteen of these were full text reviewed and all 16 were excluded because they contained no cost data (12) or concerned the wrong population. Bausone-Gazda et al. (2010) and Tuffaha et al. (2014) were retrieved by the search. Reynolds et al. (2015) was not. Three studies for full text review mentioned SecurAcath. In conclusion, no studies were found that satisfied all inclusion and exclusion criteria.

Overview of methodologies of all included economic studies

The EAC found no studies concerning the health economic aspect of the scope.

Overview and critique of the sponsor's critical appraisal for each study

The sponsor used tables to assess the quality of the 3 included studies. This was done to a reasonable standard. However, as previously noted the EAC judged that these studies were not relevant to the scope.

Does the sponsor's review of economic evidence draw conclusions from the data available?

The sponsor does not draw any conclusions from the economic evidence, but they do note that there are very few economic studies concerning securement devices for central venous access. The EAC did not find any relevant economic evidence during the systematic review.

4.2 De novo cost analysis

The sponsor submitted a de novo cost analysis using a decision tree to estimate costs associated with placement of PICC lines or CVC lines, maintenance and complications that might reasonably be influenced by the choice of securement device.

Patients

The population specified by the scope includes both adults and children receiving a PICC or CVC line. The scope specifies a number of subgroups: patients receiving a PICC line; patients receiving a CVC line; children; patients with comorbidities; patients with medium or long dwell times. It provides separate cost analyses for patients receiving a PICC line and patients receiving a CVC line. The sponsor's submission assumes a dwell time of 25 days for PICC lines and 3 days for CVC lines. The sponsor's submission does not explicitly consider children or patients with comorbidities.

The EAC considered separate evaluations of costs in patients receiving a PICC line and those receiving a CVC line as appropriate. The EAC considered the assumptions on dwell times for catheters as conservative with respect to the cost analysis. Consequently, the addition of sensitivity analysis considering medium or long dwell times would be very unlikely to change the inference arising from the analysis. The EAC considered it unlikely that sufficient data would be available to support a sensitivity analysis specifically addressing catheter securement in children or in patients with comorbidities. The EAC anticipated the possibility that youth or comorbidities would influence the rate of CRBSI. The EAC anticipated the possibility that youth or dementia would influence the rate of dislodgement by patients. The EAC regarded a sensitivity analysis on the parameters for the rate of CRBSI and the rate of dislodgement as sufficient to address concerns regarding the cost implications of the use of SecurAcath in children or patients with comorbidities. The sensitivity analysis undertaken in the sponsor's submission only partially addressed these concerns.

Technology

The technology under consideration is a novel attachment device for catheter lines consisting of a nickel anchor and a plastic flange to which the catheter is attached. The anchor is inserted subcutaneously providing a secure attachment for the catheter line. The flange can be lifted to allow cleaning around the catheter entry point without the need to remove the securement device and risk dislodgement of the catheter. Once therapy is completed the device can be removed with a 'sharp tug'. The device is intended for the securement of PICC and CVC lines in adults and children.

Comparator(s)

Traditional methods of securement of PICC and CVC lines include suturing and the use steristrips or adhesive tape. Suturing generates possible additional risks of CRBSI for patients and needlestick injuries for professionals. More recently a number of adhesive devices have been developed to replace sutures or steristrips/tape, of which StatLock is the most

commonly used. These devices adhere to the skin and hold the catheter in place. The devices need to be removed and replaced on a weekly basis to allow cleaning of the catheter entry site and minimise the risk of infection. During this time the catheter line is unsecured which poses an additional risk of dislodgement.

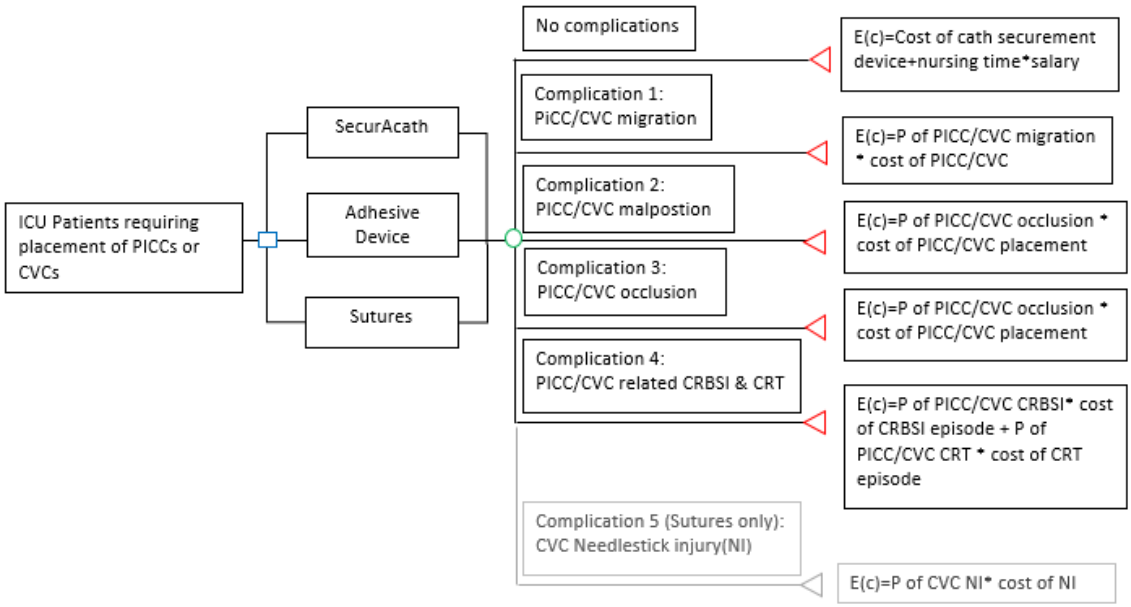
The sponsor's submission provides a comparison of SecurAcath with StatLock for PICC lines and a comparison of SecurAcath with sutures for CVC lines. No comparison with tape or steristrips is provided. The scope specifies adhesive devices (such as StatLock), sutures and Steristrips or adhesive tape as comparators for SecurAcath. The EAC decided that the manufacturer's submission had not fully addressed the specified scope in failing to include adhesive devices in particular as a comparator to SecurAcath for the securement of CVC lines.

Model structure

The sponsor's submission utilises decision trees to estimate costs associated with the choice of securement device. A decision tree does not allow the modelling of events over time. Instead, the likelihood of events occurring is reduced to a single probability over the course of the episode modelled. The decision trees in the sponsor's submission are replicated in the figure below. (Note: the diagram is reproduced from the submission including apparent typographical errors). The decision trees illustrate a comparison of SecurAcath with sutures or adhesive device for securement of either PICC or CVC lines. The submission further limits the comparators as noted above. Each comparison is composed of a very simple decision tree for each complication and a scenario of no complications whatsoever. For each complication, the expected cost is obtained by calculating the product of the probability of complication and the cost. There will be a probability of the particular complication not occurring but this arm is cancelled out because there is a 0 additional cost associated with this. The overall expected cost for a securement device is obtained by summing these products of probability and cost. The complications are not strictly treated as mutually exclusive - in

that a patient cannot experience both a CRBSI and an occlusion of the catheter line – but the sponsors approach is not complex enough to explicitly model each combination of multiple complications. The sponsor's submission states assumptions regarding indwell times of 25 days for PICC lines and 3 days for CVC lines. It appears that these assumptions informed the cost of cleaning and maintaining securement over the lifetime of the placement, but they did not inform the parameterisation of complication rates in the model.

SecurAcath model structure diagram



The EAC regarded the sponsors approach as reasonably appropriate with the caveat that the risk of complications would be likely to vary with indwell time. The EAC regarded the structure of the decision trees as acceptable. The EAC considered malposition to be vague in a clinical sense and that this term should be replaced with dislodgement. The EAC agreed with the sponsor that an assumption of short indwell times for catheters would generate a conservative estimate of any cost savings accruing from the securement with SecurAcath on the basis that device costs for SecurAcath were 'front-loaded' and with increased potential for cost savings over extended indwell periods. In summary, the EAC considered the model specification to be appropriate for the cost analysis.

Clinical parameters and variables

The sponsor's cost analysis explicitly considers the risk of five complications affected by securement of a catheter: migration of the catheter; malposition of the catheter; occlusion of the catheter line; CRBSI or catheter related thrombosis (CRT); and (for suture securement only) risk of needle-stick injury to professionals. In practice, CRBSI and CRT are treated as separate complications, and the latter does not vary in incidence across comparators. Parameters for complication probabilities are sourced from a limited number of publications. The sources consist of a mixture of peer-reviewed publications, letters, posters and grey literature. A number of parameters are sourced from a report of one Canadian hospital's experience of implementing SecurAcath along with anti-coagulant impregnated catheters (Anonymous, Covenant Health, Misericordia Parenteral Therapy, 2015). The report is not well written and the analysis and presentation of findings is limited. For instance, complication probabilities are reported, but rates per patient day are not reported. This source presents a strong risk of bias due to concerns regarding a lack of peer review or appropriate statistical guidance on the analysis and presentation of data. In addition, such grey literature is likely to present a high risk of publication bias. The use of poster presentations to source data raises similar concerns.

Specific assumptions around the clinical parameters and variables used in the sponsor's model are described and critiqued below.

- The sponsor assumed that adhesive devices and SecurAcath are applied by nurses, while sutures are applied by physicians; literature cited in support of this is Canadian/American, and some (Cordovani & Cooper, 2013) suggest that physicians were trained on the use of SecurAcath. The healthcare professional inserting the catheter or sutures in the UK may depend on the clinical environment (e.g. oncology unit versus ICU), but is likely to be a nurse. Costs of securement significantly influence overall costs and need to be revised based on UK practice.

- The model considers migration, malposition and occlusion of the catheter line as separate events. The literature contains different definitions for migration and dislodgement, and suggests that malposition may be considered as migration or dislodgement. It is unclear how the sponsor defines these events and whether malposition was considered to be equivalent to dislodgement. Dislodgement is not considered explicitly in the decision model. However, it is mentioned by the sponsor in the list of catheter-related complications included in the cost analysis (section 9.2.4). The sponsor used a probability of CVC malposition with SecurAcath of 0.03 from Cordovani and Cooper (2013). This appears to be based on 2 patients (out of 74) experiencing dislodgement, however it is unclear as the sponsor did not explicitly define malposition as dislodgement. The definitions of events relating to catheter positioning need to be clarified.
- The sponsor's submission appears to assume the same rate of CRBSI with PICC lines secured with SecurAcath and StatLock. (Table C5a in the sponsor's submission gives different probabilities for CRBSI with SecurAcath and StatLock. However, Table C14a would suggest the same rate has been used despite typographical errors in the table.) Parameters for these complications are taken from a study (Covenant Health, Misericordia Parenteral Therapy, 2014) which uses an anti-clotting catheter (ArrowChlorag+ard) in addition to SecurAcath. Concerns regarding the use of this unpublished study have been previously noted. The probabilities of the following complications are all taken from this study and the literature should be reviewed to establish if more authoritative sources are available: CRT; PICC malposition with SecurAcath; PICC occlusion with SecurAcath; CRBSI with SecurAcath, PICC migration with adhesive devices; and PICC malposition with adhesive devices.
- The sponsor assumes that sutures carry a much higher probability of CRBSI when securing a CVC compared to non-sutured devices

including SecurAcath. This appears to be sourced from a review (Frey & Schears, 2006) reporting on an RCT comparing sutures with an adhesive device for securing CVC lines in 100 children which found a probability of CRBSI of 14% with sutures versus 4% with an adhesive device. The EAC notes the dramatic impact such an assumption has on the estimate of cost savings from the use of SecurAcath with CVC lines and believes efforts should be made to find a more authoritative source of infection rates with CVC lines.

- The model assumes a reduction in CRBSI risk observed with adhesive devices when compared with suturing for securement of CVC lines is applicable to SecurAcath. The EAC accepts this assumption.
- The sponsor assumes the probability of PICC and CVC migration with SecurAcath is zero. This is based on a letter to the editor reporting early experience of physicians with the device (Cordovani & Cooper, 2013). There are a number of other sources of evidence on migration in the literature, including an RCT (Egan et al. 2013, Hughes et al. 2014, Janssens et al. 2016b, McParlan et al. 2016). The EAC believes these probabilities should be revised and based on a meta-analysis of the literature if possible.
- The sponsor based the following probabilities on a review by Frey and Schears (2006): PICC occlusion with adhesive device; CRBSI with SecurAcath for CVC; CRBSI with sutures for CVC; CVC migration with sutures; CVC occlusion with sutures; and needle stick injury. The EAC accepts that the review may report the best source of these probabilities. However, the analysis would benefit from updating these probabilities using a meta-analysis where feasible.
- The source of complication probabilities for CRBSI and CRT in the sponsor's submission is unclear. The probability of CRBSI with SecurAcath for CVC lines is given twice (with very different probabilities). Probabilities of 0.00369 from Cooper et al. (2014) and 0.04 from the review by Frey & Schears (2006) are reported. No attention appears to have been given to the fact that the former

probability is actually a rate per 1000 catheter-days whereas the latter appears to be a true probability. The EAC believes the former rate is a more appropriate source (after conversion to a probability) but notes that the latter has been used in the analysis.

- The sponsor's submission assumes the probability for CVC malposition with sutures is 0.03, with Cordovani and Cooper (2013) cited as a source. This letter to the editor does not mention the probability of malposition with sutures. A further source (Boland et al. 2003) is also cited for this probability. This source refers to a study by Ahmed and Mohyuddin (1998) examining complications associated with different insertion techniques for Hickman catheters which reported malposition of 3 out of 65 patients (4%). The EAC believes the literature should be reviewed to establish if the latter source is the most authoritative.
- The sponsor's submission assumes the probability of CVC occlusion with SecurAcath is zero based on the Cordovani and Cooper (2013) letter to the editor. This probability is not explicitly stated in the article although the authors report no device related adverse events. The EAC believes the literature should be reviewed to establish if the latter source is the most authoritative.

The sponsor's submission applies a time horizon of 3 days for securement of CVC lines and 25 days for securement of PICC lines based on mean indwell times sourced from the literature. Thus it is assumed that no long term sequelae result from complications following placement of catheters and influenced by securement. In a sensitivity analysis, a time horizon of 3 months and 6 months is considered to simulate patients with PICC lines for extended periods. The EAC agrees that a short time horizon reflecting indwell times is appropriate. The EAC also agrees that the indwell times assumed by the manufacturer are conservative with respect to any cost savings from SecurAcath.

The sponsor's submission is a cost minimisation analysis; no attempt is made to quantify the impact of securement devices on patient mortality or quality of

life. The EAC regards this approach as appropriate and within the specified scope of the analysis.

Resource identification, measurement and valuation

The sponsor states that they conducted a literature search to find information on resource use and costs for the management and securing of PICC and CVC insertions. The search included the following databases: Medline, PubMed, Embase, Medline, NHS EED, Google, Google Scholar and EconLit. Exclusion criteria are stated which limited the search to studies including costs. However, appendix 4 of the sponsor's submission states that studies which reported "estimates or measures of rates and probabilities for central catheter complications, disaggregated by type of securement device" were also included. The latter search appears to be the basis for the selection of parameter sources in the cost analysis. The sponsor states that no meta-analyses were conducted because of the heterogeneity of the studies in terms of populations of patients, securement technology (i.e. comparator type) and indwell times. Therefore, relevant single source estimates were used as parameters in the model. The sponsor states two criteria for the choice of parameter values in the model: relevance of populations and relevance of data reported.

The EAC considered the description of search strategy inadequate and did not consider the search to be systematic. The EAC regarded the inclusion and exclusion criteria as vague; these should have been presented explicitly in terms of population, interventions, outcomes, study design etc. The strategy is not described in a transparent fashion (e.g. there is no PRISMA diagram of results). The justification for not undertaking meta-analyses was deemed to be reasonable by the EAC. No explicit criteria or comparisons were presented by the sponsor in cases where the literature provided at least two estimates that could be used for the same parameter in the model. The sensitivity analysis presented by the sponsor goes some way to mitigating the concerns of the EAC.

Cost parameters in the sponsor's model relating to securement method, placement (for example, labour time), complications and adverse events were derived from the literature search described above. These are described and critiqued below.

- The cost of PICC securement was estimated by the sponsor to be £250. This was taken from a supplement published in the British Journal of Nursing (Hughes, 2014) and includes staff and X-ray costs. It is difficult to say how this figure was calculated, but the EAC found it was in line with other unit cost estimates – the recent NICE MTG 24 put the cost of conventional "blind" PICC placement at £274 (NICE, 2015).
- The cost of CVC placement was estimated by the sponsor to be £450. The source is referenced as a published HTA report (Boland et al, 2003). However, the original source of the cost is an older publication (Hamilton et al, 1993) and the £450 assumes the Hickman line (CVC) is inserted by a surgeon in the operating theatre. The same paper calculates that a CVC inserted by a nurse on the ward would cost substantially less (£150). The HTA contains its own cost analysis and puts the one-off cost (i.e. without complications) of blind insertion and image guided CVC insertion at £312 and 382, respectively. This cost assumes insertion by a nurse. After inflation the cost of CVC insertion with image guidance by a trained nurse is £440, which is very close to the estimate in the sponsor's submission.
- Although listed under consumables, costed labour time inputs are included in the model. Average time for placement is multiplied by an average wage. The average times are 40.8 minutes of nurse time for StatLock, 20.5 minutes of nurse time for SecurAcath and 4.7 minutes of doctor time for suturing – the source for these is an internal report from the manufacturer website (Interrad Medical, 2015). Unit costs per minute for staff time of £0.60 for a nurse and £1.47 for a doctor are reported in the sponsor submission, and appear to be the basis of the

overall cost estimates. However, different figures are used in the Excel spread-sheet model submitted by the sponsor for the CVC analysis using sutures. The EAC understands that suturing of CVC lines would most commonly be performed by a nurse in the UK. Further, the EAC regards a cost per patient hour including qualifications and training to be a better representation of the opportunity cost of nursing time for securement of catheters. The EAC believes labour costs should be amended accordingly.

- The cost of a CRBSI episode is taken to be £9900 from NICE MTG 25 (NICE, 2015). This report suggests some consensus around this figure in terms of expert opinion and reports that it was originally taken from a published HTA report (Hockenhull et al, 2008). The EAC could not find this cost figure in the HTA report, although £9900 seems in line with a number of studies the HTA report reviewed. The HTA report noted a wide range of estimates in the literature ($812 to $71,000) and suggested that differences arose from wide variation in additional bed days attributable to CRBSI.
- The cost of catheter related thrombosis (CRT) is reported as £250 per episode with NICE MTG25 stated as the source. However, the EAC notes that MTG25 reports this as the cost for local site infections, thus an implicit assumption about equivalence of costs has been made. The sponsor's submission is unclear regarding assumptions of any differential risk of CRT between SecurAcath and the comparators. However, the parameters listed in Table C5a mention CRT only once under the heading 'PICC related variables' and the detailed breakdown of costs in Tables C14a and C14b suggest risks of CRT were not varied across comparators. This renders the cost of the complication irrelevant to the sponsor's analysis.
- The cost per episode of needle-stick injury (NI) was estimated to be £312 and appears to have been sourced from an American paper investigating the short term economic costs of NI for acute care nurses (Won Chan et al, 2005). The study used survey data and a micro-

costing approach to arrive at an average for each NI of $235 to $328 – the EAC assumes the figure of £312 was calculated using this range. The EAC notes that a very recent systematic review of the economic costs of NI (Mannocci et al, 2016) estimated direct costs—the most relevant to the cost perspective of the model—from $48 to $1,516 (international dollars). Two studies taking a national healthcare perspective suggested direct costs per NI of $473 to $910. Therefore, the EAC suggests that £312 is reasonable but may be at the lower end of empirical estimates of direct cost.

Technology and comparator costs

A list price of £16 for SecurAcath was used in the model, which the EAC considers to be appropriate.

For adhesive devices, cost per treatment is stated to be £12, but £14 is entered in the Excel model. The information used to calculate this is sourced from a supplement published in the British Journal of Nursing (Hughes, 2014). The paper calculates the weekly equipment cost of securing a PICC with an adhesive device at £3.47 including adhesive device cost and wound closure strips. The model appears to apply a cost of four times this figure assuming four devices over 25 days. The figure used in the submission may represent an adjustment reflecting a mean of 25 days indwell (£3.47 x 25/7). The EAC regards the latter estimate as more conservative and hence to be preferred, although it notes that part weeks would incur additional costs as for a full week assuming the device is changed weekly.

The costs for sutures are sourced from the internal manufacturer report (Interrad Medical, 2015). The equipment cost is inclusive of suture, needle, and removal kit and appears to have been exchange rate adjusted to generate an estimate of £5. The EAC considers this cost estimate to be reasonable.

The sponsor assumed no equipment maintenance and training costs for all securement methods that were compared, and this was considered a reasonable assumption by the EAC.

Sensitivity analysis

The sponsor's submission included sensitivity analysis addressing parameter uncertainty. One-way sensitivity analysis was undertaken in which parameters were varied by ±20%. Four parameters were varied in the comparison of SecurAcath and adhesive devices for PICC lines: cost of SecurAcath and the probability of migration, malposition or occlusion. Five parameters were varied in the comparison of SecurAcath and suturing for CVC lines: cost of SecurAcath and the probability of migration, malposition, occlusion or CRBSI. In addition, the sponsor's submission included multi-way sensitivity analyses for the analysis of PICC lines and of CVC lines in which all of the parameters varied in the one-way sensitivity analysis were simultaneously increased or decreased by 20%. Such analysis represents an extreme value analysis as increases in each parameter would increase the overall cost of SecurAcath. The sponsor's submission suggests structural uncertainty is minimal, and states that no structural sensitivity analysis was undertaken. In fact, the sponsor's submission did undertake two structural sensitivity analyses in which the indwell time for a PICC line was increased to three months and six months. No subgroup analysis addressing comorbidities or age is presented. The EAC regards the sensitivity analysis in the sponsor's submission as insufficient in scope or justification. No justification is provided for the range over which parameters are varied, albeit the use of ±20% is commonplace. Given the limited evidence available to estimate many parameters, this range may be insufficient to capture the true uncertainty. The EAC accepts the sponsor's view that the structure of the decision tree does not present a significant risk of bias, and that sensitivity analysis of the model structure is unnecessary. The sponsor's submission assumes that the probabilities of complications are independent of time (i.e. the probability is unchanged in sensitivity analysis in which indwell times are increased). The EAC regards an

assumption of a constant hazard for complications as more appropriate, facilitating a more robust assessment of the impact of indwell times on cost. The EAC considers the literature insufficient to support subgroup analyses addressing age or comorbidities.

4.3 Results of de novo cost analysis

Base-case analysis results

The sponsor's submission estimates a saving of £41 with the use of SecurAcath instead of StatLock for securing a PICC line for a period of 25 days. The sponsor's submission estimates a saving in device placement and maintenance costs of £8 over the lifetime of the catheter placement arising from a reduction in nursing time of 20 minutes for SecurAcath, which more than offsets the additional cost of the device. In addition, the sponsor estimates further savings of £32 with SecurAcath arising primarily from a reduction in the probability of migration from 6% with StatLock to zero with SecurAcath and a reduction in the probability of malposition from 11% with StatLock to 2% with SecurAcath. The sponsor's submission assumes both complications require replacement of the PICC line at a cost of £250.

As noted earlier, the EAC has concerns regarding the source of parameters for risks of migration and malposition of PICC lines with SecurAcath. The true cost savings from a reduction in complications may be less than £32. However, they are likely to be greater than zero. The EAC regards the valuation of nursing time at £0.60 per minute to be an underestimate. An authoritative estimate of the cost per hour of patient contact time for a nurse paid at the midpoint of the NHS Agenda for change band 6 pay scale is £125, or £2.08 per minute (Unit Costs of Health and Social Care, 2015). Consequently, the EAC believes that the sponsor may have underestimated the device placement and maintenance cost savings. In summary, while the EAC has reservations regarding parameter selection, it regards the estimate of the total cost saving as reasonable. Critically, it views the likelihood that the

true costs for SecurAcath are higher than those for StatLock over the relatively short indwell time of 25 days to be highly unlikely.

The sponsor's submission estimates a saving of £1006 with the use of SecurAcath instead of suturing to secure a CVC line for a period of 3 days. Of this saving, £990 is attributable to a reduction in the risk of CRBSI from 14% to 4% at a unit cost of £9900 for treatment of CRBSI. Modest savings of £27 accrue from a reduction of the occlusion rate from 6% with sutures to 0% with SecurAcath. The cost of device placement and maintenance is £16 higher for SecurAcath. The sponsor's submission assumes the same cost of £28 for SecurAcath placement and maintenance for securing CVC lines and securing PICC lines implying total nursing time of 21 minutes for either line. In contrast, the sponsor's submission assumes a total placement and maintenance time of 5 minutes for sutures placed by a doctor at a unit cost of £1.47 per minute.

The EAC has concerns regarding parameter selection for the probability of CRBSI with sutures. The EAC accepts the likelihood of an increased risk of CRBSI with sutures. Hence the EAC regards it as highly likely that the cost savings attributable to SecurAcath from reduced complication rates are greater than zero. The EAC understands that in a UK setting it would be usual for a nurse to suture a CVC line. The consequences of assuming that a nurse sutures the line at a unit cost of £2.08 per minute and requires 5 minutes for this task as opposed to 21 minutes to place and maintain a SecurAcath device are to increase the device placement and maintenance costs for SecurAcath when compared to suturing. However, the EAC notes that an assumption that suturing takes only a quarter of the time required to place and maintain a SecurAcath device seems highly conservative. In summary, the EAC believes that the increased costs of device placement and maintenance with SecurAcath compared to suturing are likely to be of the order of £16, as estimated in the sponsor's submission. However, the costs savings through reduced CRBSI with SecurAcath are very unlikely to be as high as £990.

Sensitivity analysis results

The results presented in the sponsor's submission are robust to the sensitivity analysis they undertook (described above). The multi-way (worst case scenario) analysis generates cost savings of £17 for PICC lines secured with SecurAcath and £876 for CVC lines secured with SecurAcath. In addition, the sensitivity analysis in which the indwell time for PICC lines was increased indicated greater savings attributable to SecurAcath.

The EAC views the sensitivity analysis undertaken as insufficient. Sensitivity of the results to assumptions regarding unit costs other than the cost of a SecurAcath device should have been undertaken. Parameter values for complication rates for StatLock and suturing should have been included in the sensitivity analysis. Nevertheless, with regard to PICC lines the EAC agrees with the sponsor that the results are likely to be robust to sensitivity analysis. With regard to CVC lines, the EAC notes that large cost savings are predicted on the basis of a 14% risk of CRBSI with suturing combined with a unit cost for treatment of CRBSI of £9900. The EAC regards this as likely to be overestimated and considers it essential to test the impact of alternative assumptions regarding these parameter values.

Subgroup analysis

The sponsor provides separate cost calculations for PICC and CVC lines as already discussed. No further subgroup analysis was included with the sponsor's submission. The EAC considers the omission of any further subgroup analysis as acceptable, given the limited evidence base in the literature. However, it notes the possibility that dislodgement rates for PICC lines secured with SecurAcath may be higher than those assumed by the sponsor for a population with diminished insight into their condition who may be prone to pull out the lines.

Model validation

The sponsor's submission does not include a validation of the model. The evidence of validity offered by the sponsor is the observation that the results presented in the submission are, 'what would be expected given the clinical

performance differential of the SecurAcath device compared to adhesives and sutures.' The EAC does not regard such an observation as validation of the model. However, the EAC considers there to be limited scope for validation given the simple decision tree approach and the lack of a substantial literature in the area.

4.4 Interpretation of economic evidence

The sponsor provides very little interpretation of the economic evidence alongside their submission, except to note that their results are consistent with three reports in the literature (Cordovani et al. 2013; NICE 2015; Frey & Schears 2006 (incorrectly referenced)). The first of these reports is an early study of the efficacy of SecurAcath for CVC lines in 72 patients and the authors note, "The study was too small to confirm securement superior to sutures or to show a reduction in catheter related infections or increased operator safety." The report by NICE is an evaluation of a securement dressing designed to minimise catheter related infections when compared against traditional swabbing with antimicrobials. The EAC did not consider this report to provide evidence relevant to the economic performance of SecurAcath. The final study cited is a useful overview of the early literature. It provides evidence of the superiority of adhesive devices over tape for the securement of PICC lines, and evidence of the superiority of adhesive devices over sutures for PICC and CVC lines. Given that the sponsor's submission does not include tape for the securement of PICC lines the evidence in Frey & Schears is of limited relevance with regard to the sponsor's analysis of PICC lines. It is of greater relevance to the sponsor's analysis of the securement of CVC lines, and in support of their findings. However, the EAC notes that a number of parameters in the sponsor's analysis of the securement of CVC lines were sourced from that publication.

4.5 Additional work undertaken by the External Assessment Centre in relation to economic evidence

The EAC had a number of concerns with the cost analysis submitted by the sponsor which prompted re-estimation of the cost implications of using SecurAcath. Chiefly:

- The sponsor's submission assumes event probabilities are constant with respect to indwell times. The EAC believes that an assumption of a constant hazard rate (an exponential relationship with time) is more appropriate

- Event probabilities are sourced from a limited number of primarily non-peer-reviewed literature sources raising concerns regarding bias

- Costs of nurse time for maintenance do not reflect the cost of overheads and training or consider that maintenance is a patient contact activity for which there may be associated non-contact time.

The EAC has reviewed the available evidence on complication rates. Trial data comparing SecurAcath and StatLock is limited to one study (Janssen et al. 2016) which found a non-significant increase in migration and dislodgement rates with SecurAcath and no difference in infections. This small trial was not powered to examine complication rates and the differences are not significant. The observational data indicates reduced risks of migration and dislodgement but not infection with SecurAcath when compared to StatLock. However, this literature is primarily non peer reviewed and the quality of the analysis and reporting is weak; the use of survival analysis to compare outcomes and the reporting of event rates is notable by its absence. The EAC regarded the RCT by Yamamoto (2002) as the most authoritative source of evidence comparing StatLock with sutures; rates of complications are reported although no survival analysis is undertaken. Yamamoto reported no significant difference in dislodgements or migrations, but a significant reduction in systemic infections with StatLock compared to sutures

(confirmed, p = 0.04). The lack of survival analysis weakens these findings. Consequently, the EAC chose to re-estimate cost savings under an assumption of no difference in complication rates in the base case. The EAC did include a risk of needlestick injury with sutures on the basis that an assumption of reduced risk with sutureless securement devices was highly likely. The EAC undertook sensitivity analysis which included differential risks of migration, dislodgement and CRBSI. The EAC did not consider the risk of catheter related thrombosis or occlusion on the grounds that there was insufficient evidence to determine the relative risk by securement device.

The EAC analysis compared SecurAcath with StatLock and sutures for CVC lines. The EAC analysis of PICC lines was restricted to SecurAcath and StatLock on the advice that suturing of PICC lines is no longer considered appropriate. Three indwell times were considered for both CVC and PICC lines: 5 days (short); 25 days (medium); and 120 days (long). In the base case cost estimates were based on placement and maintenance costs over the relevant indwell time with inclusion of costs rated to the risk of needlestick injury at placement of the catheter where relevant. The sensitivity analysis included costs attributable to migration, dislodgement and CRBSI. These costs were estimated as the product of the probability of the event over the indwell period and the unit cost of the event. The EAC assumed that complication rates were independent of whether the catheter was a PICC or CVC.

The probability of complications over the relevant indwell time was calculated from a baseline event rate per day multiplied by indwell time in days and converted to a probability. Event rates were derived from Yamamoto (2002). Yamamoto reports the number of events and event rates for CRBSI and dislodgements for CVC lines secured with sutures and with StatLock. (Note that the CRBSI rate includes confirmed and suspected infections). Only the number of migration events (and not the rate) is reported. Consequently, the migration rate for sutures and StatLock was estimated on the basis of the number of migrations and the ratio of total complications and complication

rates reported. These rates were utilised to estimate the probability of complications for both CVC and PICC lines secured with StatLock and for CVC lines secured with sutures. The CRBSI rates for CVC lines reported by Yamamoto (2002) are in line with the baseline rate of 1.48 per 1000 catheter days for PICC catheters applied in the recent assessment of TegaDerm (Jenks et al, 2016).

The probability of complications with securement of either PICC or CVC lines using SecurAcath was estimated by multiplying the relevant rate for StatLock with a relative risk estimated from the meta-analysis of the observational studies comparing StatLock and SecurAcath. The meta-analysis pooled the probability of events reported across studies due to a lack of reporting of event rates. The EAC assumed an indwell time of 25 days and converted pooled event probabilities to rates on this basis. A relative risk for each complication with SecurAcath compared to StatLock was then derived as the ratio of the relevant rates. This relative risk was applied to the event rate for each complication with StatLock (from Yamamoto) to derive an event rate with SecurAcath.

Assumptions regarding placement and maintenance times are unclear in the sponsor's submission and appear inconsistent with data reported in the cited evidence. The EAC assumed a placement time of 3 minutes for StatLock based on supporting evidence cited in the sponsor's submission [ref 17] which is broadly in line with evidence from the literature (Frey 2006). The supporting evidence cited in the Sponsor's submission reports a placement time of 30 seconds for SecurAcath. The EAC chose to make the more conservative assumption that placement time would be the same as for StatLock (3 minutes). The impact of assuming a placement time of 30 seconds is addressed in a sensitivity analysis. The EAC accepted the sponsor's assumption that placement time using suturing for securement is 4.7 minutes. The EAC used mean times for dressing changes of 4.3 minutes for SecurAcath and 7.3 minutes for StatLock reported by Janssen (2016). No evidence was available on times for dressing changes with sutures hence the

EAC assumed a time of 4.3 minutes (as for SecurAcath) in the base case, and 7.3 minutes (as for StatLock) in a sensitivity analysis.

Data on the risk of NI per procedure is sparse. Estimates of approximately 1 in 10 health care workers suffering a NI in any given year are commonly reported (Panlolio et al, 2004) The sponsor's submission utilised a risk per procedure of 2% based on one injury reported in a small RCT (Frey 2006). The EAC believed this to be a likely overestimate but found a paucity of data on NI rates per procedure. The EAC replaced this estimate with a more conservative value of 1.2% based on a single NI observed in Yamamoto (2002).

The EAC accepted the cost of CRBSI (£9900) and NI (£312) submitted by the sponsor in their analysis. The EAC increased the cost of nurse time per minute from £0.60 to £2.08 on the basis of the unit cost per hour of patient contact time reported in the Unit Costs of Health and Social Care (2015). The EAC applied a cost of placement of a PICC line of £274 (after inflation) derived from detailed micro-costing undertaken as part of a health technology assessment (Boland et al. 2003). The EAC regarded the sponsor's estimate of the cost of placement of a CVC line (£450) as reasonable but noted inconsistencies in the literature cited to support it. Instead, the EAC applied a unit cost of £440 derived from Boland et al. (2003) and inflated. The sponsor's submission assumed that all migrations of catheter lines result in replacement of the line. The EAC took advice from clinical experts that replacement would only occur when the end of the catheter had moved out of the Superior Vena Cava. Therefore, the EAC assumed a lower cost of £134 for migration of PICC or CVC lines based on the average cost of rectifying catheter-tip misplacement following blind insertion of a Hickman line (after inflation) reported by Boland et al. (2003)

The EAC analysis made the following further assumptions:

- Suturing is undertaken by a band 6 nurse

- Sutures remain secure for the duration of the catheter indwell time so that no repeat suturing is necessary

- Occlusion and catheter related thrombosis rates are independent of securement device.

The table below lists the parameters applied in the analysis undertaken by the EAC.

Parameter	Value (base case)	Value (sensitivity analysis)	Source
Routine placement and maintenance times			
SecurAcath placement	3 minutes	0.5 minutes	Ref 17 (Interrad report)
StatLock placement	3 minutes		Ref 17 (Interrad report)
Suture placement	4.7 minutes		As sponsor
SecurAcath maintenance	[redacted]		Janssens 2016
StatLock maintenance	[redacted]		Janssens 2016
Suture maintenance	[redacted]	[redacted]	Janssens 2016
Hazard ratios (SecurAcath vs StatLock)			

Migration	0.8443		Meta-analysis undertaken by EAC
Dislodgement	0.1424		Meta-analysis undertaken by EAC
CRSBI	1.1441		Meta-analysis undertaken by EAC
Complication rates per 1000 catheter days			
SecurAcath migration	0	2.18	Yamamoto 2002 and meta-analysis
StatLock migration	0	1.8	Calculated from Yamamoto 2002
Suture migration	0	3.1	Calculated from Yamamoto 2002
SecurAcath dislodgement	0	0.4	Yamamoto 2002 and meta-analysis
StatLock dislodgement	0	3.6	Yamamoto 2002
Suture dislodgement	0	4.1	Yamamoto 2002
SecurAcath CRBSI	0	0.7	Yamamoto 2002 and meta-

			analysis
StatLock CRBSI	0	0.7	Yamamoto 2002
Suture CRBSI	0	3.4	Yamamoto 2002
Needlestick Injury (suture)*	1.2		Yamamoto 2002
Unit costs			
Nurse time per minute	£2.08		PSSRU 2015
Cost of CRBSI	£9900		As sponsor
Cost of Needlestick Injury	£312		As sponsor
Cost of migration of CVC line	£134		Boland 2003 (inflation adjusted)
Cost of migration of PICC line	£134		Boland 2003 (inflation adjusted)
Cost of dislodgement of CVC line	£440		Boland 2003 (inflation adjusted)
Cost of dislodgement of PICC line	£274		NICE MTG24

*rate per 1000 procedures

Sensitivity Analysis

One-way sensitivity analysis was undertaken on SecurAcath placement time and suture maintenance time as described above. Threshold analysis was undertaken to quantify the indwell time at which SecurAcath became cost saving compared to StatLock and to sutures for CVC lines and compared to StatLock for PICC lines. Multi-way sensitivity analysis considering differences in migration, dislodgement and CRBSI rates was also undertaken. Finally, the EAC undertook a probabilistic sensitivity analysis (PSA) for CVC lines with an indwell time of 5 days and PICC lines with an indwell time of 25 days. The PSA was only conducted in the multi-way sensitivity analysis models so as to capture how the parameter uncertainty in complication risk inputs would affect results. The PSA reports mean cost differences and the non-parametric 95% credible intervals derived from 5000 calculations using parameter values sampled from distributions reflecting the uncertainty in each parameter. The following parameter distributions were applied.

Parameter	Distribution	Source
SecurAcath maintenance	Gamma; mean= [redacted], se=[redacted]	Janssens 2016
StatLock maintenance	Gamma; mean= [redacted], se=[redacted]	Janssens 2016
Suture maintenance	As SecurAcath	Assumption
SecurAcath placement	Gamma; mean=3,	Ref 17 (Interrad report);

	se=0.2	se assumed
StatLock placement	Gamma; mean=3, se=0.2	Ref 17 (Interrad report); se assumed
Suture placement	Gamma; mean=4.7, se=0.2	As sponsor; se assumed
SecurAcath migration HR	Gamma; mean=0.8433, se=0.090	Meta-analyses
StatLock migration probability (baseline rate equivalent)	Beta; n=85, r=prob*85#	Calculated from Yamamoto 2002
Suture migration probability (baseline rate equivalent)	Beta; n=85, r=prob*85#	Calculated from Yamamoto 2002
SecurAcath dislodgement HR	Gamma; mean=0.1424, se=0.029	Meta-analyses
StatLock dislodgement probability (baseline rate equivalent)	Beta; n=85, r=prob*85#	Yamamoto 2002
Suture dislodgement probability (baseline rate equivalent)	Beta; n=85, r=prob*85#	Yamamoto 2002

SecurAcath CRBSI HR	Gamma; mean=1.1441, se=0.008	Meta-analyses
StatLock CRBSI probability (baseline rate equivalent)	Beta; n=85, r=prob*85#	Yamamoto 2002
Suture CRBSI probability (baseline rate equivalent)	Beta; n=85, r=prob*85#	Yamamoto 2002
Needlestick Injury (suture) probability	Beta; n=85, r= 1.02	Yamamoto 2002
Cost of CRBSI	Gamma; mean= 9900, se= 990	Sponsor; se assumed as 10% of mean
Cost of Needlestick Injury	Gamma; mean= 312, se= 31.2	Sponsor; se assumed as 10% of mean
Cost of migration of CVC line	Gamma; mean=133.62 ,se = 17.96	Boland 2003 (inflation adjusted)
Cost of migration of PICC line	Same as CVC	
Cost of dislodgement of CVC line	Gamma; mean= 440, se= 44	Sponsor; se assumed as 10% of mean
Cost of dislodgement of	Gamma; mean= 274,	Sponsor; se assumed

PICC line	se= 27.10	as 10% of mean

se, standard error; RR, relative risk; prob, probability; #probability calculated from rate over relevant indwell time - 5 days for CVC line, 25 days for PICC line

Results

Base Case

The table below gives the results from the base case analysis in which only the placement and maintenance costs of securement were considered. In this analysis complication rates are assumed to be the same across securement devices and hence they are ignored (no net differences across comparators). For short indwell times StatLock was the cheapest option. For medium or long indwell times SecurAcath was cheaper than StatLock for securing PICC lines, but sutures were the cheapest option for securing CVC lines.

Scenario	SecurAcath	StatLock	Sutures	Cheapest option	Saving
CVC line for 5 days	£22	£10	£15	StatLock	£5
PICC line for 5 days	£22	£10	-	StatLock	£12
CVC line for 25 days	£49	£66	£42	sutures	£7
PICC line for 25 days	£49	£66	-	SecurAcath	£17
CVC line for 120 days	£174	£268	£167	sutures	£7

PICC line for 120 days	£174	£268	-	SecurAcath	£94

One-way sensitivity analyses

Reduced SecurAcath placement time

The table below reports the results of assuming a placement time of 30 seconds for SecurAcath as reported in the Sponsor's promotional literature. This resulted in a modest saving of approximately £5 for SecurAcath regardless of indwell time. This was insufficient to change the ranking of SecurAcath over sutures or StatLock and the inference from the base case analysis remained unchanged.

Scenario	SecurAcath	StatLock	Sutures	Cheapest option	Saving
CVC line for 5 days	£17	£10	£15	StatLock	£5
PICC line for 5 days	£17	£10	-	StatLock	£7
CVC line for 25 days	£44	£66	£42	sutures	£2
PICC line for 25 days	£44	£66	-	SecurAcath	£22

CVC line for 120 days	£169	£268	£167	sutures	£2
PICC line for 120 days	£169	£268	-	SecurAcath	£99

Increased suture maintenance time

The table below reports the results of assuming a maintenance time of [redacted] minutes for sutures equivalent to the time reported for StatLock in Janssens (2016). Costs for maintenance of sutures over medium and long indwell times rose and SecurAcath became the cheapest securement option for both CVC and PICC lines over medium and long indwell times.

Scenario	SecurAcath	StatLock	Sutures	Cheapest option	Saving
CVC line for 5 days	£22	£10	£15	StatLock	£5
PICC line for 5 days	£22	£10	-	StatLock	£12
CVC line for 25 days	£49	£66	£61	SecurAcath	£12
PICC line for 25 days	£49	£66	-	SecurAcath	£17
CVC line for 120 days	£174	£268	£273	SecurAcath	£94
PICC line for 120 days	£174	£268	-	SecurAcath	£94

Multi-way sensitivity analysis including complication rates

The table below reports the results of including differences in rates of migration, dislodgement and CRBSI in the cost analysis. Rates of migration, dislodgement and CRBSI for StatLock and sutures are derived from the data reported in Yamamoto (2002). Rates for SecurAcath are calculated by applying risk ratios derived from the meta-analysis to the rates for StatLock

reported in Yamamoto. Costs for sutures rose sharply due to the increased risk of CRBSI now associated with suturing. Costs for StatLock also rose, relative to SecurAcath, over medium and long indwell times due to increased migration and dislodgement rates. Over indwell times of 5 days StatLock remained the cheapest option. For longer indwell times SecurAcath was the cheapest option.

Scenario	SecurAcath	StatLock	Sutures	Cheapest option	Saving
CVC line for 5 days	£64	£53	£193	StatLock	£11
PICC line for 5 days	£64	£50	-	StatLock	£14
CVC line for 25 days	£256	£281	£902	SecurAcath	£25
PICC line for 25 days	£254	£267	-	SecurAcath	£13
CVC line for 120 days	£1130	£1246	£3696	SecurAcath	£116
PICC line for 120 days	£1120	£1188	-	SecurAcath	£68

Threshold analysis and probabilistic sensitivity analysis

The threshold sensitivity analysis for the best case scenario indicated that the costs of SecurAcath dropped below those of StatLock for securing PICC lines at indwell times of 15 days or more; the costs of sutures dropped below those of StatLock for securing CVC lines at indwell times of 8 days or more. SecurAcath remained more expensive than sutures for securing CVC lines over any indwell time. The PSA generated mean cost savings of £22 (95% CI -£128 to £438) for securing PICC lines with SecurAcath compared to StatLock for an indwell time of 25 days. For a CVC line with an indwell time of 5 days the PSA generated mean cost savings of -£7 (95% CI -£210 to £47) for SecurAcath when compared to StatLock and £137 (95% CI -£31 to £574) when compared to suturing.

Consideration of the impact of characteristics of patient subgroups on results

No specific sensitivity analysis was undertaken to consider the impact of the increased risk of CRBSI associated with age or comorbidities. In the base case, where no differential CRBSI rate by securement device is assumed, an increased risk would have no impact on relative costs. In the multi-way sensitivity analysis any increased risk of CRBSI would have magnified the higher costs already estimated for sutures and the ranking of options would be unlikely to change. We did not examine the impact of age on dislodgement rates due to a lack of evidence.

Summary of the results

There is considerable uncertainty in the underlying evidence which is reflected in the large 95% confidence intervals arising from the probabilistic sensitivity analysis. Nevertheless, SecurAcath appears to be cheaper than StatLock over medium and long indwell times. This is due to savings on maintenance costs arising from a reduction in cleaning time and the need to replace StatLock on a weekly basis. The evidence on cleaning time is drawn from a small, but sufficiently powered RCT. There is additional, observational

evidence that SecurAcath may result in fewer dislodgements; the single RCT did not support this but was underpowered to evaluate this outcome. It seems likely that SecurAcath yields some reduction in dislodgements generating additional savings over StatLock. Hence, the finding that SecurAcath is cheaper than StatLock over medium and long indwell times appears robust.

Over short indwell times StatLock was the cheapest option in all scenarios analysed by the EAC. Reduced maintenance and device replacement costs are of no advantage for indwell times of less than one week. In the multi-way sensitivity analysis the increased risk of dislodgement over SecurAcath and the resultant increased costs did not outweigh the savings in placement costs for StatLock. Whilst there remains uncertainty regarding the extent to which dislodgement is increased in StatLock compared to SecurAcath the absolute risk is likely to be small over an indwell time of 5 days. Indeed, increased risks may be predominantly associated with maintenance times when the line is unsecured. Hence, the finding that StatLock is the cheapest option for short indwell times appears robust.

The greatest uncertainty arose in the comparison of SecurAcath with suturing over medium and long indwell times. In the base case suturing was modestly cheaper. This assumes that cleaning and maintenance of a sutured line takes no more time, and hence is no more costly than cleaning a line secured with SecurAcath. It also assumes that both securement devices last for the duration of the line placement. There is some evidence to show an increased risk of CRBSI with sutured lines. Such an event is costly to treat (as well as placing a significant mortality risk on the patient). Any increase in CRBSI is likely to generate costs which outweigh the very modest cost savings from suturing a CVC line. Whilst the EAC excluded the risk of CRBSI from consideration in the base case analysis, the results of the multi-way sensitivity analysis would strongly favour the selection of SecurAcath over suturing of CVC lines.

4.6 Conclusions on the economic evidence

The sponsor's submission concludes that SecurAcath is cost saving when compared to StatLock for securing PICC lines over an indwell period of 25 days. The EAC revised the sponsor's model and drew the same conclusion. The EAC found smaller savings in their base case analysis which excluded complications compared to those in the sponsor's submission, but similar results in sensitivity analysis which included complications. The EAC found that suturing was modestly cheaper than SecurAcath when only placement and maintenance costs are considered but more expensive when complications were included. Hence the EAC's reassessment was consistent with the sponsor's conclusion that SecurAcath is cost saving for securing PIC lines over medium and long indwell times.

The sponsor's submission concludes that SecurAcath is cost saving when compared to suturing for securing CVC lines over an indwell period of 3 days. The EAC drew the same conclusion in sensitivity analysis which included complication rates, albeit with smaller cost differences. The analysis undertaken by the EAC also included StatLock and found StatLock to be the cheapest option in all analysis undertaken over short indwell times. Hence the EAC concludes that whilst the sponsor's submission may be correct in predicting cost savings for SecurAcath in place of suturing, Stat Lock is very likely to be cheaper still.

The exclusion of StatLock as an option for the short time securement of CVC lines in the sponsor's submission is difficult to justify and in the EAC's opinion did not address the specified scope. It seems likely that if the sponsor had included StatLock in their analysis of the securement of CVC lines they would also have found lower costs for StatLock. Hence the EAC views the sponsor's analysis of SecurAcath for CVC lines as flawed through the exclusion of the most appropriate comparator.

The EAC accepts that suturing is unlikely to be considered as a securement option for PICC lines. The EAC had a number of concerns with the parameter

choice for complication rates in the sponsor's cost submission including the quality of the source data and the assumption that rates were independent of time. The revised analysis undertaken by the EAC addressed these limitations to the extent allowed by the literature and drew the same conclusion as the sponsor: SecurAcath is very likely to be cost saving for securement of PICC lines over medium and long indwell times.

Impact on the cost difference between the technology and comparator of additional clinical and economic analyses undertaken by the External Assessment Centre

The additional analysis undertaken by the EAC ignored differences in complications rates in the base case. The EAC's analysis estimated savings for SecurAcath of £17 when compared to StatLock for securing a PICC line for 25 days. This estimate is higher than the sponsor's estimate of savings of £8 for placement and maintenance of SecurAcath compared with StatLock reflecting the assumption of higher unit costs for labour in the EAC analysis. The sponsor estimated further savings of £32 arising from reduced complications with SecurAcath. The EAC included complications in a sensitivity analysis and found total savings of £13. The EAC found that the overall cost of complications was slightly higher with SecurAcath compared to StatLock due to a modestly raised risk of CRBSI, a very expensive complication. However, the EAC regarded the evidence on complication rates as weak.

The analysis undertaken by the EAC found SecurAcath to be £7 more expansive than sutures for securing CVC lines independent of time; the sponsor's submission estimated the additional costs at £16. The difference is primarily attributable to the assumption in the sponsor's submission of higher labour unit costs for suturing compared with placing a SecurAcath. The EAC assumed both securement methods would be undertaken by a band 6 nurse. The sponsor's submission included cost savings of £1002 attributable to a reduction in infection probability from 14% to 4% with the use of SecurAcath in place of sutures. The EAC believes it is highly likely that infection risk is dependent on indwell time and the probabilities assumed by the sponsor are unrealistic for an indwell time of 3 days. The EAC derived infection probabilities from rates reported in Yamamoto (2002) after conversion over the appropriate time period. In their sensitivity analysis the EAC estimated savings of £129 for SecurAcath when compared to sutures over 5 days. The considerable difference is primarily attributable to assumptions of 1.7% and

0.3% for the probability of infection over 5 days with sutures and SecurAcath, respectively. As noted earlier, the EAC found additional savings for StatLock over SecurAcath in all scenarios with an indwell time of 5 days.

In summary, the EAC estimated cost savings for SecurAcath when compared to StatLock for securing PICC lines over 25 days which were similar to those estimated by the sponsor. However, the EAC considered the evidence on differences in rates of complications across securement devices in a sensitivity analysis due to concerns regarding the quality of the clinical data. The EAC found both suturing and StatLock to be cheaper than SecurAcath for securing CVC lines over 5 days when considering only placement costs (there is zero maintenance at 5 days). The EAC did find suturing to be considerably more expensive than SecurAcath in sensitivity analysis including differences in CRBSI risk. However, StatLock remained the cheapest option over 5 days.

5 Conclusions

The most relevant evidence to the decision problem is the unpublished RCT results. Janssens (2016b) showed that [redacted]

The EAC's meta-analysis supports the findings of the RCT. With the exception of dislodgment, the 95% confidence intervals (CIs) for migration, total catheter-related infections and CRBSIs are similar between SecurAcath

and StatLock. The majority of the observational studies report higher pain scores during device removal in comparison with device placement and in-situ. The most relevant study for UK practice reporting pain scores (Hughes 2014) states that device removal caused the most dissatisfaction among staff and patients were complaining of pain or discomfort.

Comparative evidence and the EAC's meta-analysis of non-comparative evidence suggests that both SecurAcath and StatLock are superior to sutures for migration, dislodgment, total catheter-related infections and CRBSIs. However, it should be noted that this evidence relates to people requiring PICC lines for which currently sutures are not standard of practice.

The EAC concludes that there is insufficient evidence to determine that SecurAcath is clinically superior in effectiveness and adverse events to StatLock. There is some evidence that SecurAcath is non-inferior in effectiveness and side effects profiles to StatLock.

There is some evidence to suggest that both SecurAcath and StatLock are superior to sutures, however, this evidence is from a population requiring PICC lines, for which suturing is not relevant to clinical practice.

There is insufficient information to compare the effectiveness and safety of SecurAcath with its comparators in terms of the subgroups specified in the scope.

The EAC revised the economic model submitted by the sponsor and chose to consider the impact of differences in rates of complications in a sensitivity analysis due to concerns already highlighted regarding the quality of the clinical evidence. The EAC found that StatLock is associated with the lowest costs for PICC or CVC line securement over short indwell times. This result was robust to sensitivity analysis. For securement of PICC or CVC lines over medium and long indwell times SecurAcath was associated with lower costs than StatLock. Suturing was cheaper than either StatLock or SecurAcath over medium and long indwell times in the base case analysis which excluded evidence on differences in complication rates. However, consideration of

potential differences in CRBSI rates led to sharply higher costs for suturing. Hence the EAC concludes that it is likely that SecurAcath is associated with the lowest costs for securement of PICC or CVC lines over medium and long indwell times.

6 Implications for research

Although evidence on the effectiveness and safety of SecurAcath exist, there is limited prospective comparative evidence on SecurAcath and its comparators. Therefore, the EAC would recommend that further primary research to this end is carried out.

There is insufficient information to compare the effectiveness and safety of SecurAcath with its comparators in terms of the subgroups specified in the scope. This is especially the case for exploring the use of SecurAcath in patients requiring a short term CVC and in children and adolescents. Therefore, any further primary research should be targeting these specific patient populations.

Further research should investigate the effectiveness and safety of SecurAcath in comparison with adhesive securement devices such as StatLock but also with sutures. As sutures are mainly used clinically in short term central venous catheters it is important that attention is paid during the study design development to match this comparator with the appropriate patient population.

Studies investigating the use of SecurAcath should be adequately powered to detect difference in the outcomes of dislodgment, migration, and CRBSI. The EAC notes that national and international guidelines providing objective definitions of these outcomes exist and should be referred to as part of any prospective study design.

The EAC notes that because of the relative simplicity of the technology and the wide spread use of these devices in the NHS, a randomised control trial is feasible and should be pursued in most cases of future research.

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7 Appendix 1

Clinical Evidence search strategies

Ovid MEDLINE(R) 1946 to July Week 1 2016 and Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations July 15, 2016

1	exp Catheterization, Central Venous/	13019
2	exp Catheterization, Peripheral/	9400
3	(venous adj3 (catheter* or line*)).tw.	15272
4	(central adj3 (catheter* or line*)).tw.	15745
5	((non tunnelled or non-tunnelled or tunnelled or hickman or broviac or cook) adj catheter*).tw.	800
6	exp Catheters, Indwelling/	16933
7	(implantable vascular access device* or IAVD or PortACath).tw.	93
8	(peripherally inserted central catheter* or PICC).tw.	1062
9	exp Central Venous Catheters/ or CVC.mp.	3841
10	cvad.mp.	428
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	47272
12	securement.mp.	147
13	secure.mp.	17245
14	stabili$ation.mp.	1
15	dressing$.mp.	20829
16	exp Sutures/ or sutures.mp.	30883
17	steristrip$.mp.	21
18	adhesive$.mp.	67646
19	12 or 13 or 14 or 15 or 16 or 17 or 18	133308
20	11 and 19	1003
21	securacath.mp.	2
22	statlock.mp.	19
23	grip-lok.mp.	0
24	griplok.mp.	0
25	20 or 21 or 22 or 23 or 24	1008

Embase 1974 to 2016 Week 29

1	exp central venous catheter/	16549
2	exp central venous catheterization/	7990
3	(venous adj3 (catheter* or line*)).tw.	21004
4	(central adj3 (catheter* or line*)).tw.	22684
5	((hickman or broviac or cook) adj catheter*).tw.	821
6	exp vascular access device/	16549
7	(implantable vascular access device or IAVD or PortACath).tw.	129
8	(peripherally inserted central catheter or PICC).tw.	1799
9	cvad.mp.	744
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	37283
11	securement.mp.	254
12	secure.mp.	23849
13	stabili$ation.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	2
14	dressing$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	29829
15	exp Sutures/ or sutures.mp.	56652
16	steristrip$.mp.	73
17	adhesive$.mp.	61435
18	11 or 12 or 13 or 14 or 15 or 16 or 17	167387
19	10 and 18	1143
20	securacath.mp.	7
21	statlock.mp.	47
22	grip-lok.mp.	1
23	griplok.mp.	1
24	19 or 20 or 21 or 22 or 23	1173

Cochrane

Search run on 21/07/2016, total number of studies retrieved = 184

1	Catheterization Central Venous
2	MeSH descriptor: [Catheterization, Central Venous] explode all trees
3	Catheterization Peripheral
4	MeSH descriptor: [Catheterization, Peripheral] explode all trees
5	Catheters Indwelling
6	MeSH descriptor: [Catheters, Indwelling] explode all trees
7	venous adj3 (catheter* or line*)
8	central adj3 (catheter* or line*)
9	(non tunnelled or non-tunnelled or tunnelled or hickman or broviac or cook) adj catheter*
10	implantable vascular access device* or IAVD or PortACath
11	peripherally inserted central catheter* or PICC
12	Central Venous Catheters or CVC
13	MeSH descriptor: [Central Venous Catheters] explode all trees
14	cvad
15	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14
16	securement
17	secure
18	stabilization
19	stabilisation
20	dressing
21	sutures
22	steristrip
23	adhesive
24	#16 or #17 or #18 or #19 or #20 or #21 or #22 or #23
25	#15 and #24
26	securacath
27	statlock

28	grip-lok
29	griplok
30	#25 or #26 or #27 or #28 or #29

Economic Evidence search strategies

Ovid MEDLINE(R) 1946 to August Week 1 2016 and Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations August 05, 2016

1	*exp Catheterization, Central Venous/*	*13019*
2	*exp Catheterization, Peripheral/*	*9400*
3	*(venous adj3 (catheter* or line*)).tw.*	*15272*
4	*(central adj3 (catheter* or line*)).tw.*	*15745*
5	*((non tunnelled or non-tunnelled or tunnelled or hickman or broviac or cook) adj catheter*).tw.*	*800*
6	*exp Catheters, Indwelling/*	*16933*
7	*(implantable vascular access device* or IAVD or PortACath).tw.*	*93*
8	*(peripherally inserted central catheter* or PICC).tw.*	*1062*
9	*exp Central Venous Catheters/ or CVC.mp.*	*3841*
10	*cvad.mp.*	*428*
11	*1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10*	*47272*
12	*securement.mp.*	*147*
13	*secure.mp.*	*17245*
14	*stabili$ation.mp.*	*1*
15	*dressing$.mp.*	*20829*
16	*exp Sutures/ or sutures.mp.*	*30883*
17	*steristrip$.mp.*	*21*
18	*adhesive$.mp.*	*67646*
19	*12 or 13 or 14 or 15 or 16 or 17 or 18*	*133308*
20	*11 and 19*	*1003*
21	*securacath.mp.*	*2*
22	*statlock.mp.*	*19*
23	*grip-lok.mp.*	*0*
24	*griplok.mp.*	*0*
25	*20 or 21 or 22 or 23 or 24*	*1008*
26	*(economic$ or cost$).mp.*	*708879*
27	*25 and 26*	*103*

Embase 1974 to 2016 Week 32

1	exp central venous catheter/	16549
2	exp central venous catheterization/	7990
3	(venous adj3 (catheter* or line*)).tw.	21004
4	(central adj3 (catheter* or line*)).tw.	22684
5	((hickman or broviac or cook) adj catheter*).tw.	821
6	exp vascular access device/	16549
7	(implantable vascular access device or IAVD or PortACath).tw.	129
8	(peripherally inserted central catheter or PICC).tw.	1799
9	cvad.mp.	744
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	37283
11	securement.mp.	254
12	secure.mp.	23849
13	stabili$ation.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	2
14	dressing$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	29829
15	exp Sutures/ or sutures.mp.	56652
16	steristrip$.mp.	73
17	adhesive$.mp.	61435
18	11 or 12 or 13 or 14 or 15 or 16 or 17	167387
19	10 and 18	1143
20	securacath.mp.	7
21	statlock.mp.	47

22	grip-lok.mp.	1
23	griplok.mp.	1
24	19 or 20 or 21 or 22 or 23	1173
25	(economic$ or cost$).mp.	1171357
26	24 and 25	200

Cochrane Database of Systematic Reviews : Issue 8 of 12, August 2016

Database of Abstracts of Reviews of Effect : Issue 2 of 4, April 2015

Cochrane Central Register of Controlled Trials : Issue 7 of 12, July 2016

Cochrane Methodology Register : Issue 3 of 4, July 2012

Health Technology Assessment Database : Issue 3 of 4, July 2016

NHS Economic Evaluation Database : Issue 2 of 4, April 2015

About the Cochrane Collaboration : Issue 7 of 12, July 2016

#1	Catheterization Central Venous
#2	MeSH descriptor: [Catheterization, Central Venous] explode all trees
#3	Catheterization Peripheral
#4	MeSH descriptor: [Catheterization, Peripheral] explode all trees
#5	Catheters Indwelling
#6	MeSH descriptor: [Catheters, Indwelling] explode all trees
#7	venous adj3 (catheter* or line*)
#8	central adj3 (catheter* or line*)
#9	(non tunnelled or non-tunnelled or tunnelled or hickman or broviac or cook) adj catheter*
#10	implantable vascular access device* or IAVD or PortACath
#11	peripherally inserted central catheter* or PICC
#12	Central Venous Catheters or CVC
#13	MeSH descriptor: [Central Venous Catheters] explode all trees
#14	cvad
#15	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14
#16	securement

#17	secure
#18	stabilization
#19	stabilisation
#20	dressing
#21	sutures
#22	steristrip
#23	adhesive
#24	#16 or #17 or #18 or #19 or #20 or #21 or #22 or #23
#25	#15 and #24
#26	securacath
#27	statlock
#28	grip-lok
#29	griplok
#30	#25 or #26 or #27 or #28 or #29
#31	economic* or cost*
#32	#30 and #31
(442 results)	