# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Medical technology consultation: GID-MT582 Kurin Lock for blood culture collection

## Supporting documentation – Committee papers

The enclosed documents were considered by the NICE medical technologies advisory committee (MTAC) when making their draft recommendations:

1. **EAG assessment report** – an independent report produced by an external assessment group who have reviewed and critiqued the available evidence.
2. **Assessment report overview** – an overview produced by the NICE technical lead which highlights the key issues and uncertainties in the company's submission and assessment report.
3. **Scope of evaluation** – the framework for assessing the technology, taking into account how it works, its comparator(s), the relevant patient population(s), and its effect on clinical and system outcomes. The scope is based on the sponsor's case for adoption.
4. **Company submission of evidence** – the evidence submitted to NICE by the notifying company.
5. **Expert questionnaires** – expert commentary gathered by the NICE team on the technology.
6. **EAG correspondence log** – a log of all correspondence between the external assessment group (EAG) and the company and/or experts during the course of the development of the assessment report.
7. **Company fact check comments** – the manufacturer's response following a factual accuracy check of the assessment report.

Please use the above links and bookmarks included in this PDF file to navigate to each of the above documents.

NICE medical technology consultation supporting docs:

Document cover sheet

Assessment report: Kurin Lock for Blood Culture Collection

EAG team: Ayesha Rahim, Megan Dale, Susan O'Connell, Simone Willis, Huey Yi Chong, Megan Dale, Michael Beddard.

Project lead(s): Ayesha Rahim

Information specialist: Simone Willis

Clinical evidence reviewer: Ayesha Rahim, Susan O'Connell

Economic evidence reviewer: Megan Dale

EAG sign-off: Rhys Morris

| Version number | Brief description of changes | Author/reviewer (e.g. J Smith) | Date (DD/MM/YY) | Date sent to NICE (if applicable) |
|---|---|---|---|---|
| 0.1 | Working draft | AR | 07/06/2023 | |
| 0.2 | Added searching details | SW | 21/06/2023 | |
| 0.3 | Working draft continued | AR | 23/06/2023 | |
| 0.4 | Clinical and economic sections merged | AR | 14/07/2023 | |
| 0.5 | Amendments post-internal review | AR | 18/07/2023 | |
| 0.6 | Integration into the NHS section moved | AR | 18/07/2023 | |
| 1.0 | Draft Report to NICE | AR | 19/07/2023 | 19/07/2023 |
| 1.1 | Amendments post NICE comments | AR | 24/07/2023 | |
| 1.2 | Further changes made in preparation for final submission. | AR | 26/07/2023 | |
| 1.3 | Internal CEDAR check | SO'C / RM / MD | 27/07/2023 | |
| 1.4 | Amendments post internal check | AR/MD | 28/07/2023 | |
| 1.5 | Finalising version for submission | AR/MD | 01/08/2023 | |
| 2.0 | Final report to NICE | AR | 01/08/2023 | 01/08/2023 |
| 2.1 | Post fact check edits | MD/AR | 07/08/2023 | |
| 3.0 | Post fact check version to NICE | AR | 08/08/2023 | 08/08/2023 |
| 4.0 | Following additional comments from NICE | MD/AR | 21/08/23 | 21/08/23 |

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

# Medical technologies guidance
# MT582 Kurin Lock for Blood Culture Collection
# External Assessment Group report

Produced by: CEDAR

Authors: Ayesha Rahim (Healthcare Scientist)

Megan Dale (Principal Healthcare Scientist)

Simone Willis (Information Specialist)

Dr Susan O'Connell (Principal Healthcare Scientist)

Dr Huey Yi Chong (Health Economist)

Dr Rhys Morris (CEDAR Director)

Correspondence to: CEDAR, Cardiff Medicentre, Heath Park, Cardiff CF14 4UJ

Date completed: 01/08/2023

Contains confidential information: Yes.

Number of attached appendices: 6

## Purpose of the assessment report

The purpose of this External Assessment Group (EAG) report is to review and critically evaluate the company's clinical and economic evidence presented in the submission to support their case for adoption in the NHS. The report may also include additional analysis of the submitted evidence or new clinical and/or economic evidence. NICE has commissioned this work and provided the template for the report. The report forms part of the papers considered by the Medical Technologies Advisory Committee when it is making decisions about the guidance.

## Declared interests of the authors

Description of any declared interests with related companies, and the matter under consideration. See NICE's Policy on managing interests for board members and employees.

None.


## Acknowledgements

CEDAR wish to thank the following clinical experts for their contribution to the development of this report:

- Mr Andrew Barton, Nurse Consultant IV Therapy and Vascular Access, IVAS Lead Nurse, Frimley Health NHS Foundation Trust.
- Dr David Partridge, Consultant Microbiologist, Sheffield Teaching Hospitals Foundation Trust.
- Ms Jane Hodson, Lead IV Practitioner, Guy's and St Thomas' NHS Foundation Trust.
- Dr Mustafa Atta, Consultant Medical Microbiologist, Kings College Hospital NHS Foundation Trust.




## 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

## List of Tables



## List of Figures

## Abbreviations

| Term | Definition |
|---|---|
| A&E | Accident and Emergency |
| AKI | Acute kidney injury |
| BCC | Blood Culture Contamination |
| BNF | British National Formulary |
| CI | Confidence Interval |
| DAPS | Directly Accessed Pathology Services |
| DSA | Deterministic sensitivity analysis |
| EAG | External Assessment Group |
| ED | Emergency Department |
| HRG | Healthcare Resource Groups |
| ICU | Intensive Care Unit |
| ISDD | Initial specimen diversion device |
| LOS | Length of stay |
| ITT | Intention to treat |
| MIB | Medtech innovation briefing |
| MAUDE | Manufacturer and User Facility Device Experience |
| MHRA | Medicines & Healthcare products Regulatory Agency |
| MTEP | Medical Technologies Evaluation Programme |
| NCC | National Cost Collection |
| NHS | National Health Service |
| NICE | National Institute for Health and Care Excellence |
| NICE CG | NICE Clinical Guideline |
| NICE MTG | NICE Medical Technology Guidance |
| NTT | Non touch technique |
| PHW | Public Health Wales |
| PLICS | Patient level information and costing system |
| PP | Per protocol |
| PSA | Probabilistic sensitivity analysis |
| PSSRU | Personal Social Services Research Unit |
| RCT | Randomised Controlled Trial |
| SD | Standard Deviation |
| SOC | Standard of care |
| TFC | Treatment function code |
| UK | United Kingdom |
| USA | United States of America |
| WHO | World Health Organisation |

# 1. Executive summary

## *1.1. Background*

### 1.1.1. The technology and clinical context

Kurin Lock (Iskus Health Ltd) is a CE-marked class IIa medical device, intended for use in collecting blood culture samples. The Kurin Lock device consists of a needle, a flash chamber to collect, isolate and display the first 0.15 mL of blood drawn, and a tube to collect the remaining blood sample which goes on to be cultured and analysed.

Blood culture samples are commonly taken in the secondary care setting to identify the presence of bloodstream infections. Where the bloodstream infection is bacterial, this is commonly referred to as sepsis. Patients may be tested for bloodstream infections in the emergency department (accident and emergency (A&E)) or while as an inpatient on a ward.

The innovative aspect of the Kurin Lock device is the flash chamber which diverts and contains the first 0.15 mL of blood. The intended purpose of this mechanism is to avoid contamination of the blood sample by isolating the blood that potentially contains microbes located on the skin at the site of venepuncture, and reduce the rate of false positive bloodstream infection results.

### 1.1.2. Decision problem

Kurin Lock is intended for use in secondary care, for people who have blood culture samples taken where bloodstream infections are suspected. This includes in A&E, intensive care units and other general inpatient wards. Specific subgroups that may benefit from Kurin Lock include populations where circumstances may make taking blood samples more difficult, and the risk of contamination is consequently higher. For example, taking blood samples from children or from intravenous drug users. The comparator for Kurin Lock is standard blood culture collection, without any diversion of the initial blood drawn during sampling. The key outcome to consider for Kurin Lock is the blood culture contamination rate. Other outcomes to be considered are rates of antibiotic use, length of hospital stay and use of further microbiological investigations or medical interventions.

The company submission largely aligned with the decision problem; the populations, intervention and comparators reported in the evidence were relevant. Blood culture contamination rates were widely reported as an outcome across the evidence base. However, the EAG considered there to be a lack of robust evidence that reported downstream outcomes that occurred as a result of the change in blood culture contamination rates. In particular, there was limited data related to Kurin Lock on how introduction of the device impacted on patients' length of stay and antibiotic use.

Clinical experts consulted during this assessment agreed that Kurin Lock was appropriate for use in secondary care blood culture sampling pathway, to reduce blood culture contamination rates.

## *1.2. Summary of clinical evidence*

### 1.2.1. Key studies and results

The EAG included 12 studies in total (reported in 14 publications). Four studies are reported in peer-reviewed full text publications (Arenas 2021, Burnie 2021, O'Sullivan 2019, Rhew 2021). The remaining 8 studies are reported across 5 abstracts (Allain 2018, Arnaout 2021, Baxter 2020, Ostwald 2021b, Sutton 2018b) and 5 posters (Atta 2022, Hodson 2022, Ostwald 2021a, Parsons 2023, Sutton 2018a).

Results from 4 key studies indicate that, following implementation of Kurin Lock, reductions in blood culture contamination (BCC) rates compared with standard care (Table 1). The results reported in the studies represented by abstract and poster publications also suggest that Kurin Lock is effective in reducing BCC rates.

**Table 1: Blood culture contamination rate results from 4 key studies.**

| Study | BCC Rate without Kurin Lock | BCC rate with Kurin Lock |
|---|---|---|
| Arenas (2021) | 5.2% | 0.3% |
| Burnie (2021) | 2.92% | 1.42-1.52% |
| O'Sullivan (2019) | 1.71% | 0.44% |
| Rhew (2022) | 3.1% | "<2.1%" |

Abbreviations: BCC: Blood culture contamination.

The impact of the Kurin Lock device on blood culture contamination rates reported in the studies represented by poster and abstract publications aligns with the results

from the studies reported in peer-reviewed full text publications. Detailed results relating to BCC rates are reported in section 6.3.1

There is limited data relating to the impact on length of hospital stay and use of unnecessary antibiotics associated with the Kurin Lock device across the evidence base. Generally, any reference to length of stay and antibiotic use was based on assumptions and calculations using historical data relating to the costs associated with blood culture contamination, outside of the context of Kurin Lock implementation. These outcomes are discussed in section 6.3.2 and section 6.3.3.

### 1.2.2. Quality appraisal summary

As assessed by a recognised critical appraisal checklist, the studies by Arenas (2021), Burnie (2021) and Rhew (2021) were considered to be of low quality. The study by O'Sullivan (2019) was considered to be of medium quality. Details of these quality assessments are summarised in section 6.2 with the full checklists in Appendix B.

The EAG notes that there may be variation in clinical practice relating to the criteria that trigger the ordering of a blood culture test; such variation may be present in the included studies, but it is not clear in any of the study methodologies how participants were selected to be referred for a blood culture test.

One aspect of the studies that is not reported in detail, except for in the study by Arenas (2021), is the methods of laboratory analysis that may lead to a sample result being deemed a false positive. Variations in determining and defining a false positive blood culture result between studies may limit the generalisability of the results. All 4 studies that have been critically appraised by the EAG are based in the USA, where baseline blood culture contamination rates are notably lower than those in the UK. The EAG notes that in studies where Kurin Lock was implemented as part of wider quality improvement projects (Burnie 2021, Rhew 2021), it is less clear how much of the effect on contamination rates can be attributed to the device alone.

## *1.3. Summary of economic evidence, including model results*

### 1.3.1. Economic evidence

No full economic analyses relating to Kurin Lock were identified by the EAG, although 2 clinical studies reported limited data for costs associated with BCC (Burnie 2021, Ostwald 2021a/2021b) (section 11.1, Table 12).

Additional studies identified by the EAG (n=9) and the company (n=11) did not involve the Kurin Lock device but provided relevant information about the costs associated with contaminated blood cultures or economic information for similar competitor devices, are summarised in Table 11.

### 1.3.2. Economic model, including EAG changes

The company model was clearly laid out and appropriate for the decision scope, using a decision tree with a time horizon of hospital discharge and NHS perspective.

The EAG accepted the use of studies based in the USA for length of stay data, as no acceptable UK alternative was identified for the A&E base case setting. This remains an evidence gap and additional sensitivity highlights the importance of length of stay, particularly in areas with lower daily stay costs, or lower baseline contamination rates.

The EAG changed the costing method to be in line with daily stay costs used in previous assessment reports. This, together with other minor cost adjustments, reduced the cost saving from £73 to £8 per patient in an A&E setting with a baseline contamination rate of 9% (Table 2). Lower baseline contamination rates would reduce the cost saving, and may result in the introduction of Kurin Lock becoming cost incurring. This is examined further in two-way sensitivity tables (section 11.3: Table 19,Table 20,

Table ***21***).

**Table 2 Cost saving per patient, A&E setting. Company and EAG base case**

| | Company's results | EAG results |
|---|---|---|
| Device | -£36 | -£38 |
| BC testing (initial and subsequent) | £1 | £1 |
| Antibiotics | £4 | £1 |

| | | |
|---|---|---|
| Length of stay | £104 | £44 |
| **Total** | **£73** | **£8** |

Scenario modelling for ICU settings demonstrated that where the daily hospital cost is higher, the cost saving is greater and is also more robust to changes in length of stay or baseline contamination rate (Table 3).

**Table 3 EAG cost saving per patient in alternative settings**

| | EAG base case (A&E) | EAG ICU scenario |
|---|---|---|
| Device | -£38 | -£38 |
| BC testing (initial and subsequent) | £1 | £0 |
| Antibiotics | £1 | £0 |
| Length of stay | £44 | £78 |
| **Total** | **£8** | **£41** |

The company also submitted a general hospital scenario. This is based on length of stay data from a UK study on the cost of contaminated blood cultures, but the EAG has strong reservations concerning the appropriateness of the data for this scenario and its interpretation (section 11.3).

## *1.4. Key points for decision makers*

**Table 4: Summary of key points for decision makers, identified by the EAG.**

| Key point | Description |
|---|---|
| Limited peer-reviewed robust data | The evidence for Kurin Lock consisted of 4 peer-reviewed studies based in the USA. The remaining evidence consisted of posters and abstracts with limited study details and results; 3 studies were based in a UK NHS setting. |
| Lack of data for economic consequences relating directly to Kurin Lock | There is a lack of data relating directly to Kurin Lock for consequences such as length of stay or antibiotic use, that inform economic modelling. |
| Length of stay | Length of stay duration is uncertain, and is a key driver of the economic model. In addition, the costs for length of stay have some uncertainty as there is no direct evidence. |
| Baseline blood contamination rates | Kurin Lock is only cost saving if baseline blood contamination rates are high, as stated in company model. If baseline rates are lower, Kurin Lock shifts towards being no longer cost saving. |

Abbreviations: NHS: National Health Service; UK: United Kingdom; USA: United States of America.

# 2. Decision problem

The company has proposed some variation to the decision problem outlined in the scope. The company stated that the population specified in the scope, 'people who need a blood culture test within a secondary care setting' should be changed to 'people who need a blood culture'. The company's rationale for this is that while a large proportion of blood cultures are taken in the secondary care setting, some blood cultures are performed in the community and Kurin Lock could be used in these settings. The EAG recognises that blood cultures are occasionally performed outside of secondary care and Kurin Lock could therefore be implemented in these settings. However, the literature search performed by the company focused on Kurin Lock in a hospital setting and the economic model provided is based on patients within secondary care. A clinical expert advised that blood cultures for microbiological analysis are rarely received from primary care. Therefore, the EAG do not consider this variation in the scope to be valid in the context of this assessment and will focus on the use of Kurin Lock in the secondary care setting.

The company provided clarification of the terminology used to describe subgroups to be considered, the intervention and the comparator(s). The company also clarified that while all outcomes listed in the scope are relevant, the blood culture contamination rate should be considered the 'main outcome'. The EAG considers these clarifications to be informative but does not consider the clarifications to represent variation to the scope (**Table *5***).

### Table 5: Variation to the scope as proposed by the company

| Decision problem | Scope | Proposed variation in company submission | EAG comment |
|---|---|---|---|
| **Population** | People who need a blood culture test within a secondary care setting | People who need a blood culture | The EAG does not consider this variation in scope to be valid in the context of this assessment. |
| **Subgroups to be considered** | • People who present with signs or symptoms of infection<br>• People at increased risk of infections such as those who are immunocompromised<br>• People in whom sampling blood can be challenging for example intravenous drug users or children. | Blood cultures are taken to identify patients with bacteraemia. There are many signs and symptoms in a patient which may suggest bacteraemia and clinical judgement is required,<br>but the following indicators should be taken into account when assessing a patient for signs of bacteraemia or sepsis:<br>• core temperature out of normal range;<br>• focal signs of infection;<br>• abnormal heart rate (raised), blood pressure (low or raised) or respiratory rate (raised);<br>• chills or rigors;<br>• raised or very low white blood cell count; and<br>• new or worsening confusion.<br>• Could it be Sepsis? | The EAG agrees that this information provided by the company is for clarification purposes only and does not represent a variation to the scope. |
| **Intervention** | Kurin blood culture collection including Kurin Lock | Kurin® Blood Culture Collection Set with Kurin Lock® Technology | The EAG agrees that this information provided by the company is for clarification purposes only and does not represent a variation to the scope. |
| **Comparator(s)** | Standard blood culture collection (tubes and container) | Standard blood culture collection methods including standard winged butterfly sets with tubes and adaptor | The EAG agrees that this information provided by the company is for clarification purposes |

| Decision problem | Scope | Proposed variation in company submission | EAG comment |
|---|---|---|---|
| | | caps (closed system). Also, standard safety needle and syringe method (open system) for collecting a blood culture is common practice. | only and does not represent a variation to the scope. |
| **Outcomes** | The outcome measures to consider include:<br>• Blood culture contamination rate<br>• Positive and negative predictive values<br>• Rates of antimicrobial prescriptions<br>• Use of unneeded antibiotic treatment<br>• Unnecessary further interventions such as laboratory tests to rule out suspected bacteraemia<br>• Treatment delays<br>• Length of hospital stay<br>• Rates of hospital-acquired infection<br>• Patient-reported outcome measures such as health-related quality of life<br>• Patient-reported experience measures<br>• Device-related adverse events | All of these are relevant, but for clarification the main outcome is by significantly lowering the rates of contaminated blood cultures clinicians improve the clinical value and accuracy of blood cultures. Essential the diagnostic value is more accurate, and therefore the knock-on consequences to the patient and healthcare system as detailed are avoided. | The EAG agrees that this information provided by the company is for clarification purposes only and does not represent a variation to the scope. |

# 3. Overview of the technology

Kurin Lock (Iskus Health Ltd) is a CE-marked class IIa medical device, intended for use in collecting blood culture samples. The Kurin Lock device consists of a needle, a flash chamber to collect, isolate and display the first 0.15 mL of blood drawn, and a tube to collect the remaining blood sample which goes on to be cultured and analysed.

The innovative aspect of this technology is the flash chamber which diverts and contains the first 0.15 mL of blood that is drawn during blood sample collection. The intended purpose of this mechanism is to isolate the blood that potentially contains microbes located on the skin at the site of venepuncture, to avoid contamination of the blood sample and reduce the rate of false positive bloodstream infection results.

The regulatory documents submitted by the company, including certification of CE marking and instructions for use, were deemed satisfactory by the EAG.

The company submission lists 14 different versions of the Kurin Lock device. The company stated there is no impact on the generalisability of evidence across these various versions of the device and they exist to facilitate the different methods of taking blood culture samples that are used in clinical practice such as variations in the bottles used to collect samples and the taking of blood samples from freshly inserted peripheral intravenous cannulas instead of via standard venepuncture.

# 4. Clinical context

Blood culture samples are commonly taken in the secondary care setting to identify the presence of bloodstream infections. Where the bloodstream infection is bacterial, this is commonly referred to as sepsis. There are several symptoms that indicate a patient may have a bloodstream infection, including breathlessness, delirium, changes in the skin’s colour (blue, grey or pale), and rashes. Sepsis may also be suspected in people who appear acutely unwell with no obvious cause. Where a bloodstream infection is suspected, taking blood samples for culturing is performed alongside general clinical assessments such as measuring heart rate, oxygen saturation and

temperature. Other samples may be taken such as urine and swabs from wounds to identify potential causative organisms.

Patients may be tested for bloodstream infections in the emergency department (accident and emergency (A&E)) or while as an inpatient on a ward. Clinical experts stated that A&E would be a suitable place to introduce Kurin Lock as this is where blood culture contamination (BCC) rates are consistently high, in addition to other secondary care settings such as inpatient wards. Experts also commented that Kurin Lock may be particularly useful in situations where circumstances may make taking blood samples more difficult, and the risk of contamination is consequently higher. For example, taking blood samples from children or from intravenous drug users. The company has positioned Kurin Lock as a suitable device to be used in secondary care settings, including in emergency care. The EAG considers the company's description of the clinical context to be appropriate and relevant to the decision problem.

The general accepted procedure for taking blood culture samples involves cleaning the patient's skin, disinfecting the blood culture bottles ready to be filled, applying a tourniquet to the patient to perform venepuncture and filling 2 bottles with blood samples (an aerobic bottle and an anaerobic bottle). It is recommended that 2 samples are taken, from different sites, to increase the chance of identifying disease-causing microorganisms in the bloodstream and to help identify potential skin flora contaminants at the analysis stage (UK HSA, 2022). Aseptic technique should be employed throughout the procedure. A step-by-step description of the procedure can be found in the summary of the PHW: ANTT Clinical Guideline for Blood Culture Collection in Table 7.

When blood is sampled, bacteria from the skin at the site of puncture can be drawn into the blood sample. Samples are cultured in the laboratory and any microorganisms that are present are analysed and identified. Microorganisms that originated in the skin, rather than in the blood, can therefore produce a false-positive result. This can potentially have significant consequences for the patient, the laboratory, and the hospital system. False-positive results that

have occurred due to skin flora contamination can be detected by the laboratories conducting analysis, but often only after the downstream events have already been triggered such as antibiotic provision and admission to hospital.

Once a blood sample is drawn and sent for processing and analysis, any organisms present in the sample are grown in laboratory conditions for a minimum of 5 days. Positive result turnaround times are heavily patient and organism-dependent; clinical experts commented that positive results are usually available within 24-48 hours of incubation. Preliminary negative results are usually provided within 48 hours, and confirmed after the 5 days of growth has elapsed. Antibiotics are routinely commenced based on the initial signs and symptoms of a bloodstream infection, prior to the result of a blood culture test. Clinical experts advised antibiotics are given to 90% of patients who undergo blood culture sampling, prior to any result being received. Based on the result of the blood culture analysis, antibiotics may be changed or withdrawn, based on clinical judgement and in line with antimicrobial stewardship guidelines. One expert commented that a blood culture result is not considered the sole, definitive marker of sepsis and that the primary purpose of a blood culture test is to identify the disease-causing organism to facilitate selection of the most appropriate antibiotic.

There are various consequences reported to be associated with false-positive blood culture results. As described by clinical experts, these consequences can impact the patient, the laboratories that analyse blood culture samples and hospital systems as a whole (Table 6).

**Table 6: Potential impacts on patients, laboratories and hospitals of false-positive blood culture results due to contamination with skin flora.**

| Context | Potential impact of false positive blood culture result |
|---|---|
| **Patient** | • Unnecessary or inappropriate antibiotics given<br>• Long-term indwelling lines and/or catheters removed unnecessarily in an attempt to eliminate cause of suspected infection<br>• Increase in length of hospital stay while further treatment and investigations occur |

| Context | Potential impact of false positive blood culture result |
|---|---|
| **Laboratory** | • Repeated samples and analysis where contamination is suspected and further analysis is required<br>• Subsequent increased demand on resources such as culture medium and staff time |
| **Hospital** | • Increased costs associated with providing antibiotics, length of stay and further investigations<br>• Contribution to development of antibiotic resistance as a result of increased/unnecessary antibiotic provision |

Key recommendations relating to taking blood samples for culture and microbiological blood culture analysis, taken from guidelines identified as relevant to the decision problem, are summarised in **Table *7***.

The following NICE guidelines were identified as relevant to managing sepsis and healthcare-associated infections, but are not discussed in detail as they were deemed to be not directly relevant to the decision problem:

- NG51 Sepsis: recognition, diagnosis and early management
- CG139 Healthcare-associated infections: prevention and control in primary and community care
- PH36 Healthcare-associated infections: prevention and control

## Table 7: Relevant guidance

| Guidance | Recommendations |
|---|---|
| PHW: ANTT Clinical Guideline for Blood Culture Collection | Preparation: Consent patient, assess veins visually and patient or nurse cleans arm<br><br>Step 1: With clean hands clean tray according to local policy<br><br>Step 2: Gather equipment and place around tray<br><br>Step 3: Clean hands with alcohol hand rub or soap and water<br><br>Step 4: Prepare equipment using a non-touch technique (NTT)<br><br>Step 5: Apply disposable apron and label bottles<br><br>Step 6: Clean hands with alcohol hand rub or soap and water<br><br>Step 7: Scrub bottle ports for 15 seconds using 2% chlorhexidine & 70% alcohol wipe<br><br>Step 8: Position arm on drape and pillow<br><br>Step 9: Apply disposable tourniquet, identify a vein, relax tourniquet<br><br>Step 10: Clean hands with alcohol hand rub or soap and water<br><br>Step 11: Re-tighten tourniquet<br><br>Step 12: Apply non-sterilised gloves<br><br>Step 13: Clean skin – 2% chlorhexidine / 70% alcohol applicator, back and forth & left to right strokes for 30 seconds. Allow to dry<br><br>Step 14: Puncture vein (DO NOT RE-PALPATE). Draw blood<br><br>Step 15: Inoculate blood into bottles using a NTT. Release tourniquet<br><br>Step 16: Apply an appropriate dressing to the puncture site<br><br>Step 17: Dispose of sharps<br><br>Step 18: Clean tray according to local policy<br><br>Step 19: Dispose of gloves<br><br>Step 20: Clean hands with alcohol hand rub or soap and water |

| Guidance | Recommendations |
|---|---|
| WHO Guidelines on Drawing Blood | **Procedure for drawing blood: strategies for infection prevention and control:**<br>**DO:**<br>• carry out hand hygiene (use soap and water or alcohol rub), and wash carefully, including wrists and spaces between the fingers for at least 30 seconds (follow WHO's 'My 5 moments for hand hygiene')<br>• use one pair of non-sterile gloves per procedure or patient<br>• use a single-use device for blood sampling and drawing<br>• disinfect the skin at the venepuncture site<br>• discard the used device (a needle and syringe is a single unit) immediately into a robust sharps container<br>• use the one-hand scoop technique, where recapping of a needle is unavoidable<br>• seal the sharps container with a tamper-proof lid<br>• place laboratory sample tubes in a sturdy rack before injecting into the rubber stopper<br>• immediately report any incident or accident linked to a needle or sharp injury, and seek assistance; start PEP as soon as possible, following protocols<br>**DO NOT:**<br>• forget to clean your hands<br>• use the same pair of gloves for more than one patient<br>• wash gloves for reuse<br>• use a syringe, needle or lancet for more than one patient<br>• touch the puncture site after disinfecting it<br>• leave an unprotected needle lying outside the sharps container<br>• recap a needle using both hands<br>• overfill or decant a sharps container<br>• inject into a laboratory tube while holding it with the other hand<br>• delay post-exposure prophylaxis (PEP) after exposure to potentially contaminated material; beyond 72 hours, PEP is NOT effective<br>**Monitoring and evaluation**<br>A monitoring and evaluation system should be in place to offer surveillance of management of phlebotomy services and adverse events, and to document improvements.<br>One indicator to be included would be the number (and percentage) of laboratory test results lost due to errors or poor quality; for example:<br>• blood culture contamination rate<br>• blood transfusion adverse events<br>• haemolysis<br>• number of specimens with illegible or missing paperwork or labels number of specimens that could not be processed due to inadequate sample volumes |

| Guidance | Recommendations |
|---|---|
| UK Standards for Microbiology Investigations B37: investigation of blood cultures (for organisms other than Mycobacterium species) | **Factors affecting isolation of causative organisms**<br>**Clinical:**<br>Method of collection<br>• Studies have shown that discarding the first 10mL aliquot of blood taken from vascular catheters has no effect on the contamination rate of these samples and that, even following strict sterile precautions; samples taken from central venous catheters have higher contamination rates than those taken from peripheral or arterial lines<br>• Changing needles between venepuncture and inoculation of the bottles is not recommended because this carries a risk of needle stick injury.<br>Number and timing of samples:<br>• For the majority of patients, two blood culture sets are recommended. A second or third set taken from a different site not only increases yield but also allows recognition of contamination<br>• In most conditions other than endocarditis, bacteraemia is intermittent, given it is related to the fevers and rigors which occur 30-60 minutes after the entry of organisms into the bloodstream. Samples should be taken as soon as possible after a spike of fever.<br>Previous antimicrobial therapy<br>• Ideally, blood samples should be taken prior to antimicrobial treatment. When already receiving antimicrobials, blood culture should be collected just before the next dose is due when antimicrobial concentration in the blood is at the lowest.<br>Volume of blood<br>• Blood culture volume is the most significant factor affecting the detection of organisms in bloodstream infection. There is a direct relationship between blood volume and yield, with approximately a 3% increase in yield per mL of blood cultured. False negatives may occur if inadequate blood culture volumes are submitted.<br><br>**Contamination**<br>• Contamination of blood cultures complicates interpretation and can lead to unnecessary antimicrobial therapy and increased costs. In general, contamination target rates are set at less than 3%. Several criteria are used to differentiate between contamination and true bacteraemia and to determine the clinical significance of a positive result. These include the identity of the organism, the number of positive sets, the number of positive bottles within a set, quantity of growth, and clinical and laboratory data (including source of culture). Prevention of contamination can be achieved through appropriate skin and bottle preparation, obtaining cultures from peripheral venepuncture instead of vascular catheters, and through training and intervention measures. |

## Special considerations, including issues related to equality

There were no special considerations identified in the scope. The company stated there are no issues relating to equality and that the Kurin Lock device

can be used on people of all ages. The EAG did not identify any issues relating to equality for this assessment.

# 5. Clinical evidence selection

## *5.1. Evidence search strategy and study selection*

The company conducted searches in one database (Medline via PubMed) and on the company website. The search strategy included free text terms, which were targeted towards the device name. However, no index terms were used. It is unclear how many studies the company identified in total and the number of duplicate records was not reported. The company did not search clinical trial registers or conduct searches for adverse events.

The inclusion criteria used for screening by the company were as follows:

- Population: Blood cultures collection studies which used Kurin or initial specimen diversion device (ISDD) within a secondary care setting
- Intervention and comparators: Kurin blood culture collection, including Kurin Lock, ISDD devices; Standard of care: Standard blood culture collection (tubes and container)

Whilst the inclusion criteria relating to the population identified the context for the intervention (i.e. secondary care setting), they did not identify the population appropriately (i.e. people who need a blood test). The inclusion criteria for the intervention and comparator were appropriate to the decision problem.

As only one database had been searched by the company and some key concepts had not been adequately captured by the search terms, the EAG were not confident that all relevant literature had been identified and, therefore, conducted their own systematic searches. Additionally, the EAG were not confident that the inclusion criteria had been adequately defined for the company selection process. Details of the company and EAG searches are provided in Appendix A.

The EAG literature searches identified a total of 264 records. Two EAG researchers screened the 264 records by title and abstract in accordance with the scope. Of these, 218 were excluded as they did not meet the scope, leaving 46 records for screening against the criteria of the decision problem. The 46 publications were retrieved and reviewed by two EAG researchers, in addition to 2 publications included in the company submission that were not picked up through the EAG searches. There were no disagreements on inclusion and exclusion of the 48 publications screened in total. 34 publications were excluded, leaving 14 publications for inclusion, representing 12 unique studies: 4 full-text publications (Arenas 2021, Burnie 2021, O'Sullivan 2019, Rhew 2021) and 10 abstracts/posters (Allain 2018, Arnaout 2021, Baxter 2020, Atta 2022, Hodson 2022, Ostwald 2021a, Ostwald 2021b, Parsons 2023, Sutton 2018a, Sutton 2018b).

It should be noted that a record relating to the study by Hodson (2022) was identified during EAG searches and deemed relevant, but only a URL linking to the study details published on the Kurin Lock company website was found when searching for the associated publication. The company submission included a poster publication relating to the Hodson (2022) study which matched the study details published on the Kurin Lock webpage identified by the EAG; this poster was therefore used by the EAG for data extraction purposes.

## *5.2. Included and excluded studies*

The EAG has included 12 studies in total (reported in 14 publications). Four studies are reported in peer-reviewed full text publications (Arenas 2021, Burnie 2021, O'Sullivan 2019, Rhew 2021). The remaining 8 studies are reported across 5 abstracts (Allain 2018, Arnaout 2021, Baxter 2020, Ostwald 2021b, Sutton 2018b) and 5 posters (Atta 2022, Hodson 2022, Ostwald 2021a, Parsons 2023, Sutton 2018a).

This is largely consistent with the evidence included in the company submission. The company submission lists the same 12 unique studies, 4 of these being peer-reviewed full text publications. The type of publications (abstract or poster) associated with the remaining 8 included studies were

unclear, and the EAG sought clarification from the company regarding this. **Table *8*** summaries the studies identified by the company and by the EAG, including the types of associated publications. The EAG notes that no additional information was identified in the 2 publications identified by the EAG that were not included by the company (Ostwald 2021b, Sutton 2018b).

**Table 8: Studies identified by the company and the EAG.**

| Study | Associated publication | Publication type | Identified by company | Identified by EAG |
|---|---|---|---|---|
| Allain 2018 | Allain 2018 | Abstract | ✓ | ✓ |
| Arenas 2021 | Arenas 2021 | Full text publication | ✓ | ✓ |
| Arnaout 2021 | Arnaout 2021 | Abstract | ✓ | ✓ |
| Atta 2022 | Atta 2022 | Poster | ✓ | ✓ |
| Baxter 2020 | Baxter 2020 | Abstract | ✓ | ✓ |
| Burnie 2021 | Burnie 2021 | Full text publication | ✓ | ✓ |
| Hodson 2022 | Hodson 2022 | Poster | ✓ | ✓ |
| Ostwald 2021 | Ostwald 2021a | Poster with supplementary text | ✓ | ✓ |
| | Ostwald 2021b | Abstract | ✗ | ✓ |
| O'Sullivan 2019 | O'Sullivan 2019 | Full text publication | ✓ | ✓ |
| Parsons 2023 | Parsons 2023 | Poster | ✓ | ✓ |
| Rhew 2021 | Rhew 2021 | Full text publication | ✓ | ✓ |
| Sutton 2018 | Sutton 2018a | Poster with supplementary text | ✓ | ✓ |
| | Sutton 2018b | Abstract | ✗ | ✓ |

Details of the 12 studies included by the EAG (covered by 14 publications) are summarised in Table 9.

## Table 9: Studies selected by the EAG as the evidence base

| Study name and location | Design and intervention(s) | Participants and setting | Outcomes | EAG comments |
|---|---|---|---|---|
| Allain 2018<br><br>**Location:** USA<br><br>**Duration: Unclear.** 3 months with Kurin Lock analysed.<br><br>**Aims:** to investigate the impact of introducing Kurin Lock into blood culture sampling processes.<br><br>**Green:** meets scope | **Design:** Before/after study.<br><br>**Intervention:** Kurin Lock<br><br>**Green:** meets scope | **Participants:** Emergency department patients requiring blood culture samples (n = not reported).<br><br>**Exclusions:** None reported.<br><br>**Setting:** Emergency department in USA hospital.<br><br>**Green:** meets scope | • Blood culture contamination rate<br>• Estimated associated impact on costs<br><br>**Green:** meets scope | Abstract with limited study details.<br><br>Estimated cost savings of implementing Kurin Lock calculated, based on assumed costs associated with false positive blood culture results. |
| Arenas 2021<br><br>**Location**: USA<br><br>**Duration:** 16 months<br><br>**Aims**: to test 2 commercially available devices to reduce the blood culture contamination rate in an emergency department. | **Design**: Prospective and retrospective trial.<br><br>**Intervention**: 2 different blood diversion devices (device A and device B).<br><br>**Green**: meets scope | **Participants**: Emergency department patients requiring blood culture samples (n = 4030 samples).<br><br>**Exclusions**: None reported.<br><br>**Setting**: Emergency department in USA hospital.<br><br>**Green**: meets scope | • Blood culture contamination rate<br><br>**Green**: meets scope | Full text peer reviewed publication.<br><br>2 devices not identified in publication. Company submission indicated that device B is Kurin Lock.<br><br>Part of an ongoing quality improvement projects, however previous |

| Study name and location | Design and intervention(s) | Participants and setting | Outcomes | EAG comments |
|---|---|---|---|---|
| **Amber**: second blood specimen diversion device assessed in addition to Kurin Lock, which is not relevant to the scope. | | | | improvement strategies were reported as unsuccessful. |
| Arnaout 2021<br><br>**Location**: USA<br><br>**Duration**: 10 week period at one site, followed by second 10 week period at a second site. Washout phase in-between.<br><br>**Aims**: to assess the effectiveness of a blood diversion device<br><br>**Green**: meets scope | **Design**: Multi-phase prospective crossover trial<br><br>**Intervention**: Kurin Lock<br><br>**Green**: meets scope | **Participants**: Emergency department patients requiring blood culture samples (n = 5675 samples taken, 5661 analysed).<br><br>**Exclusions**: None reported.<br><br>**Setting**: 2 emergency departments in USA hospital.<br><br>**Green**: meets scope | • Blood culture contamination rate<br><br>**Green**: meets scope | Abstract with limited study details.<br><br>Device not named in abstract, company submission indicates the device is Kurin Lock.<br><br>Authors noted that second emergency department site had both a level 1 trauma centre and transplant program. |
| Atta 2022<br><br>**Location**: UK | **Design**: Before/after study. | **Participants**: Emergency department patients requiring | • Blood culture contamination rate | Poster with limited study details. |

| Study name and location | Design and intervention(s) | Participants and setting | Outcomes | EAG comments |
|---|---|---|---|---|
| **Duration**: 4 weeks<br><br>**Aims**: to determine, if the introduction of Kurin Lock will reduce the number of false-positive blood cultures.<br><br>**Green**: meets scope | **Intervention**: Kurin Lock<br><br>**Green**: meets scope | blood culture samples (n = 381 samples).<br><br>**Exclusions**: None reported.<br><br>**Setting**: Emergency department in NHS hospital.<br><br>**Green**: meets scope | • Estimated impact on length of stay<br>• Estimated associated impact on costs<br>• Staff adherence<br><br>**Green**: meets scope | Number of patients from whom samples were taken is unclear. |
| Baxter 2020<br><br>**Location**: USA<br><br>**Duration**: Not reported.<br><br>**Aims**: to investigate the impact of introducing Kurin Lock on blood culture contamination rates.<br><br>**Green**: meets scope | **Design**: Before/after study.<br><br>**Intervention**: Kurin Lock<br><br>**Green**: meets scope | **Participants**: Emergency department patients requiring blood culture samples (n = not reported).<br><br>**Exclusions**: None reported.<br><br>**Setting**: Emergency department in USA hospital.<br><br>**Green**: meets scope | • Blood culture contamination rate<br>• Length of stay<br>• Antibiotic provision<br>• Estimated associated impact on cost<br>• Staff adherence<br><br>**Green**: meets scope | Abstract with limited study details.<br><br>Device not named in abstract, company submission indicates the device is Kurin Lock. |
| Burnie 2021<br><br>**Location**: USA | **Design**: Before/after study. | **Participants**: Emergency department patients requiring | • Blood culture contamination rate | Full text peer reviewed publication. |

| Study name and location | Design and intervention(s) | Participants and setting | Outcomes | EAG comments |
|---|---|---|---|---|
| **Duration**: 6 months.<br><br>**Aims**: to investigate the impact of introducing Kurin Lock on blood culture contamination rates.<br><br>**Green**: meets scope | **Intervention**: Kurin Lock<br><br>**Green**: meets scope | blood culture samples (n = not reported).<br><br>**Exclusions**: None reported.<br><br>**Setting**: Emergency department in USA hospital.<br><br>**Green**: meets scope | • Estimated associated impact on costs<br><br>**Green**: meets scope | Impact of BCC on length of stay and associated cost of admission reported, not results linked to Kurin Lock implementation.<br><br>Site had previously introduced other quality improvement measures, some with no effect and others that resulted in some improvement in blood culture contamination rates. |
| Hodson 2022<br><br>**Location**: UK<br><br>**Duration**: 5 months.<br><br>**Aims**: to determine if the introduction of Kurin Lock reduces the number of contamination rates in an A&E department.<br><br>**Green**: meets scope | **Design**: Before/after study.<br><br>**Intervention**: Kurin Lock<br><br>**Green**: meets scope | **Participants**: Emergency department patients requiring blood culture samples (n = 533).<br><br>**Exclusions**: None reported.<br><br>**Setting**: A&E department in NHS hospital.<br><br>**Green**: meets scope | • Blood culture contamination rate<br><br>• Estimated associated impact on costs<br><br>**Green**: meets scope | Poster with limited study details. |

| Study name and location | Design and intervention(s) | Participants and setting | Outcomes | EAG comments |
|---|---|---|---|---|
| Ostwald 2021a<br><br>Ostwald 2021b<br><br>**Location**: USA<br><br>**Duration**: 2 months (initial study period) and 3 months (second study period with revised device).<br><br>**Aims**: to investigate the impact of introducing Kurin Lock on blood culture contamination rates in a paediatric emergency department.<br><br>**Green**: meets scope | **Design**: Before/after study.<br><br>**Intervention**: Kurin Lock<br><br>**Green**: meets scope | Participants: Paediatric emergency department patients requiring blood culture samples (n = 341 samples in first study period, n = 905 samples in second study period).<br><br>Exclusions: None reported.<br><br>Setting: USA paediatric emergency department.<br><br>**Green**: meets scope | • Blood culture contamination rate<br><br>• Mean cost of recall or admission due to false positive blood culture<br><br>• Estimated associated impact on costs<br><br>**Green**: meets scope | Abstract and poster with supplementary information identified.<br><br>Data extracted from poster with supplementary information.<br><br>Downstream impacts such as reduced length of stay and antibiotic use mentioned, but not quantified.<br><br>A cost analysis is mentioned, but it is unclear to what extent the reported cost savings are based on observed data or assumptions. |
| O'Sullivan 2019<br><br>**Location**: USA<br><br>**Duration**: 3 months.<br><br>**Aims**: to evaluate if a minimal-risk blood | **Design**: Before/after study.<br><br>**Intervention**: Kurin Lock<br><br>**Green**: meets scope | **Participants**: Emergency department patients requiring blood culture samples (n = not reported).<br><br>**Exclusions**: None reported. | • Blood culture contamination rate<br><br>• Estimated impact on associated costs<br><br>**Green**: meets scope | Full text peer reviewed publication. |

| Study name and location | Design and intervention(s) | Participants and setting | Outcomes | EAG comments |
|---|---|---|---|---|
| diversion device could be used successfully to reduce the rate of false-positive blood cultures.<br><br>**Green**: meets scope | | **Setting**: Emergency department in USA hospital.<br><br>**Green**: meets scope | | |
| Parsons 2023<br><br>**Location**: UK.<br><br>**Duration**: Not reported.<br><br>**Aims**: to determine if the introduction Kurin Lock will reduce the number of false positives in an emergency department.<br><br>**Green**: meets scope | **Design**: Before/after study.<br><br>**Intervention**: Kurin Lock<br><br>**Green**: meets scope | **Participants**: Emergency department patients requiring blood culture samples (n = 464 samples).<br><br>**Exclusions**: None reported.<br><br>**Setting**: Emergency department in NHS hospital.<br><br>**Green**: meets scope | • Blood culture contamination rate<br><br>• Estimated impact on length of stay<br><br>• Estimated associated impact on costs<br><br>**Green**: meets scope | Poster with limited study details. |
| Rhew 2021<br><br>**Location**: USA.<br><br>**Duration**: Not explicitly stated. Graphs suggest 1 year. | **Design**: Implementation study (before/after).<br><br>**Intervention**: Kurin Lock (peripheral IV blood draws) | **Participants**: Emergency department patients requiring blood culture samples (n = not reported).<br><br>**Exclusions**: None reported. | • Blood culture contamination rate<br><br>**Green**: meets scope | Full text peer reviewed publication.<br><br>Device not named in abstract, company submission indicates the device is Kurin Lock. |

| Study name and location | Design and intervention(s) | Participants and setting | Outcomes | EAG comments |
|---|---|---|---|---|
| **Aims**: to evaluate the use of an automated blood culture collection system when drawing blood cultures from a peripheral IV and to evaluate the effectiveness of implementing evidence-based policies, procedures, practice, products, and patient care to reduce blood culture contamination rates.<br><br>**Green**: meets scope | **Green**: meets scope | **Setting**: 4 USA emergency departments based in one integrated hospital system.<br><br>**Green**: meets scope | | Kurin lock was introduced as part of wider improvement measures at the same point in time. |
| Sutton 2018a<br><br>Sutton 2018b<br><br>**Location**: USA<br><br>**Duration**: 9 months total (4 with intervention, 5 without).<br><br>**Aims**: to investigate the efficacy of an engineered passive | **Design**: Before/after study.<br><br>**Intervention**: Kurin Lock<br><br>**Green**: meets scope | **Participants**: Emergency department patients requiring blood culture samples (n = 4220 samples).<br><br>**Exclusions**: None reported.<br><br>**Setting**: Phlebotomy and emergency department in single USA hospital.<br><br>**Green**: meets scope | • Blood culture contamination rate<br><br>• Estimated associated impact on costs<br><br>**Green**: meets scope | Abstract and poster with supplementary information identified.<br><br>Data extracted from poster with supplementary information. |

| Study name and location | Design and intervention(s) | Participants and setting | Outcomes | EAG comments |
|---|---|---|---|---|
| blood diversion device in preventing blood culture contaminates.<br><br>**Green**: meets scope | | | | |

Abbreviations: A&E: Accident and Emergency; BCC: Blood Culture Contamination; ED: Emergency Department; NHS: National Health Service; UK: United Kingdom; USA: United States of America.

# 6. Clinical evidence review

## *6.1. Overview of methodologies of all included studies*

The 4 studies reported in peer-reviewed full text publications investigated the impact of implementing the Kurin Lock device into blood culture sampling processes within secondary care settings.

One study (Arenas 2021) trialled 2 different blood specimen diversion devices in an emergency department in the USA (device A and device B), one of which was the Kurin Lock device. Blood culture contamination (BCC) rates observed when the 2 devices were implemented were compared with the BCC rate observed when standard care (no blood specimen diversion device) was used. The company submission indicated that device B was the Kurin Lock device.

The remaining 3 studies investigated the outcomes associated with using Kurin Lock device when blood culture samples were taken, compared to outcomes where no device or diversion technique was implemented (Burnie 2021, O'Sullivan 2019, Rhew 2021). Two of these studies were based in emergency departments located in the USA (Burnie 2021, O'Sullivan 2019). One of the studies investigated the use of Kurin Lock devices in drawing blood culture samples from peripheral IVs across 4 emergency departments based in one integrated hospital system in the USA (Rhew 2021).

The remaining 8 studies were reported in abstract and poster publications, with limited detail on study methodologies. Six of these studies were quality improvement projects by design where Kurin Lock was trialled to evaluate the impact on BCC rates in secondary care settings (Atta 2022, Allain 2018, Baxter 2020, Hodson 2022, Ostwald 2021a, Parsons 2023). One study is described as a multi-phase prospective crossover trial where Kurin Lock was implemented in one site for a 10 week initial period, followed by implementation in a second site for another 10 week period, with a washout phase in-between (Arnaout 2021). The remaining study is described as a quasi-experimental study and investigated the efficacy of Kurin Lock in preventing blood culture contaminants (Sutton 2018a). Three of these studies were based in UK NHS Trusts (Atta 2022, Hodson 2022, Parsons 2023).

All of the studies compared use of the Kurin Lock device with using no device (standard procedure). Most studies were reported in limited detail in the form of abstract and poster publications.

## 6.2. Critical appraisal of studies and review of company's critical appraisal

The company did not include critical appraisals of the included studies. A table summarising how each study was relevant to the decision problem included brief limitations of 9 of the 12 studies and details on how each study was funded. Where the limitations of the studies were described, these included the poster publications being non-peer reviewed/not published in journals and 3 of the 4 peer-reviewed full-text publications being single-centre studies. The company stated that 11 studies were hospital-delivered and funded, with 2 of these studies receiving the Kurin Lock device free of charge (Hodson 2022, Atta 2022). The remaining study is described by the company as hospital-delivered but supported by a grant from the Kurin Lock manufacturer. It is stated by the company that the design, analysis and manuscript drafting were not influenced by the manufacturer (O'Sullivan 2019).

The EAG critically appraised the 4 studies reported in peer-reviewed full text publications using a recognised critical appraisal checklist.

The EAG notes that it is difficult to assess the quality of the studies against recognised critical appraisal checklists, as they are not formal clinical trials in their design. The studies are best described as quality improvement projects in various secondary care settings. Two EAG reviewers decided the JBI Case Series critical appraisal checklist was the most appropriate checklist to assess the quality of the studies. The detailed critical appraisal checklists can be found in Appendix B.

The studies by Arenas (2021), Burnie (2021) and Rhew (2021) were considered to be of low quality. In the 3 studies, it is not clear which patients were included, and based on what criteria, if any. Whether consecutive or complete inclusion of participants was achieved is also unclear. Demographic

or clinical information of any participants is not reported. Results are reported relatively clearly in the studies by Burnie (2021) and Arenas (2021), but not by Rhew (2021). Information about the presenting site is included by Burnie (2021) and Rhew (2021), but not by Arenas (2021). Statistical analysis was considered appropriate in all 3 studies.

The study by O'Sullivan (2019) was considered to be of medium quality. The study authors state that all patients visiting a designated emergency department between April and June 2017, inclusive, were included in the study. Outcomes are reported clearly and statistical analysis is appropriate. There is information about the presenting site, which is described as an "869-bed level 1 trauma centre". However, there is no demographic or clinical information of any participants reported.

It is not clear in any of the study methodologies how participants were selected to be referred for a blood culture test. The EAG notes that there may be variation in clinical practice relating to the criteria that triggers the ordering of a blood culture test; such variation may be present in the included studies. Clinical experts indicated that general signs of systemic infection would initiate the starting of antibiotics, and a blood culture test would then be ordered to confirm the type of causative microorganism to inform selection of appropriate treatment.

One aspect of the studies that is not reported in detail, except for in the study by Arenas (2021), is the methods of laboratory analysis that may lead to a sample result being deemed a false positive. It should be considered that variations in determining and defining a false positive blood culture result across studies may limit the generalisability of the study results.

The company submission states that baseline blood culture contamination rates have been observed to be lower in USA studies compared with baseline blood culture contamination rates reported in UK studies. The EAG has not explored this beyond the studies included in this assessment, but agree that the evidence identified does suggest that baseline contamination rates are generally lower in USA studies, compared with UK studies. It should be noted

that the information on BCC rates in the UK is from abstracts / posters only and advises caution in making comparisons with data from the USA based studies.

The EAG notes that in studies where Kurin Lock was implemented as part of wider quality improvement projects (Burnie 2021, Rhew 2021), it is less clear how much of the effect on contamination rates can be attributed to the device alone.

The 10 abstracts and posters included by the EAG were not critically appraised using formal checklists due to a lack of detail. While these posters and abstracts can provide a useful representation of real-world evidence of the efficacy of Kurin Lock, the EAG cautions against over-interpretation of the results given the limited data on methods and outcomes reported and the lack of peer review publications associated with the studies.

## *6.3. Results from the evidence base*

The primary outcome reported across the evidence base is the blood culture contamination (BCC) rate. The majority of studies compared BCC rate when Kurin Lock is implemented into practice, compared with standard practice where no blood diversion technique is used. In addition to the BCC rates, the relative reduction in BCC rate is reported in some studies. Detailed results relating to BCC rates are reported in section 6.3.1.

Two studies used retrospective data on unnecessary length of stay associated with false-positive blood culture results observed during period of standard care, to calculate the number of bed days that could potentially be saved by implementing Kurin Lock (Atta 2022, Parsons 2023). One study reported the unnecessary length of stay calculated to be associated with false-blood culture results during a period of standard care, but did not link this to the potential impact that implementing Kurin Lock may have (Burnie 2021). One study calculated the average increase in length of stay associated with a BCC in practice, however it is unclear if this value was calculated during standard care periods or during the trial period where Kurin Lock was implemented (Baxter 2020). Results relating to length of stay are discussed in section 6.3.2

Two studies briefly commented on the observed impact of introducing Kurin Lock on antibiotic use, but no quantifications of these outcomes were reported (Burnie 2021, Ostwald 2021a/2021b). One study reported on the number of patients spared from receiving unnecessary antibiotics, but no information on how this number was calculated is given (Baxter 2020). Results relating to antibiotic use are discussed in section 6.3.3.

Staff adherence and satisfaction were discussed in 3 studies (Atta 2022, Baxter 2020, Ostwald 2021a/2021b) and 1 study reported on facilitators of successful implementation (Rhew 2021). Results relating to staff adherence and satisfaction, in addition to implementation facilitation, are discussed briefly in section 6.3.4.

A table detailing all relevant study results can be found in Appendix B.

### 6.3.1. Blood culture contamination rates

The evidence for BCC rates comes from 4 studies represented by full text publications (Arenas 2021, Burnie 2021, O'Sullivan 2019, Rhew 2021) and 8 studies represented by 10 posters and abstracts (Allain 2018, Arnaout 2021, Atta 2022, Baxter 2020, Hodson 2022, Ostwald 2021a/2021b, Parsons 2023, Sutton 2018a/2018b).

The study by Arenas (2021) analysed the blood culture contamination (BCC) rate recorded when standard procedure was used for blood culture sampling, compared with the BCC rates observed when 2 separate initial specimen diversion devices were used for blood culture sampling, one of which is the Kurin Lock device. The BCC rate when standard procedures were used, for 1293 samples, was 5.2%. The BCC rate when Kurin Lock was used, for 1312 samples, was 0.3%.

The study by Burnie (2021) reported on the impact of introducing the Kurin Lock device into the blood culture sampling process on BCC rates. The Kurin Lock device was trialled following implementation of other measures in an attempt to reduce BCC rates; this included implementation of a blood culture sample collection kit, designating dedicated teams for blood culture collection, and reeducation of staff on the blood culture collection procedure. These initial measures resulted in a slight decrease in BCC rates, prior to the introduction of the Kurin Lock device. The BCC rate observed during the period when the initial quality improvement measures were implemented was 2.92%. The BCC rate observed with Kurin Lock was 1.42% and then 1.51% the following year.

The study by O'Sullivan (2019) reported on BCC rates in the 3 most recent months prior to introducing the Kurin Lock device, compared with the BCC rates observed in the 3 most recent months where Kurin Lock was implemented. The rates in the 3 months without Kurin Lock were 1.4, 1.6 and 2.1% respectively. The rates in the 3 months with Kurin Lock were 0.4, 0.5 and 0.4% respectively. The BCC rates with Kurin Lock were found to be statistically significantly lower than the BCC rates without Kurin Lock ($p<0.05$). Overall, the average BCC rate was 0.44% over the 3 months with Kurin Lock

implemented, compared with an average BCC rate of 1.71% over the 3 months without Kurin Lock implemented; this translated into an average reduction in contaminations of 74.1%.

The study by Rhew (2021) reported on BCC rates from 4 hospitals that implemented the Kurin Lock device, as part of a wider quality improvement project. BCC rates for each hospital were reported in bar graphs only and these values were not extracted. The authors stated that BCC rates fell from 3.1% to 1.3% and then to 0% when using Kurin Lock over the 5 week trial period, it is not clear how these rates were calculated and how they relate to the values displayed in the bar graphs included in the study.

The number of samples used in the calculation of BCC rates is not reported by Burnie (2021), O'Sullivan (2019) or Rhew (2021).

Three studies, represented by poster publications, reported the results of quality improvement projects in UK NHS Trusts (Atta 2022, Hodson 2022, Parsons 2023). Blood culture contamination (BCC) rates appeared reduced with the introduction of the Kurin Lock device. Hodson (2022) reported this reduction to be statistically significant ($p=0.045$). Statistical significance of results is not reported in the remaining 2 studies. Five studies, represented by poster and abstract publications, reported the results of introducing the Kurin Lock device into emergency departments in the USA (Allain 2018, Arnaout 2021, Baxter 2020, Ostwald 2021a/2021b, Sutton 2018a/2018b). Three of the 5 studies reported on statistical significance of results and stated that BCC rates were significantly reduced after the introduction of Kurin Lock ($p<0.05$) (Arnaout 2021, Ostwald 2021a/2021b, Sutton 2018a/2018b). The remaining 2 studies reported a decrease in BCC rates post-Kurin Lock implementation.

The BCC rates pre and post-Kurin Lock reported across the evidence base are summarised in Table 10.

## Table 10: Blood culture contamination (BCC) rate results

| Study (setting) | Blood culture contamination (BCC) rate |
|---|---|
| **Allain 2018** (USA ED) | • Overall contamination rate from 2013-2016 ranged from 2.1% to 1.6%<br>• Annual average BCC rate pre-Kurin in 2016: 1.6% (99 contaminations)<br>• BCC rate 3 months post-Kurin Lock in 2017: 0.8% (8 contaminations)<br><br>Number of samples included in each rate calculation not reported. |
| **Arenas 2021** (USA ED) | 4030 samples included in total (device A and device B).<br>At baseline, the emergency department had contamination rates of between 3% to 4.7%.<br><br><u>Device B (Kurin Lock) results</u><br>• BCC rate in control group: 5.2% (1293 samples)<br>• BCC rate with Kurin Lock: 0.3% (1312 samples)<br>• Mean incidence of BCC in the device B group was 0.23 (0.13-0.37) times the incidence of BCC in the control group (based on statistical model prediction) |
| **Arnaout 2021** (USA EDs) | <u>Overall BCC rate (5661 samples)</u><br>• Standard procedure: 2.9%<br>• With Kurin Lock: 1.9%<br>p = 0.018<br><br><u>Emergency department 1 BCC rates (1719 samples)</u><br>• Standard procedure: 1.4%<br>• With Kurin Lock: 1.1%<br>p = 0.57<br><br><u>Emergency department 2 BCC rates (3942 samples)</u><br>• Pre-Kurin Lock: 3.5%<br>• With Kurin Lock: 2.3%<br>p = 0.024<br><br>BCC rates reduced by 1% overall, with a 34% relative reduction.<br>Statistically significant difference in BCC rate observed overall and at ED 2, but not ED 1. |
| **Atta 2022** (UK A&E) | • Baseline BCC in emergency department: 9% (8.91% in graph)<br>• BCC with Kurin Lock (381 samples included): 3.1% (3.19% in graph)<br>• An overall relative reduction of 65.5% |
| **Baxter 2020** (USA ED) | • BCC rate without Kurin Lock: 4.93%<br>• BCC rate with Kurin Lock: 1.66%<br>• Overall reduction in BCC rates of 66%. |

| Study (setting) | Blood culture contamination (BCC) rate |
|---|---|
| **Burnie 2021** (USA ED) | BCC rate at baseline:<br>• 2.92% in 2018<br><br>BCC rate with Kurin Lock:<br>• 1.42% in 2019<br>• 1.51% in 2020 (48% improvement from 2018 rate)<br><br>Introduction at a second site for 6 months (additional data, not associated with the original study period)<br>• BCC rate at baseline: 4.96%<br>• BCC rate with Kurin Lock: 1.6% |
| **Hodson 2022** (UK A&E) | • BCC rate pre-Kurin Lock: 6% (1343 samples)<br>• BCC rate with Kurin Lock: 1.9% (2% reported in text) (533 samples)<br><br>Statistically significant difference between 2 rates, p=0.045 |
| **Ostwald 2021a**<br>**Ostwald 2021b**<br>(USA Paediatric ED) | Retrospective analysis of BCC rates in department ranged from 0.45 to 5.63%.<br><br><u>First study period:</u><br>Overall BCC rate: 1.5% (stated by authors, figures suggest rate is 1.17%)<br>• 0 instances of contamination observed in 303 samples drawn with Kurin Lock (0%)<br>• 4 instances of contamination observed in 38 samples drawn without Kurin Lock (10.5%)<br>p=0.0001, significant difference in BCC rate observed post-Kurin Lock introduction.<br><br><u>Second study period (modified tubing):</u><br>Overall BCC rate: 0.22%<br>• 0 instances of contamination observed in 872 samples drawn with Kurin Lock (0%)<br>• 2 instances of contamination observed in 33 samples drawn without Kurin Lock (6.06%)<br>p=0.0001, significant difference in BCC rate observed post-Kurin Lock introduction. |
| **O'Sullivan 2019** (USA ED) | BCC rates in 3 most recent months prior to intervention:<br>• March 2017: 1.4%<br>• February 2017: 1.6%<br>• January 2017: 2.1%<br><br>BCC rates in 3 most recent months where Kurin Lock was implemented:<br>• June 2017: 0.4%<br>• May 2017: 0.5%<br>• April 2017: 0.4%<br><br>Significantly lower BCC rate consistently observed with Kurin Lock compared to BCC rates observed without Kurin Lock. Reductions in BCC rate ranged from 65% to 82% ($p<0.05$ for 9 comparisons made).<br><br>Overall, the average BCC rate was 0.44% over the 3 Kurin Lock months compared with the average BCC rate of 1.71% over the 3 non-Kurin Lock months. Average reduction of 74.1%. |

| Study (setting) | Blood culture contamination (BCC) rate |
|---|---|
| **Parsons 2023** (UK A&E) | • BCC rate at baseline: 5%<br>• BCC rate with Kurin Lock: 2.6%<br>• Overall reduction of 48% |
| **Rhew 2021** (USA EDs) | *Monthly BCC rates for 4 hospitals not extracted from bar graphs, values not reported in text.*<br><br>Authors state BCC rates fell from 3.1% to 1.3% to 0% when using Kurin Lock over the 5 week trial period. Ultimately, the overall system wide BCC rate fell to less than 2.1%. |
| **Sutton 2018a**<br>**Sutton 2018b**<br>(USA ED) | • Pre-intervention BCC rate (1953 samples): 0.025 (2.6%), 95% CI (0.019-0.033)<br>• Post-Kurin Lock BCC rate (2267 samples): 0.012 (1.2%), 95% CI (0.008-0.017)<br><br>Statistically significant difference between 2 rates, $p<0.05$. |

Abbreviations: A&E: Accident and Emergency; BCC: Blood Culture Contamination; CI: Confidence Interval; ED: Emergency Department; UK: United Kingdom; USA: United States of America.

### 6.3.2. Length of hospital stay

Length of hospital stay is not listed as a formal outcome in the methods of any of the included studies. It is however, briefly discussed in 4 studies and is listed as an outcome relevant to the decision problem in the scope.

Atta (2022) reported that implementation of Kurin Lock and the resulting reduction in blood culture contamination (BCC) could potentially release 1,444 bed days in the department the study took place in and 5,041 Trust-wide. No further detail on how these values were calculated is reported.

Parsons (2023) reported that implementation of Kurin Lock would create the opportunity to free 359 bed days in the emergency department alone, and 1,836 bed days Trust-wide. No further detail on this statement is provided.

Burnie (2021) commented on the average length of additional hospital length of stay associated with BCC in general (2.65 days), but did not make any comment on how implementing the Kurin Lock device impacted length of stay in their study population. Baxter (2020) calculated that, based on data from 3 different months, patients with BCC spent an average of 3.97 additional days in hospital. It is unclear if this figure was calculated during a period of using standard care or during a period of using Kurin Lock.

### 6.3.3. Use of unnecessary antibiotic treatment

The provision of unnecessary antibiotics is not listed as a formal outcome in the methods of any of the included studies. It is however, briefly discussed in 3 studies and is listed as an outcome relevant to the decision problem in the scope.

Baxter (2020) reported that during the trial period, 144 patients were spared from receiving unnecessary antibiotics. It is not detailed how this value was calculated and the trial period length is not reported.

Burnie (2021) commented that nearly 250 patients have 'benefitted' from the Kurin Lock device being implemented, which includes decreased exposure to unnecessary antibiotics. No exact values in relation to this statement are reported.

Ostwald (2021a/2021b) reported that the second trial period of the study resulted in decreased unnecessary antibiotic use. No further detail is provided.

### 6.3.4. Staff adherence and satisfaction

Staff adherence and satisfaction with using the Kurin Lock device is not listed in the scope as an outcome relevant to the decision problem, but it is discussed briefly in 3 studies.

Atta (2022) commented that the reduction in blood contamination rate is associated with staff adherence of using the Kurin Lock device, with results becoming evident when staff adherence is at 80%. In a graph, there is a reported compliance rate of 92.05% associated with a contamination rate of 0.00% in 'week 2'. The EAG notes that the order of the weeks listed on the X-axis of the graph are in a non-consecutive order. This is not discussed in the text.

Baxter (2020) reported that adherence of staff with using the device averaged between 70 and 75% during the trial period with Kurin Lock.

Ostwald (2021a/2021b) conducted a staff survey to assess attitudes of nurses using the Kurin Lock device during the study period. It is reported that 45% of

nurses found the device to be ‘easy to use’ and 85% of nurses found that the device ‘made sense’. However, after the first study period there were complaints that the length of tubing included in the Kurin Lock kits were too long and bulky to be used for paediatric patients. As a result, the tubing was modified prior to the second study period.

## 7. Adverse events

The company stated that no adverse events have been reported in association with the Kurin Lock device. It is unclear if any searches of databases were conducted by the company to identify adverse events.

The EAG conducted searches of MAUDE and MHRA databases. Seven medical device reports (MDRs) relating to 5 presumed unique events were found on the MAUDE database where the Kurin Lock device was mentioned in the event description. The 5 events were reported between February 2020 and January 2023.

Of the 5 event reports, 3 had responses from the manufacturer which advised that the issue was not related to the Kurin Lock device. The remaining 2 event reports did not contain formal responses from the manufacturer. Both were reported on the same day, and it is unclear if these are duplicate reports for the same event. The events were described as the safety needle not fully retracting post-blood collection, resulting in a risk of needlestick injuries. The event descriptions state that the manufacturer withdrew the batch of devices and provided replacements with an older needle version. The EAG sought further information on these 2 events from the company; the company stated they were not aware of any product failures in the UK.

There are no adverse events reported in the evidence base. Clinical experts stated they were not aware of any device malfunctions or safety concerns related to the Kurin Lock device.

## 8. Evidence synthesis and meta-analysis

Meta-analysis of results was not conducted by the company. The company calculated the pooled average reduction in the BCC rate as a result of Kurin

Lock implementation to be 67.5%. However, unlike formal meta-analysis, a pooled average does not consider heterogeneity of the studies and does not assign appropriate weightings to studies with varying sample sizes. The EAG advises caution should be taken when interpreting this pooled average.

The EAG does not consider meta-analysis to be appropriate due to there being:

- Very limited peer-reviewed published evidence and therefore a significant risk of bias in the results available.
- A lack of detail on study participants and sample sizes included in studies, meaning it would be difficult to identify and extract appropriate data to include in any meta-analysis.
- The majority of the evidence is based in the USA, where healthcare systems operate differently to those in the UK; clinical and system variations would likely undermine the generalisability of any results. It is stated by the company that BCC rates have been observed to be generally lower at baseline in the USA than the UK.

## 9. Ongoing studies

There were no ongoing studies identified as relevant to the decision problem. The company stated that they are actively engaging in talks to introduce Kurin Lock to a number of locations across the NHS.

# 10. Interpretation of the clinical evidence

Overall, the clinical evidence suggests that Kurin Lock is a safe and effective method of reducing blood culture contamination (BCC) rates. The EAG considers it reasonable to assume the downstream benefits of reducing false-positive blood culture results, such as reducing unnecessary antibiotic use and decreasing length of hospital stay, may be achieved with the implementation of Kurin Lock. However, while evidence exists linking a reduction in false-positive rates with downstream events such as reduced antibiotic use and length of stay in a wider context (Skoglund 2019), the EAG did not identify any Kurin Lock studies reporting these outcomes beyond broad estimations and assumptions. Therefore, the EAG considers there to be a significant gap in the evidence linking implementation of the Kurin Lock device with downstream benefits of reducing false-positive blood culture results.

One clinical expert commented that the proposed downstream benefits of implementing Kurin Lock, including reducing length of stay and reducing use of unnecessary antibiotics are reasonable assumptions but stated that this data had not been recorded or collected in the trial that took place in their NHS Trust. The same expert commented that adding the Kurin Lock device to the standard blood culture collection kits would mean that any general trends observed in unnecessary antibiotic use and increased length of stay as a result of false positive blood culture results could then be linked back to the introduction of the Kurin Lock device.

The company stated that it should be acknowledged that length of stay and antibiotic use can be impacted by a multitude of factors that are independent from false-positive bloodstream infection results. This was reiterated by a clinical expert, who stated this may lead to difficulty in accurately collecting these outcomes.

While the majority of the evidence identified is non-peer reviewed and available only as poster or abstract publications and this should be considered when assessing the quality and robustness of the evidence; the EAG notes that results from the poster and abstract publications align with the results

reported in the full-text peer reviewed publications indicating that Kurin Lock is effective in reducing contamination of blood cultures. The EAG accepts that these results may constitute real-world evidence and are considered relevant to the decision problem.

The majority of the studies (9 out of 12) identified were conducted in secondary care settings in the USA, which limits generalisability of the results to an NHS population due to variations in clinical practice, including factors such as pathways for patient admission, investigations, antibiotic use and length of hospital stay. In addition, the results suggest that there are differences in baseline contamination rates in the USA and UK however the reason for this is not clear. Clinical experts did not comment on the generalisability of evidence from the USA to a UK NHS setting.

# 11. Economic evidence

## *11.1. Published economic evidence*

### Search strategy and selection

The company conducted a separate search for economic evidence. The company searched one database (Medline via PubMed) using free text terms, however, no index terms were used. The date limit on the search strategy was broad, covering the dates 1983 to 2023, although only studies published in 1998 or later were eligible for inclusion. The company search strategy identified 91 records. Additionally, grey literature searches were conducted for economic evidence related to initial specimen diversion devices. Details of grey literature searches were not provided. Inclusion criteria for the economic evidence was appropriately detailed in accordance with the decision problem and is provided in Appendix A.

To ensure that all relevant and recent literature had been identified, the EAG conducted a combined search for both clinical and economic evidence, which identified a total of 264 records. Details of the company and EAG search strategies are provided in Appendix A.

### Published economic evidence review

No full economic analyses relating to Kurin Lock were identified by the EAG, however 8 of the clinical studies included by the EAG contained limited references to costs (Allain 2018, Atta 2022, Baxter 2020, Burnie 2021, Ostwald 2021a/2021b, O'Sullivan 2019, Parsons 2023, Sutton 2018a/2018b).

The EAG combined searches identified 9 studies that included cost analysis, but were excluded according to the scope, as they did not include the use of Kurin Lock. Although they do not include direct economic evidence for Kurin Lock, they do provide some relevant information about the costs associated with contaminated blood cultures, or reported economic information for studies on similar competitor devices. The company also identified 11 studies that did not include Kurin Lock, but contained relevant cost information. The studies identified during the EAG and company searches are listed in Table 11, and key results briefly summarised in the following sections.

**Table 11: Summary of additional economic studies**

| Study | Setting | Included by EAG | Included by Company | In Scope? |
|---|---|---|---|---|
| Alahmadi 2010 | UK, hospital | N | Y | No, cost of BCC |
| Buzzard 2021 | USA, ED | Y | N | No, competitor device |
| Dempsey | mixed | N | Y | No, systematic review |
| Geisler 2019 | USA | Y | Y | No, competitor device |
| Lalezari 2020 | Israel, ED | Y | Y | No, competitor device |
| Klutcher 2022 | USA, ED | N | Y | No, cost of BCC |
| McAdam 2017 | n/a | Y | N | No, editorial |
| Rupp 2017 | USA | Y | Y | No, competitor device |
| Salcedo 2019 | USA, ED | Y | N | No, cost of BCC |
| Sheppard 2008 | USA | N | Y | No, cost of BCC |
| Skoglund 2019 | USA, ED | Y | Y | No, competitor device |
| Tompkins 2022 | USA | Y | N | No, competitor device |
| Walzman 2001 | USA, ED | N | Y | No, cost of BCC |
| Zwang 2006 | USA | N | Y | No, cost of BCC |

Abbreviations: BCC: Blood Culture Contamination; ED: Emergency Department; UK: United Kingdom; USA: United States of America.

**Results from the economic evidence**

The EAG have reported any estimation of cost savings that is mentioned in the included Kurin Lock clinical studies in **Table *12***. None of the studies add significantly to the available economic evidence because they either:

- Did not report change in bed days or costs
- Applied an assumed saving to the reduction in BCCs
- Report a cost or change in length of stay per BCC, rather than due to introducing Kurin Lock.

**Table 12 Summary of economic evidence from included clinical papers**

| Study (setting) | Comparator | Baseline contamination rate | Reduction in bed days | Cost per BCC | Comments |
|---|---|---|---|---|---|
| UK Kurin Lock | | | | | |
| **Atta 2022** (UK A&E) | Kurin Lock, before/after | 9% | Not reported | £5,000 assumed | Cost savings appear to be based on applying £5,000 per BCC to the observed decrease in BCC. |
| **Hodson 2022** (UK A&E) | Kurin Lock, before/after | 6% | No cost savings reported | | |
| **Parsons 2023** (UK A&E) | Kurin Lock, before/after | 5% | 5 assumed | £5,000 assumed | Costs and bed days appear to be based on assumptions applied to the observed decrease in BCC. |
| Non-UK, Kurin Lock | | | | | |
| **Allain 2018** (USA ED) | Kurin Lock, before/after | 1.6% | Not reported | $5,200 assumed | Based on applying cost saving to number of BCC, minus device cost. |
| **Arenas 2021** (USA ED) | Kurin Lock vs other ISDD vs SoC | 3 - 5.2% | No cost savings reported | | |
| **Arnaout 2021** (USA EDs) | Kurin Lock, before/after | 2.9% overall 1.4 – 3.5% ED | No cost savings reported | | |
| **Baxter 2020** (USA ED) | Kurin Lock, before/after | 4.93% | 3.97 extra days per BCC | $4,000 assumed | Based on applying cost saving to number of BCC. Appears not to include device cost. |
| **Burnie 2021** (USA ED) | Kurin Lock, before/after | 2.92 – 4.96% | 2.65 extra days per BCC | $5,863 per BCC from data | Data collected analysed over 1 month pre introduction. No cost analysis post introduction |
| **Ostwald 2021** | Kurin Lock, before/after | 0.45 to 5.63% | Not reported | Mean cost of calling a | Data was taken from administrative records |

| Study (setting) | Comparator | Baseline contamination rate | Reduction in bed days | Cost per BCC | Comments |
|---|---|---|---|---|---|
| (USA Paediatric ED) | | | | patient back in and/or admission due to BCC was £1,907 | |
| **O'Sullivan 2019** (USA ED) | Kurin Lock, before/after | 1.4 – 2.1% | Not reported | $5,000 assumed | Costs calculated based on this assumption and including device costs, but method unclear. |
| **Rhew 2021** (USA EDs) | Kurin Lock, before/after | 3.1% | No cost savings reported | | |
| **Sutton 2018a Sutton 2018b** (USA ED) | Kurin Lock, before/after | 2.6% | Not reported | $7,500 assumed | Reports including cost of equipment, cultures and BCC, no details given. |

Abbreviations: A&E: Accident and Emergency; BCC: Blood Culture Contamination; ED: Emergency Department; ISSD: Initial Specimen Diversion Device; SoC: Standard of Care; UK: United Kingdom; USA: United States of America.

A brief description of key results reported in additional papers that do not include Kurin Lock is shown in Table 13, including the parameters that are used in the submitted company model (these are also used in the EAG model).

**Table 13 Summary of economic papers identified in submission and by EAG**

| Study | Used for company model? | Used for EAG model? | Baseline BCC | BCC change | Change in LOS | Key results | Comments |
|---|---|---|---|---|---|---|---|
| Alahmadi 2010 (UK, hospital) | Y, follow up tests, hospital LOS | Y, follow up tests, hospital LOS | 4.7% | n/a/ | 5.44 mean days per BCC | Mean difference of £5,001.5 total cost (95% CI 2.8 – 8.1 days)<br>Key difference was in LOS, smaller differences in antibiotic costs, microbiology, radiology and haematology tests. | 42% of BCC were from ICU, with higher costs than other hospital areas.<br>Total costs are reported as a mean difference, detailed costs are reported as median for each arm. |
| Buzzard 2021 (USA, ED) | N | N | 7.47%, | 2.59% ITT 0.86% PP | 0.1 hospital days (ITT) | Baseline of 7.47%, reduced to 2.59% ITT. Per protocol reduced to<br>No significant difference in LOS (2.31 vs 2.41 hospital days; 0.84 vs 0.68 ICU days), antibiotic duration or repeat blood cultures (ITT analysis only) | It is unclear if total hospital costs were calculated or based on an assumption. A value of $8,750 per contaminant was stated, and a total hospital cost of $1,120,000 before the intervention and $383,690 (ITT) post intervention.<br>Compliance likely to be difference between ITT and PP. |
| Dempsey (mixed, mainly USA) | N | N | unclear | n/a | 1-22 days for BCC compared with 1-17 days for negative cultures | Total additional hospital costs were between $2,923 and $5,812 per BCC. Direct costs only (pharmacy and microbiology) were an additional $305-$1,389 per BCC | Authors reported BCC rates of up to 84% but this was for a specific evaluation of BCC. The 11 included studies included Alahmadi, Zwang and Waltzman.<br>BCC rates reporting appears inconsistent between rate for all samples or rate within positive tests. |
| Geisler 2019 (USA) | N | N | 1.89% from data, 4.2% pooled analysis | n/a | 2.35 days per BCC | BCC incremental costs of $4,818 of which $3198 was hospital stay, $625 additional tests and IV access, $494 antimicrobial therapy, $373 hospital | Model using retrospective matched data and survival analysis<br>Does not include cost of ISSD |

| Study | Used for company model? | Used for EAG model? | Baseline BCC | BCC change | Change in LOS | Key results | Comments |
|---|---|---|---|---|---|---|---|
| | | | | | | acquired complications and $127 extra blood cultures | |
| Lalezari 2020 (Israel ED) | Y, ICU LOS | Y, ICU LOS | 5% | 1.6% | 2.35 days per BCC | 5,791 New Israeli Shekels per BCC, with the majority of this being due to daily hospital costs. Costs were also included for blood culture collection, processing and testing and antibiotics. | The majority of blood cultures were stated as being from the emergency room. |
| Klutcher, 2022 (USA, ED) | N | N | 7.3% | n/a | 1.3 days unadjusted | BCC significantly increased LOS, antibiotic duration (6.2 vs 5.2 days), hospital charges ($36,008 vs $28,875), AKI (36.7% vs 26.3%), echocardiograms (27.4% vs 19.2%), and in-hospital mortality (8% vs 4.6%). | Considers patient risk factors for BCC. |
| McAdam 2017 (editorial, n/a) | N | N | n/a | n/a | n/a | n/a | Editorial only, data not extracted by EAG |
| Rupp 2017 (USA) | Y bacteraemia risk, empiric antibiotics | Y bacteraemia risk, empiric antibiotics | 1.78% | 0.22% | Not reported | None applicable to economics | This study is used in the economic model, but does not include any cost data other than applying an assumed cost to the number of BCC. |
| Salcedo 2019 (USA, ED) | N | N | 2.8% | n/a | Not reported | Of contaminated cultures, only 12.7% given antibiotics due to test result. None were admitted due to test result, but 92.3% admitted for another diagnosis. Total costs per BCC $170 | Differentiated between treatment due to contamination, or due to other comorbidities. This may underestimate impact. |
| Sheppard 2008 (USA) | N | N | 5% | 1.1% | Overall LOS unchanged | 75% of patients with blood culture tests were admitted.<br>Calculation of cost of providing phlebotomy and lab service compared to an assumed cost per BCC | Compares previous care with introduction of phlebotomist and dedicated laboratory technician |

| Study | Used for company model? | Used for EAG model? | Baseline BCC | BCC change | Change in LOS | Key results | Comments |
|---|---|---|---|---|---|---|---|
| Skoglund 2019 (USA, ED) | Y, antibiotics, LOS | Y, antibiotics, LOS | 6% | 0.22% | 2 days per BCC | $272 cost saving per blood culture in overall hospital costs, $28 in direct costs.<br>Main drivers reported as baseline contamination rate and duration of antibiotics for direct costs (not including length of stay) | Decision tree economic analysis comparing an ISDD with standard care in the emergency department. Clinical data based on hospital database records. |
| Tompkins 2022 (USA) | N | N | 2.3% | 0% | Not reported | 2.3% vs 0% BCC for phlebotomists, nurses had a 0.8% BC rate. | Introduction of ISDD on inpatient and ED.Considers central-line-associated bloodstream infection (CLABSI)<br>24% from intensive care. |
| Walzman, 2001 (USA, ED) | N | N | 0.9% | n/a | Not reported | 79/87 patients with BCC had complete follow up.<br>7 were admitted as inpatients, with total costs of $20,227, almost all of which was general hospitalisation cost. The total cost for all patients for outpatient or community care was $12,003, including 54 with a primary care visit and 31 visits to ED. | Paediatric febrile population<br>This paper compared the cost of false positive tests ($32,230) with the cost of routine testing ($719,340), with BCC adding a mean of $3.40 per culture. |
| Zwang, 2006 | N | N | 6% | n/a | 3 days | LOS difference costed at $8,750 per BCC<br>Laboratory charges were $161 per true negative BC, and $311 per false positive BC. | Charges taken from institutional database and adjusted using a cost to charge ration. |

Abbreviations: AKI: acute kidney injury; BCC: blood culture contamination; ED: emergency department; ICU: intensive care unit; ITT: intention to treat; LOS: length of stay; PP: per protocol.

## *11.2. Company de novo cost analysis*

### Economic model structure

The company submitted a decision tree model comparing the use of Kurin Lock with standard care in an Accident and Emergency setting. They used duration of hospital stay as the time horizon, no discounting and an NHS perspective, all of which were appropriate. The model used a mixed population of 85% adults (12 years and older) and 15% pediatric patients (ONS 2022). Additional scenarios were provided for ICU and general hospital settings, and results were also presented for adults (12 years and older) and paediatric (up to 12 years old) patients.

The model structure reflected the scope and the clinical pathway appropriately, as shown in Figure 1, taken from the company model. The structure is the same for BC collection by either Kurin Lock or standard methods.

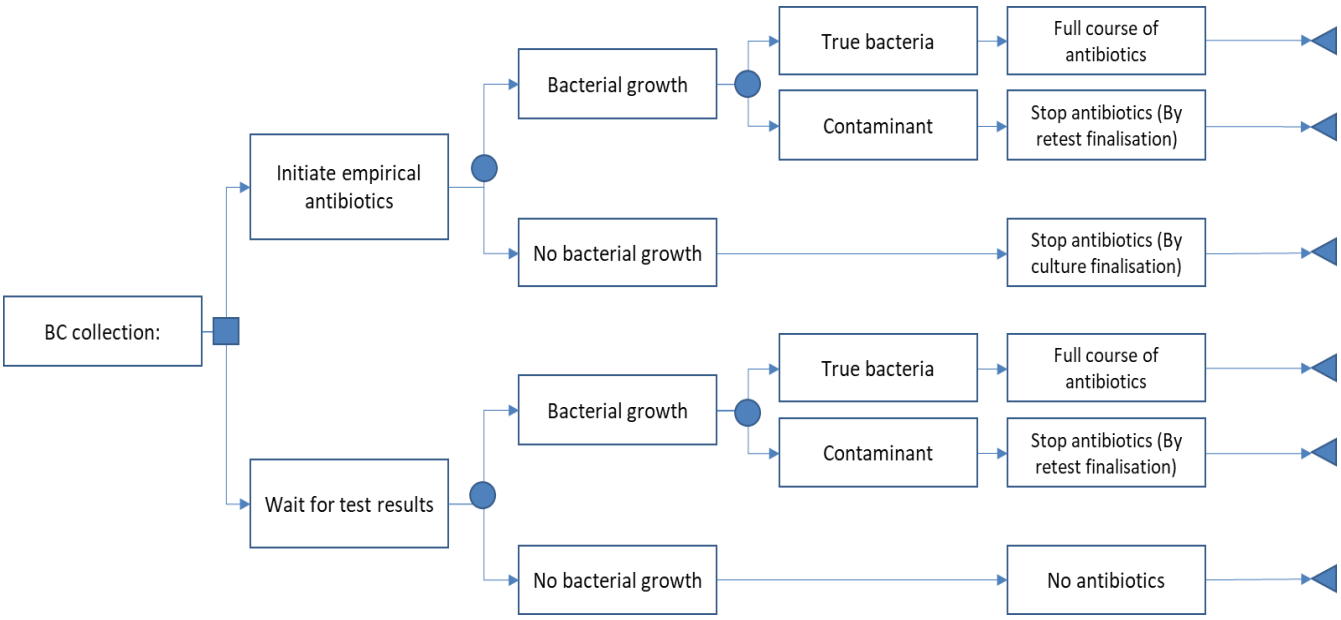



**Figure 1 Economic model structure (taken from company model)**

Assumptions from the company, and EAG comments are described in Table 14 and additional assumptions identified by the EAG in Table 15. Note that the assumptions and justifications are abbreviated, with the full version available in the company submission.

## Table 14 Modelling assumptions

| Assumption | Justification | EAG comments |
|---|---|---|
| The model assumes that the baseline risk of bacteraemia is 7.4%, which is applied to both arms of the model.(Rupp 2017) | The model assumes that the underlying risk of bacteraemia is the same in each arm of the model. Therefore the choice of base line risk in the model will not influence the final results as the number of patients identified and associated treatment costs will be equal in each arm and thus cancel out. This figure is included for completeness. | The EAG accept this and do not have any additional comments. |
| The model assumed a base line contamination rate for SoC of 9% in the A&E (Atta 2022). | Kurin Lock was trialled in the A&E at King's Princess Royal Hospital to determine if the introduction of an ISDD would reduce the number of false-positive blood cultures. The baseline contamination rate at the trial hospital A&E was 9%. | The EAG accept this, and note that expert advice was that although general hospital rates would be lower, contamination rates of up to 10% may be seen in A&E. It was noted that Rupp (2017) reported baseline contamination of 1.22% in an A&E setting in the USA, and that in the UK, Hodson (2022) report 6% and Parsons (2023) report 5%, both in A&E. |
| The model assumed that the reduction in blood culture contamination rate for Kurin Lock is at 65.5% (Atta 2022). | A trial of Kurin Lock at King's College Hospital, London, demonstrated that the introduction of an initial specimen diversionary device reduces the number of false-positive blood cultures by 65.5%. This parameter is explored in sensitivity analysis. | The EAG accept this value for the base case, but note that the potential reduction may be dependent on the baseline contamination rate, and the introduction of a bundle of improvements together with Kurin Lock. |
| It was assumed that all patients with a positive, or the suspicion of, bacteraemia would receive (empiric) vancomycin. (Skoglund 2019) | While other antibiotics therapies are available, the choice of treatment is unlikely to be influenced by the method of blood sample collection. Due to the relative low cost, and for simplicity, only vancomycin is considered for treatment of bacteraemia. | The EAG do not agree that this is likely, based on discussion with clinical experts. This may be a difference between practice in the USA and UK.<br>The EAG have replaced vancomycin with an alternative, however the impact was minor |
| In scenario analysis the model assumed that a patient receiving ≤3 days of vancomycin underwent 1 or more serum concentration assays (Liu 2011) | The administration of vancomycin often necessitates pharmacokinetic monitoring. In the base case this is conservatively excluded. | This is not included in the base case, and is not included by the EAG in any setting as experts did not consider vancomycin to be commonly used, and did not normally require any additional testing. |
| The model assumed no adverse events of vancomycin. (Patel, 2022) | As, the cost of a serum concentration is included in the model to account for monitoring of vancomycin administration, adverse events associated with the rapid infusion of vancomycin were not included. | This is a conservative assumption as more antibiotic would be delivered to the standard care arm. |
| The model assumed that two blood cultures were drawn | It was assumed that one Kurin Lock or SoC set can be used to draw two bottles for blood culture testing. The | The EAG agreed that two blood cultures per collection, and two separate collections would be the |

| Assumption | Justification | EAG comments |
|---|---|---|
| per collection and that the contamination rates were the same irrespective of the number of bottles drawn. (PHE 2021) | gold standard is two samples (aerobic and anaerobic), from two sites so utilising two sets and four bottles. | normal procedure based on expert advice. |
| The model does not consider false negative patients (Assumption) | There is no evidence to suggest that the method of blood culture collection would result in different levels of false negative patients (i.e. patients with bacteraemia being mis-diagnosed). | The EAG agree that the level would be expected to be the same in both arms, and therefore would not then impact on the model results. |
| No impact on hospital acquired infection and/or on the associated mortality is assumed | There is a small increased risk of hospital acquired infections linked to length of stay. This has been conservatively excluded from the analysis. | The EAG agree that this is a conservative assumption and have not made any changes. |

**Table 15 Additional assumptions identified by the EAG**

| Assumption | Comment |
|---|---|
| Blood collection only occurs at one point in time for any single patient | Patients may require more than one set of blood cultures if a false positive or negative is suspected and confirmation required. This would reduce the cost savings due to Kurin Lock, due to the higher cost of the device. Additional testing is included in one way sensitivity analysis |
| All false positive results would cause an impact on patient treatment | The evidence for Kurin Lock is based on reduction of false positives, but there is no direct evidence of the consequences being realised. It is possible that not all false positives have the modelled impact on treatment. |
| All patients with a blood culture test taken would be admitted from A&E | Expert opinion is that a small number would not be admitted, and their recall would be more likely to be an additional appointment than multiple days in hospital. No data was identified to include this in the model. |

### Economic model parameters

The following sections detail the clinical and resource use parameters used in the economic model and any changes made by the EAG. Both the parameters used by the company and any changes made by the EAG are summarised in Table 16 and Table 17.

### Clinical parameters and variables

The key points for consideration in the clinical parameters are:

- Some key data comes from papers in the US, where the normal standard of care may differ from the UK.
- It is unclear for some papers if results are per blood test or per patient.

- None of the papers for Kurin Lock report length of stay or antibiotic use, data for these parameters are taken from other sources, based on false positive tests. The EAG did not change the values of these parameters in the base case.

Baseline contamination rates: This is the contamination rate observed prior to the introduction of Kurin Lock. The majority of papers refer to a recommended standard of <3% (Arenas 2021, Burnie 2021, O'Sullivan 2019, Rhew 2021), but literature and clinical experts agree that there is wide variation in practice, with A&E being one of the settings with the highest contamination rate observed. The range of values from included studies were from 1.6% (Allain, 2018) to 9.0% (Atta, 2022) (**Table *12***) and are described in more detail in Table 10 of the clinical evidence. The company used 9% in the model, and the EAG agreed that this was reasonable as it is based on a UK NHS source with an A&E setting, and reflects discussions with clinical experts. Some A&E settings will have lower baseline contamination rates.

A lower baseline contamination rate would mean less opportunity for Kurin Lock to reduce false positives. In the model a standard percentage reduction is applied to the baseline contamination rate, and therefore a lower initial value will reduce the difference between Kurin Lock and the comparator. This is investigated in the one way sensitivity analysis and additional two way sensitivity tables.

There are alternative methods to reduce contamination rates, with success reported in some studies (Bentley 2016, Bool 2020). However, a number of the Kurin Lock studies noted that alternative methods had been implemented with limited success prior to the introduction of Kurin Lock.

Efficacy of Kurin Lock: The model uses a 65.5% reduction based on an NHS pre and post service evaluation (Atta, 2022). This reduction was observed in A&E for 381 samples (it is unclear how many patients), and is used for all the modelled scenarios. The company calculated reductions for all their included studies, and these ranged from 32.3% (Rhew, 2021) to 86.4% (Arenas, 2021).

The EAG accept the company parameter, and have used the range of alternative values in the EAG sensitivity analysis.

Antibiotic regimen: None of the papers identified for Kurin Lock reported the type of antibiotic that would normally be used. The model is based on the use of Vancomycin for all patients who receive antibiotics, based on papers based in the USA (Skoglund, 2019, Souvenir 1998) and Israel (Lalezari 2019). Clinical experts advised that a range of different antibiotics may be used within the NHS, and the EAG have included alternative costs, however this does not result in any large changes in the modelled cost savings.

Vancomycin does require the use of serum assays at regular intervals, this was conservatively excluded from the submitted base case, and is also excluded from the EAG base case.

**Table 16 Clinical parameters used in the company's model and changes made by the EAG**

| Parameter | Company submission | Source | EAG value | Comment |
|---|---|---|---|---|
| Bacteraemia and contamination rates | | | | |
| Baseline bacteraemia risk (in the A&E) | 7.4% | Rupp et al. 2017 | No change | Reported in single centre study of A&E department, USA, 904 patients and 1808 blood cultures. The model uses the same rate across all settings and is not sensitive to change |
| Standard of care rate of blood culture contamination (false positives), in the A&E | 9% in A&E | Atta et al. 2022 | No change | Reported as 9% in text and 8.91% in graph in UK based abstract. Experts advised that rates in A&E may be up to 10%, although other UK sources (Hodson, 2022, Parsons, 2023) have lower rates, and studies in the USA have reported rates as low as 1.78% in A&E (Rupp, 2017) |
| Reduction of BC contamination by using Kurin Lock | 65.5% | Atta et al. 2022 | No change | The EAG accept this is reasonable as it is reported by Atta (2022) in an NHS A&E setting, and investigate alternatives in the sensitivity analysis. |
| Antibiotic use | | | | |

| Parameter | Company submission | Source | EAG value | Comment |
|---|---|---|---|---|
| Probability of starting empiric antibiotics prior to initial BC results | 71% | Skoglund et al. 2019 | No change | This may be different in the UK and the antibiotic prescribed is different. Expert opinion was that it could be up to 90% in an A&E setting, and this has been used in sensitivity analysis but has only a small impact |
| Probability of starting antibiotics following a positive BC | 100% | Assumption | No change | EAG accept this as reasonable and reflecting expert advice. |
| Stopping empirical antibiotics by culture finalisation (true negative, no BC growth), in the A&E (days) | 3.0 | Skoglund et al. 2019 | No change | EAG received expert opinion that some initial results may be received from 24 hours, but cultures would continue until 5 days for certainty. |
| Stopping empirical antibiotics by the identification of false positive result (following initial positive BC), in the A&E (days) | 4.0 | Skoglund et al. 2019 | No change | The EAG accept this is reasonable given the comments above. |
| Stopping empirical antibiotics following confirmed bacteraemia (true positive, following initial positive BC), in the A&E (days) | 10.0 | Skoglund et al. 2019 | No change | The EAG accept this information |
| Length of stay | | | | |
| Length of stay duration for a patient with a true negative BC, in the A&E (days) | 5.0 | Skoglund et al. 2019 | No change | EAG accept this, as based in ED setting, but note that it is a US study. Alahmadi (2010) had a duration of 8 days based in Northern Ireland, and across all hospital settings. |
| Length of stay duration for a patient with a false positive (contaminated) BC, in the A&E (days) | 7.0 | Skoglund et al. 2019 | No change | As above |
| Length of stay duration for a patient with a true positive (bacteraemia) BC, in the A&E (days) | 9.0 | Skoglund et al. 2019 | No change | As above |

Use of antibiotics: The model assumes that 71% of patients who have a blood culture sample taken will be given antibiotics at the same time point, based on clinical samples. This is taken from a non-Kurin Lock study in the USA (Skoglund, 2019). The EAG has not found alternative values, and has accepted this parameter. However, clinical experts indicated that this number

could be as high as 90% and this is considered in the EAG sensitivity analysis. Overall the antibiotic costs and duration have a small impact on the model compared to the length of stay.

Length of stay: Data for length of stay in the base case (A&E setting) is taken from Skoglund (2019), which has an appropriate A&E setting, but is from the USA where the typical length of stay may be different to that expected in the NHS. No Kurin Lock papers were identified that reported length of stay in an NHS setting for an A&E setting, however Alahmadi (2010) report the additional length of stay across a general hospital in Northern Ireland, for patients with false positive blood culture results as 5 days (this data is used in a scenario analysis for general hospital use). The EAG therefore accepts the use of data from Skoglund as being a reasonable estimate, and conservative compared to the use of Alahmadi (2010) which is NHS based, but not specific to A&E. It is noted however that 42% of the contaminated blood cultures included in Alahmadi were from an ICU setting, which may also influence the length of stay.

**Resource identification, measurement and valuation**

Device costs in the submitted model were: Kurin Lock costs £19.50 per set (company value), compared to approximately £1.50 for standard blood collection equipment (NICE MIB 297). The EAG updated the comparator costs to be £0.48, based on a mean value of all blood collection sets available through NHS supply chain (2023). The costs per set ranged from [redacted]

The model assumes that each blood collection time point requires two blood samples from two sites, and therefore two devices. Experts agree that taking two samples is the best practice, although there may be some locations where this does not always happen. Expert advice indicated that repeat blood cultures may be taken if there is a positive result, and clinical indications require it. Therefore, the EAG investigated the impact of repeat testing of 50% of the positive blood culture results. This would, in the EAG base case, result in a use of 2.11 devices per patient for Kurin Lock, and 2.16 for SOC. These values are within the parameter range for device use that is considered in the

EAG sensitivity analysis, and therefore no additional sensitivity analysis was completed.

Blood culture processing costs: The company included a cost for processing all blood cultures, which is applied equally to both arms, and is accepted by the EAG. The first processing is done for all blood cultures to give a positive (true positive and false positive) or negative (true negative) result. A second processing cost is applied to all positive blood cultures to confirm which ones are true positives. Due to the reduced contamination rate with Kurin Lock, there is a slight cost saving of less than £1 associated with these.

Adult and paediatric patients: The company defined paediatric as aged under 12 years, based on the dose recommendations for Vancomycin. They calculated the proportion of those aged 12 and over in the general population (ONS 2022), and used this when calculating the antibiotic and length of stay costs. The EAG preferred to use a more standard definition of adults as over 18, as used by the NHS cost collection, and therefore suitable for length of stay costing. When calculated from ONS data (2022) for the general population this resulted in 81% adults in the EAG base case.

Antibiotics costs: As discussed in clinical parameters Table 16 and resource use Table 17, the EAG has costed an alternative antibiotic regimen, based on expert advice. This results in only a small difference in the model findings.

Length of stay costs: The submitted base case is for A&E, and uses a daily cost of a ward stay that is derived from patient level data for one NHS Trust, and is described as a non-elective short stay cost. This is applied as a daily cost for the duration of the patient stay. The EAG does not have access to the same data, however the costs of £844 for an adult or £1,092 for a child are very high compared to other economic models (NICE MTG71, MTG75). Therefore, the EAG used NHS reference cost data to derive alternative daily stay costs. The EAG used a non-elective short stay cost as the initial admission for the first day of stay, and then calculated excess stay costs for additional days. This is also in line with approaches used previously in NICE assessment reports. Both costs were taken from publicly available NHS Cost

Collection data. Non-elective short stay was based on 2019-20 data, and inflated using PSSRU inflation rates to avoid any impact of Covid on the costing. Excess bed day costs were taken from 2017-18 data, as the last point at which they were reported, and inflated using the same method. For both adult and paediatric patients, HRG groups were chosen that included sepsis with no intervention, or single or multiple interventions with, or without complications, or fever of unknown origin.

The EAG also explored alternative methods of deriving daily length of stay costs from the reference cost, resulting in adult costs of £440 to £550 per day, and these values are encompassed in sensitivity analysis. Full calculation details are shown in Appendix D: Length of stay calculations.

**Table 17 Cost parameters used in the company's model and changes made by the EAG**

| Parameter | Company value | Source | EAG value | Comment |
|---|---|---|---|---|
| Kurin lock device | £19.50 | Company submission | No change | |
| Alternative | £1.50 | NICE MIB | £0.48 | Mean cost of blood collection sets NHS supply chain (2023) |
| Number of blood tests per patient | 2 | | No change | The EAG have considered the possibility that 50% of patients with a positive blood culture will have an additional test in the sensitivity |
| Collection and process of blood culture collection | | | | |
| Microbiology test | £10.18 | 2020-21 NCC Direct Access DAPS https://www.england.nhs.uk/publication/2020-21-national-cost-collection-data-publication/ | £8.53 | 2021:22 NCC Direct Access Pathology |
| Biochemistry test | £1.85 | | £1.55 | |
| Haematology test | £3.63 | | £2.96 | |
| Total | £15.66 | | £13.04 | Sum of items above is applied to all blood cultures. It is applied a second time to positive blood cultures. |
| Antibiotics costs | | | | |
| Vancomycin (cost per vial) | £11.25 | British National Formulary (BNF). Medical forms for vancomycin. Ennogen Healthcare Ltd. 2023. | | Identified, and correct price for the item specified |

| Parameter | Company value | Source | EAG value | Comment |
|---|---|---|---|---|
| Vancomycin serum concentration assay† | £72.93 | NHS England. National Cost Collection for the NHS. National schedule of NHS costs 2021/22 Code: PHCD00026. | n/a | This is not the cost for the assay, however this is not included in either the company or EAG base case or any subsequent EAG scenarios. |
| Alternative regimens, based on clinical expert advice | | | | |
| IV Gentamycin: | | | £1.20 per vial | Gentamicin 80mg/2ml solution, Advanz Pharma, 10 in pack, £12, BNF 2023 |
| Cost per day per patient treated | £35.99 | | £6.52 | EAG calculation assumes whole vials must be used 4 mg/kg daily in 3 divided doses |
| Daily stay in hospital costs | | | | |
| Daily cost of stay in a ward (adult) | £844 | 2020-21 NCC PLICS data Non elective short episode, Treatment Function code excl Paediatrics, Primary Diagnosis ICD10 T808 and T809 | See below | The EAG do not have access to PLICS data, but do not agree that a short episode is an appropriate method |
| Non-elective short stay for infection (adult) | | | £970 | EAG base case value, adult for initial admission. HRG groups WJ06A-J and WJ07, 2019/20 inflated to 2021/22 using PSSRU from £921 |
| Non-elective Excess days for infection adult | | | £329 | EAG base case value, adult for additional days. HRG groups WJ06A-J and WJ07, 2017/18 inflated to 2021/22 using PSSRU from £301 |
| Daily cost of stay in a ward (paediatric) | £1,092 | 2021-22 NCC TFC 420 (Paediatrics) and all Paediatric sub specialties (TFC 211 - 290) Non elective short episodes / | | The EAG do not agree that applying a short episode cost daily is an appropriate method |
| Non elective short stay for infection (paediatric) | | | £1,150 | EAG base case value, paediatric for initial admission HRG groups PW16B - E, 2019/20 inflated to 2021/22 using PSSRU from £1,093 |
| Non elective Excess days for infection (paediatric) | | | £585 | EAG base case value, paediatric for additional days HRG groups PW16B - E, 2017/18 inflated to 2021/22 using PSSRU |

| Parameter | Company value | Source | EAG value | Comment |
|---|---|---|---|---|
| | | | | from £535 |
| Weighted non elective short stay for infection (adult and paediatric) | | | £1,004 | EAG base case value for initial admission<br>Weighted based on 85% adults and 15% paediatric |
| Weighted non elective excess days for infection (adult and paediatric) | | | £377 | EAG base case value for additional days<br>Weighted based on 85% adults and 15% paediatric |

**Sensitivity analysis**

The company included one way sensitivity analysis using a 10% variation for most variables. The cost of Kurin Lock was not included in the sensitivity analysis, and the majority of length of stay inputs were varied by a fixed amount, which the company reported as based on literature, rather than 10%. The EAG updated variables to 20% and additionally increased ranges for baseline BCC, daily cost of stay, duration of stay and probability of empiric antibiotics to reflect the range of available evidence and clinical advice. The full details are available in

Appendix E: One way sensitivity analysis.

The changes for A&E setting were:

- Baseline contamination rate low value was 2%, reflecting the lower figures reported in some papers. The high value remained at 20%.
- The proportion of people given empiric antibiotics was increased to a high value of 90% to reflect expert opinion.
- Length of stay was adjusted so that the sensitivity analysis was carried out on the difference between false positive and true negative LOS
- Daily bed costs were adjusted to show the total daily cost rather than adult and paediatric separately, and the range was adjusted to have a high value of £800
- Number of blood samples taken was not adjusted, but it was confirmed that the range encompassed in the one way sensitivity range.

Two-way sensitivity analysis was completed by the company considering the baseline contamination rate and reduction in contamination using Kurin Lock. This has been updated for the EAG base case in Table 19 and the EAG have added additional sensitivity analysis comparing the baseline contamination rate with:

- the difference in length of stay between true negative and false positive
- the cost of an additional day in hospital

Probabilistic sensitivity analysis was also reported, with again a 10% variation across all included variables. The EAG increased this variation to 20% and re-ran the analysis after updating to the EAG base case. Cost variables were analysed using a gamma distribution and probabilities  used a beta distribution in an appropriate method. This approach gives an indication of the combined impact of variation in all parameters, but there is insufficient data for most variables to be able to estimate the actual variability of the parameter.

**Scenarios**

The company also submitted scenarios for adult and paediatric populations, and intensive care and general hospital settings, as described in Table 24 of their submission. The EAG has re-run these scenarios with the updated EAG parameters where appropriate, and full details of these are in

Appendix F: Scenario analysis inputs and results.

The changes to adult and paediatric scenarios changed only the antibiotic dose (and cost) and the cost of a daily hospital stay.

The ICU and hospital scenarios updated the baseline contamination rate, length of stay, duration of antibiotics and, for ICU, a higher daily hospitalisation cost.

## *11.3. Results from the economic modelling*

### Base case results

The company base case, for a mixed adult and paediatric population in an A&E setting resulted in a cost saving of £73 per patient, and a saving of 0.06 false positives. This is primarily derived from the reduction of bed days associated with a lower false positive blood culture rate. The EAG base case result for the same population and setting is a cost saving of £8 per patient. The difference is almost entirely due to the lower daily cost used by the EAG (reduced from £880 to £377 per day).

**Table 18 Summary of base case results**

| | Company's results | | | EAG results | | |
|---|---|---|---|---|---|---|
| | Technology | Comparator | Cost saving per patient | Technology | Comparator | Cost saving per patient |
| Device | £39 | £3 | **-£36** | £39 | £1 | **-£38** |
| BC processing | £16 | £16 | **£0** | £13 | £13 | **£0** |
| Confirmation tests | £2 | £3 | **£1** | £1 | £2 | **£1** |
| Antibiotics | £100 | £104 | **£4** | £18 | £19 | **£1** |
| Length of stay | £4,716 | £4,820 | **£104** | £2,647 | £2,692 | **£44** |
| **Total** | **£4,872** | **£4,945** | **£73** | **£2,719** | **£2,727** | **£8** |
| Avoided events | | | | | | |
| False positives | 0.03 | 0.09 | **0.06** | 0.03 | 0.09 | **0.06** |
| Days of antibiotics | 2.77 | 2.88 | **0.11** | 2.77 | 2.88 | **0.11** |

| | Company's results | | | EAG results | | |
|---|---|---|---|---|---|---|
| | Technology | Comparator | Cost saving per patient | Technology | Comparator | Cost saving per patient |
| Bed days | 5.36 | 5.48 | **0.12** | 5.36 | 5.48 | **0.12** |

## Sensitivity analysis results

The EAG re-ran the one-way sensitivity analysis and probabilistic sensitivity analysis for the EAG base case, and using an increased 20% variation for all PSA variables and those one-way variables that were not determined separately. All included variables, high and low values and the results are listed in

Appendix E: One way sensitivity analysis.

The one way sensitivity analysis showed that even with the reduced cost saving of the EAG base case, and the use of a 10% variation as submitted by the company, the only included variables that cause the model to be cost incurring are the length of stay. However following the EAG adjustments to sensitivity ranges, the length and cost of stay, rate of BC contamination at baseline and the reduction due to Kurin Lock all have the potential to mean Kurin Lock is cost incurring, or cost neutral, as shown in

Figure ***2***.

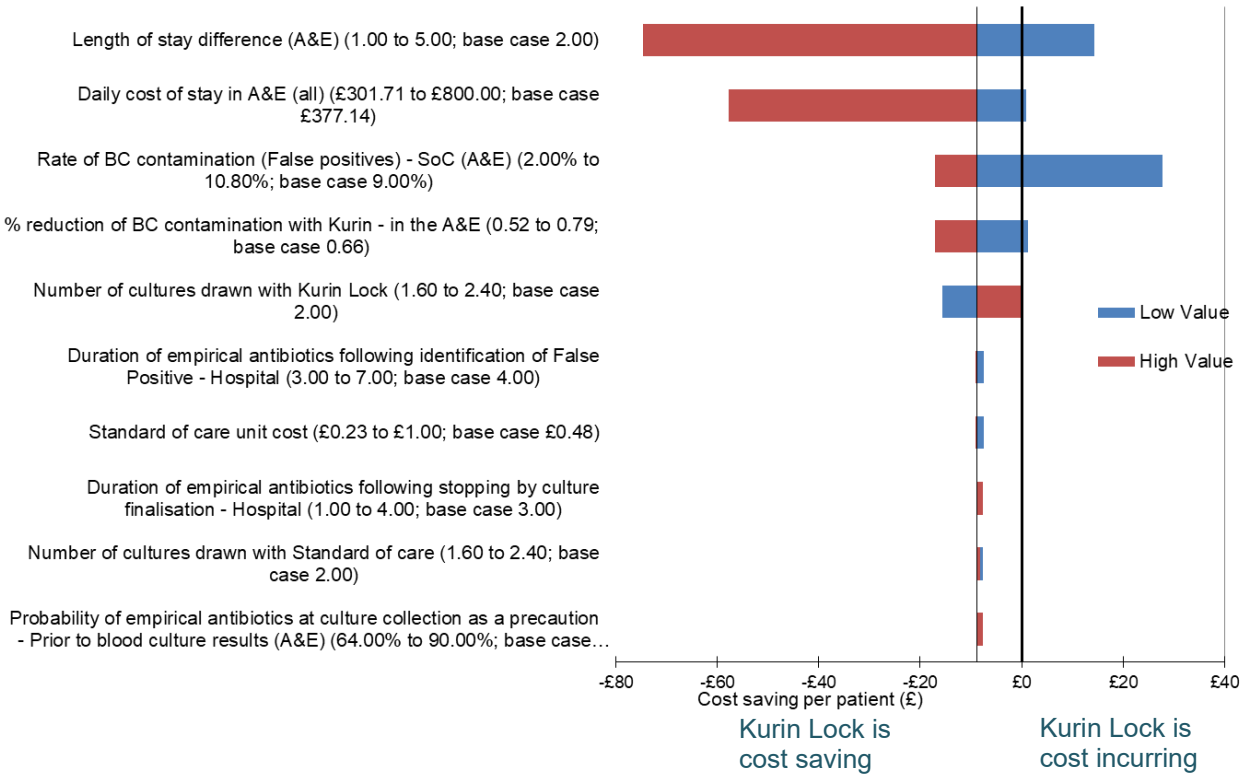



**Figure 2 Tornado diagram for EAG base case, A&E setting**

Two-way sensitivity analysis results are reported using the EAG base case and comparing baseline contamination rate with:

- reduction in contamination using Kurin Lock (Table 19)
- the difference in length of stay between true negative and false positive (Table 20)

- the cost of an additional day in hospital (
- Table ***21***)

Comparing these tables, it can be seen that at baseline contamination rates of less than 3% there is very little probability of Kurin Lock being cost saving, as modelled. Equally at baseline contamination rates of 9% or more there is a high probability of cost savings. For baseline contamination rates in between there is less certainty, although a break-even point of around 7% appears plausible.

The probabilistic sensitivity analysis, using a 20% variance on the EAG base case resulted in a 62% probability of Kurin Lock being cost saving.

**Table 19 Two way sensitivity analysis of baseline risk of BCC, and percentage reduction in contamination rate with Kurin Lock (A&E setting)**

| | | Baseline risk of BC contamination with SoC (ED) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| % reduction of BC contamination with Kurin | £8 | 1% | 2% | 3% | 4% | 5% | 6% | 7% | 8% | 9% | 10% |
| | 10.0% | -£37 | -£36 | -£36 | -£35 | -£34 | -£33 | -£33 | -£32 | -£31 | -£30 |
| | 20.0% | -£36 | -£35 | -£33 | -£32 | -£30 | -£29 | -£27 | -£26 | -£24 | -£22 |
| | 30.0% | -£36 | -£33 | -£31 | -£29 | -£26 | -£24 | -£22 | -£19 | -£17 | -£15 |
| | 40.0% | -£35 | -£32 | -£29 | -£26 | -£22 | -£19 | -£16 | -£13 | -£10 | -£7 |
| | 50.0% | -£34 | -£30 | -£26 | -£22 | -£19 | -£15 | -£11 | -£7 | -£3 | £1 |
| | 60.0% | -£33 | -£29 | -£24 | -£19 | -£15 | -£10 | -£5 | -£1 | £4 | £9 |
| | 65.5% | -£33 | -£28 | -£23 | -£18 | -£13 | -£7 | -£2 | £3 | **£8** | £13 |
| | 70.0% | -£33 | -£27 | -£22 | -£16 | -£11 | -£5 | £0 | £6 | £11 | £17 |
| | 80.0% | -£32 | -£26 | -£19 | -£13 | -£7 | -£1 | £6 | £12 | £18 | £24 |
| | 90.0% | -£31 | -£24 | -£17 | -£10 | -£3 | £4 | £11 | £18 | £25 | £32 |
| | 100.0% | -£30 | -£22 | -£15 | -£7 | £1 | £9 | £17 | £24 | £32 | £40 |

**Table 20 Two way sensitivity analysis of baseline risk of BCC, and difference in bed days between true negative and false positive blood cultures (A&E setting)**

| Reduction in days in hospital between true negative and false positive results | Baseline risk of BC contamination with SoC (ED) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **£8** | 1% | 2% | 3% | 4% | 5% | 6% | 7% | 8% | 9% | 10% |
| 1.0 | -£35 | -£33 | -£30 | -£28 | -£25 | -£22 | -£20 | -£17 | -£14 | -£12 |
| 1.5 | -£34 | -£30 | -£26 | -£23 | -£19 | -£15 | -£11 | -£7 | -£3 | £1 |
| 2.0 | -£33 | -£28 | -£23 | -£18 | -£13 | -£7 | -£2 | £3 | **£8** | £13 |
| 2.5 | -£32 | -£25 | -£19 | -£13 | -£6 | £0 | £6 | £13 | £19 | £25 |
| 3.0 | -£30 | -£23 | -£15 | -£8 | £0 | £7 | £15 | £23 | £30 | £38 |
| 3.5 | -£29 | -£20 | -£12 | -£3 | £6 | £15 | £24 | £32 | £41 | £50 |
| 4.0 | -£28 | -£18 | -£8 | £2 | £12 | £22 | £32 | £42 | £52 | £62 |
| 5.0 | -£26 | -£13 | £0 | £12 | £25 | £37 | £50 | £62 | £75 | £87 |
| 6.0 | -£23 | -£8 | £7 | £22 | £37 | £52 | £67 | £82 | £97 | £112 |

**Table 21 Two way sensitivity analysis of baseline risk of BCC, and daily cost of hospital stay (A&E setting)**

| Daily cost of hospital stay | Baseline risk of BC contamination with SoC (ED) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| £8 | 1% | 2% | 3% | 4% | 5% | 6% | 7% | 8% | 9% | 10% |
| £200 | -£35 | -£32 | -£30 | -£27 | -£24 | -£21 | -£18 | -£16 | -£13 | -£10 |
| £300 | -£34 | -£30 | -£26 | -£22 | -£18 | -£13 | -£9 | -£5 | -£1 | £3 |
| £400 | -£33 | -£27 | -£22 | -£16 | -£11 | -£6 | £0 | £5 | £11 | £16 |
| £500 | -£31 | -£25 | -£18 | -£11 | -£4 | £2 | £9 | £16 | £22 | £29 |
| £600 | -£30 | -£22 | -£14 | -£6 | £2 | £10 | £18 | £26 | £34 | £42 |
| £700 | -£29 | -£19 | -£10 | -£1 | £9 | £18 | £27 | £37 | £46 | £55 |
| £800 | -£27 | -£17 | -£6 | £5 | £15 | £26 | £36 | £47 | £58 | £69 |
| £900 | -£26 | -£14 | -£2 | £10 | £22 | £34 | £46 | £58 | £70 | £82 |
| £1,000 | -£25 | -£12 | £2 | £15 | £28 | £42 | £55 | £68 | £81 | £95 |

**Additional results**

ICU scenario: The ICU setting shows a higher cost saving per person, despite the lower baseline contamination rate. This is largely due to the much higher daily cost incurred in ICU. Although the EAG cost saving is less than that in the company submission, it remains high at £41 per patient.

Hospital scenario: The hospital scenario uses data based on an economic paper from the NHS in Northern Ireland (Alahmadi, 2010). The authors found an increase of 5 bed days per false positive blood culture, and this change in length of stay lead to the general hospital scenario being cost saving. The bed day costs are the same as for A&E. The difference in bed day savings between the hospital scenario and the base case are as likely to be due to differences between health care systems or hospitals as they are to be due to differences between A&E and general hospital. It is also noted that the 42% of the BCC reported in Alahmadi (2010) came from ICU, and these were not matched for settings with the comparator cases. Therefore, the difference in length of stay, and cost, may be overestimated.

## *11.4. The EAG's interpretation of the economic evidence*

The EAG revised the following parameters or calculations (Table 22), however the only change that had a notable impact was the change in the daily cost of a ward stay. The reasons for changes are discussed more fully in the resource use parameters section.

**Table 22 Summary of EAG changes and their impact on the model**

| EAG change | Impact on model |
|---|---|
| Reduced daily stay cost in A&E and hospital setting to £377 per day (weighted for adults and paediatric population). | Large reduction in cost saving |
| Reduction in ICU daily cost due to using 2019/20 costs inflated, avoiding any impact of Covid. | Small reduction in cost saving for ICU scenario only |
| Change to antibiotic regimen, based on expert advice resulting in a decreased daily cost | Very small reduction in cost saving |

| EAG change | Impact on model |
|---|---|
| Change to antibiotic cost calculation to use whole vials only | Negligible increase in cost saving |
| Change to blood processing cost to £13 per processing | Negligible reduction in cost saving |
| Change to comparator costs, based on NHS supply chain data. | Small reduction in cost saving |
| Change to adult / paediatric weighting to reflect NHS cost collection definition of paediatric as aged 18 or under. | Small increase in cost saving |

The EAG noted that the main driver for the model is the length of stay difference (and its associated cost) that is attributed to reducing false positive blood cultures. There is reasonable and consistent evidence that Kurin Lock can reduce the number of false positive blood cultures, although these are generally not from peer reviewed publications, or high-quality studies, particularly in the UK. There is evidence that false positive blood cultures are associated with longer hospital stays and higher costs. None of this evidence is directly linked to Kurin Lock, however some of it is related to a similar device, and it is plausible to expect a similar impact. The daily cost of hospitalisation used by the EAG is much lower than the submitted model, but is in line with approaches used in other MTEP assessments.

The baseline contamination rate is also a driver for the model, with lower rates changing the result to cost incurring. The length of stay and baseline contamination rates were investigated further in two-way sensitivity tables, showing that there is a low range of contamination rates where Kurin Lock is unlikely to be cost saving, but also a mid-range where there is considerable uncertainty.

The other variables that have any significant impact on the model results are the reduction in blood culture contamination due to Kurin Lock and the number of cultures drawn with Kurin Lock.

There may be some system benefits in reducing the amount of antibiotics given, however the majority of patients will receive antibiotics at the point of testing based on clinical symptoms, and the cost impact is small.

There may also be system and patient benefits that have not been captured in the model for some patient populations. Expert advice mentioned that a reduction in false positives could avoid the unnecessary changes in central line catheters. This has not been included in the company submission, or in any detail in the clinical and economic papers included.

The baseline contamination rate is known to be variable across different settings and locations. The rate used in the model reflects expert opinions of possible rates for A&E, but is higher than some alternative sources in the literature. The modelling suggests that where there are high baseline contamination rates Kurin Lock could reduce these, and the additional cost of the device would be offset by savings in bed days. Where alternative methods have been employed to reduce the baseline contamination rate it is likely that Kurin Lock will be cost incurring, unless it is a setting with a high daily cost, such as ICU.

# 12. Integration into the NHS

There is limited evidence that is generalisable to the NHS, with no peer-reviewed published evidence pertaining to use of the technology in the UK. The evidence for the use of Kurin Lock in the UK is limited to 3 posters reporting on quality improvement projects in the NHS.

The EAG do not consider there to be any significant change in the current care pathway if Kurin Lock was adopted in the NHS. Clinical experts agreed that Kurin Lock does not change the standard procedure for taking blood culture samples. Clinical experts advised that the standard recommended process of taking of 2 samples for every blood culture would remain in place

should Kurin Lock be introduced, as it improves sensitivity of the testing and improves the chances of detecting disease-causing microorganisms, in addition to being a method of identifying skin flora contaminants.

Training for staff to use Kurin Lock is minimal, with the company and clinical experts stating the training takes no more than a few minutes.

The EAG recognises that other quality improvement measures, independent of introducing additional devices, may be effective at reducing blood culture contamination. This includes re-education of staff on aseptic technique, streamlining blood culture sampling processes, and implementing dedicated teams for blood culture sampling. However, based on the evidence and comments from clinical experts, the EAG recognises that there may be certain contexts and circumstances where Kurin Lock may be particularly beneficial such as in A&E departments where contamination rates are observed to be consistently high. Additionally, there may be subgroups where the use of Kurin Lock is particularly beneficial such as groups where it may be difficult to take a blood sample (e.g. paediatric patients and IV drug users).

The EAG recognises that the initial outlay of purchasing Kurin Lock devices is high, in comparison to standard care, and should be considered alongside the potential downstream cost-savings that may occur as a result of reducing BCC rates. Reductions in length of stay are the largest potential cost-saving, but there is very limited UK data published. It may be beneficial to examine any locally available data on the length of stay associated with BCC, in order to determine the potential for realising cost savings.

# 13. Conclusions

## *13.1. Conclusions from the clinical evidence*

Overall, the evidence suggests the Kurin Lock device is an effective mechanism for reducing blood culture contamination (BCC) rates in a secondary care setting. The majority of the available evidence has been generated in an emergency department/A&E setting which is an important subgroup identified by the clinical experts, as this is where BCC rates are consistently highest.

The EAG notes that the majority of the evidence is non-peer reviewed, therefore the EAG cannot be certain that the evidence presents an unbiased estimate of the technology's clinical effectiveness. Some of the studies implemented Kurin Lock as part of wider quality improvement projects, where other strategies to reduce BCC may also have had an impact on the rates reported.

The EAG considers there to be a gap in evidence on downstream system impacts directly related to the implementation of the Kurin Lock device. Reductions in length of hospital stay (LOS), use of antibiotics and repeat blood culture draws are described by the company as key benefits of Kurin Lock and listed in the scope as relevant outcomes. However, these outcomes are not reported in the evidence base beyond brief estimations. Although these outcomes are not reported in the Kurin Lock studies, there is evidence that a reduction in BCC rates does result in a reduction in LOS and antibiotic use (Skoglund 2019). Therefore, the EAG considers that the proposed downstream benefits of implementing Kurin Lock are likely to be realised.

Clinical experts commented on the difficulty in quantifying downstream benefits, but some clinical experts stated that it could be achieved, provided the variations in practice between sites are reflected in the study designs. The EAG considers it would be feasible for this data to be collected while implementing Kurin Lock as part of quality improvement projects in secondary care, but recognises there may be extra personnel required to collect and analyse the data, if it is not being collected already, as indicated by a clinical expert.

## *13.2. Conclusions from the economic evidence*

The submitted model reflects the scope and the current clinical pathway within the NHS. Key limitations are that the model is based on clinical evidence from studies based in the USA, studies that do not include Kurin Lock, and non-peer reviewed Kurin Lock studies in the UK.

The submitted model is for a mixed adult and paediatric population in an A&E setting. The model assumes that most patients (71%) will receive antibiotics based on clinical assessment at the point of blood culture collection, and all will be admitted into hospital. The modelled cost savings are based on Kurin Lock reducing the number of false-positive tests, and that a patient with a false-positive test would have a longer length of stay and antibiotic treatment compared to a patient with a true negative test. The key drivers are length of hospital stay, daily cost of hospital stay, the baseline BCC rate and the reduction in BCC due to Kurin Lock.

Several key clinical parameters (length of stay and antibiotic use) are based on studies from the USA in the submitted model. This was accepted by the EAG due to limitations in alternative UK based sources. The EAG did not change any clinical parameters, but carried out additional sensitivity analysis to reflect the uncertainty.

Cost parameters used appropriate UK sources, however the EAG disagreed with company assumptions for the daily hospital stay cost, and changed this from ££8 per day (based on non-elective short stay costs) to £377 per day (based on excess bed day costs).

The EAG changes resulted in a reduction in the cost saving from £73 per patient to £8 per patient, when considered in an A&E setting with a baseline contamination rate of 9%. Lower baseline BCC rates will reduce the cost saving, and may result in the introduction of Kurin Lock becoming cost incurring. Scenario modelling for ICU settings demonstrated that where the daily hospital cost is higher, the cost saving is more robust to changes in length of stay or baseline BCC rate.

# 14. Summary of the combined clinical and economic sections

The clinical evidence suggests that implementation of Kurin Lock results in a reduction of blood culture contamination (BCC) rates. However, there is a significant lack of robust, peer-reviewed evidence. Additionally, there is a lack of data collected and reported for downstream outcomes that may occur as a result in reducing BCC rates, including length of hospital stay and antibiotic use.

The EAG note that some of the included Kurin Lock studies are quality improvement projects that involved other methods of reducing BCC rates and so the benefits observed may not be directly attributable to the Kurin Lock device.

The economic modelling indicates that whether the Kurin Lock device is cost-saving or cost-incurring is heavily dependent on length of stay (and associated costs) as well as the baseline BCC rates. Kurin Lock is more likely to be cost-saving if length of stay costs are higher (e.g. in an ICU setting) or where the baseline BCC rates are higher, for example in A&E.

The majority of clinical evidence and data used in the economic model is based in the USA, which may not be reflective of the UK NHS. For example, the pathways for patient admission, investigations, antibiotic use and length of hospital stay are likely to be different in the USA healthcare system in comparison to the UK NHS.

# 15. Implications for research

The current evidence base suggests that Kurin Lock is an effective method of reducing blood culture contamination rates. The EAG identified the following gaps in the evidence base: limited peer-reviewed robust evidence, a lack of cost data relating directly to Kurin Lock, a lack of data relating to downstream system impacts of Kurin Lock and limited evidence from a UK NHS setting.

To address these evidence gaps, the EAG have identified the following research approaches to be considered by decision makers:

- Kurin Lock studies with larger populations and longer study periods that are based in the UK. The collected outcomes should include downstream impacts such as length of stay and antibiotic, in addition to the primary outcome of blood culture contamination rates. The EAG notes this data could be collected in a real-world evidence setting e.g. from quality improvement projects in the NHS.

- Collection of cost data associated with aforementioned downstream impacts such as cost of length of stay, cost of antibiotics provided, costs of further investigations and blood culture processing for patients who have had blood culture samples taken with Kurin Lock

Overall, the EAG considers Kurin Lock is an effective method of reducing blood culture contamination rates, which has the potential to have a positive impact on downstream events such as length of hospital stay and antibiotic use. However, there are uncertainties in the clinical and cost data that need to be addressed.

# 16. References

Alahmadi Y, Aldeyab M, McElnay J, Scott M, Elhajji FD, Magee F, et al. Clinical and economic impact of contaminated blood cultures within the hospital setting. Journal of Hospital Infection. 2011;77(3):233-6.

Allain M. Top Scoring Abstracts From the 2018 National Association of Clinical Nurse Specialists Annual Conference: Not Your ‘‘Average’’ ED: A CNS-Led Project That Reduced Blood Culture Contaminations in One Emergency Department to Below Expected Levels. Clinical Nurse Specialist. 2018:E1-E

Arenas M, Boseman GM, Coppin JD, Lukey J, Jinadatha C, Navarathna DH. Asynchronous Testing of 2 Specimen-Diversion Devices to Reduce Blood Culture Contamination: A Single-Site Product Supply Quality Improvement Project. Journal of emergency nursing. 2021;47(2):256-64.e6.

Arnaout S, Ellison RT, Greenough TC, Wedig A, Mitchell MJ, St John L, et al. Prospective Trial of Passive Diversion Device to Reduce Blood Culture Contamination. Open Forum Infectious Diseases. 2021;8(SUPPL 1):S70.

Atta M, Mcguire R. Reducing False Positive Blood Cultures in an Adult NHS Emergency Department using an Kurin. 2022.

Baxter M, Cook C, James A. Passive Engineering Controls Result in Sustained 66% Reduction in Blood Culture Contamination. Infection Control & Hospital Epidemiology. 2020;41(S1):s342-s3.

Bentley J, Thakore S, Muir L, Baird A, Lee J. A change of culture: reducing blood culture contamination rates in an Emergency Department. BMJ Qual Improv Rep. 2016 Jun 6;5(1)

Bool M, Barton MJ, Zimmerman PA. Blood culture contamination in the emergency department: An integrative review of strategies to prevent blood culture contamination. Australas Emerg Care. 2020;23(3):157-165.

British National Formulary, BNF. Medical forms for vancomycin, Ennogen Healthcare Ltd. 2023. Available from: https://bnf.nice.org.uk/drugs/vancomycin/medicinal-forms/. Accessed on: July 2023

Burnie J, Vining S. Clinical Nurse Specialist Practice Impact on Emergency Department Blood Culture Contamination. CLINICAL NURSE SPECIALIST. 2021;35(6):314-7.

Buzard BA, Evans P, Schroeder T. Evaluation of an Initial Specimen Diversion Device (ISDD) on Rates of Blood Culture Contamination in the Emergency Department. Kansas journal of medicine. 2021;14:73-6.

Geisler BP, Jilg N, Patton RG, Pietzsch JB. Model to evaluate the impact of hospital-based interventions targeting false-positive blood cultures on economic and clinical outcomes. The Journal of hospital infection. 2019;102(4):438-44.

Hodson J, Stebbing J, Graham C, O' Donnell S. Reducing False-Positive Blood Cultures in Adult A&E using a Initial Specimen Diversion Device. Available from: https://www.kurin.com/reducing-false-positive-blood-cultures-in-adult-ae-using-a-initial-specimen-diversion-device/.

Lalezari A, Cohen MJ, Svinik O, Tel-Zur O, Sinvani S, Al-Dayem YA, et al. A simplified blood culture sampling protocol for reducing contamination and costs: a randomized controlled trial. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2020;26(4):470-4.

McAdam AJ. Reducing Contamination of Blood Cultures: Consider Costs and Clinical Benefits. CLINICAL INFECTIOUS DISEASES. 2017;65(2):206-7.

NICE Guideline NG51: Sepsis: recognition, diagnosis and early management (2017). Available from: Overview | Sepsis: recognition, diagnosis and early management | Guidance | NICE

NICE Clinical Guideline CG139: Healthcare-associated infections: prevention and control in primary and community care (2017). Available from: Overview | Healthcare-associated infections: prevention and control in primary and community care | Guidance | NICE

NICE Public Health Guideline PH36: Healthcare-associated infections: prevention and control (2011). Available from: Overview | Healthcare-associated infections: prevention and control | Guidance | NICE

O'Sullivan DM, Steere L. Reducing false-positive blood cultures: Using a blood diversion device. Connecticut Medicine. 2019;83(2):53-6.

Ostwald CM. Reduction of False-positive Blood Culture Rates Using a Passive Blood Diversion Device in an Urban Academic Pediatric Emergency Department. American Journal of Infection Control. 2021b;49(6, Supplement):S3.

Ostwald CM, Whitsell K, editors. Reduction of False Positive Blood Culture Rates using a Passive Blood Diversion Device in an Urban Academic Pediatric Emergency Department. Poster Presentation APIC; 2021a.

Patel S, Preuss CV, Bernice F. Vancomycin. StatPearls [internet]: StatPearls Publishing; 2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK459263/ Accessed August 2023

Public Health England, UK Standards for Microbiology Investigations B37: investigation of blood cultures (for organisms other than Mycobacterium species) (2019). Available from: UK SMI B 37: investigation of blood cultures (for organisms other than Mycobacterium species) - GOV.UK (www.gov.uk)

Public Health Wales: Aseptic Non-Touch Technique (ANTT), a national standardised approach to aseptic technique (2023). Available from: ANTT - Public Health Wales (nhs.wales)

Rhew D, Childress C. Decreasing blood culture contamination rates when using an initial peripheral IV: implementing the 5 P's and using a closed system device. Nur Primary Care. 2021;5(3):1-6.

Rupp ME, Cavalieri RJ, Marolf C, Lyden E. Reduction in Blood Culture Contamination Through Use of Initial Specimen Diversion Device. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2017;65(2):201-5.

Salcedo DAT, Powers-Fletcher M, Smulian AG. Minimal impact of blood culture contaminants on patient care decisions may limit cost-effectiveness of interventions to reduce contamination rates. Open Forum Infectious Diseases. 2019;6(Supplement 2):S676.

Skoglund E, Dempsey CJ, Chen H, Garey KW. Estimated Clinical and Economic Impact through Use of a Novel Blood Collection Device To Reduce Blood Culture

Contamination in the Emergency Department: a Cost-Benefit Analysis. Journal of clinical microbiology. 2019;57(1).

Sutton J, Fritsch P, Moody M, Dinaro K, Holder C, editors. Preventing Blood Culture Contamination using a Novel Engineered Passive Blood Diversion Device. Association for Professionals in Infection Control; 2018a June 13-15; Minneapolis.

Sutton J, Fritsch P, Moody M, Dinaro K, Holder C. A novel solution to prevent blood culture contamination using an engineered passive blood diversion device. American Journal of Infection Control. 2018b;46(6):S63.

Tompkins LS, Tien V, Madison AN. Getting to zero: Impact of a device to reduce blood culture contamination and false-positive central-line-associated bloodstream infections. Infection control and hospital epidemiology. 2022:1-5.

WHO Guidelines on Drawing Blood: Best Practices in Phlebotomy. Geneva: World Health Organization; 2010. Available from: WHO guidelines on drawing blood: best practices in phlebotomy

Zimmerman FS, Assous MV, Zevin S, Wiener-Well Y. Reducing blood culture contamination using an initial specimen diversion device. American journal of infection control. 2019;47(7):822-6.

# 17. Appendices

**List of Appendices:**

## *Appendix A: Clinical and economic evidence identification*

### Company search strategy, screening criteria and process for clinical evidence

A literature search was performed in one database, Medline (PubMed), using free text terms. The search was limited to studies published in the English language and between the period January 2017 to 23rd April 2023. A search was also performed on the company website. It was noted that the company were aware of all studies related to Kurin Lock, and these studies were available on the company website.

PubMed search strategy: “Kurin” or “Kurin Lock Blood culture collection” and “initial specimen diversion device”

| Database/other source | Database provider | Database segment/version | Date search conducted | No of results |
|---|---|---|---|---|
| Medline | PubMed | 1.0 | April 20th 2023 | 14 (identified) |
| https://www.kurin.com/studies/ | | | April 20th 2023 | 10 |

The eligibility criteria for including studies was as follows:

Population: Blood cultures collection studies which used Kurin or ISDD within a secondary care setting.

Intervention and comparators: Kurin blood culture collection, including Kurin Lock, ISDD devices

Standard of care: Standard blood culture collection (tubes and container)

### Company study selection for clinical evidence

After screening records from PubMed by title and abstract, 8 records were included. Details on full-text screening were not provided. It was noted that screening was conducting independently but details of the process were not provided.

**Company search strategy, screening criteria and process for economic evidence**

A literature search was performed in one database, Medline (PubMed), using free text terms. The search was limited to studies published in the English language and between the period January 1983 to 16th March 2023. Grey literature searches were also conducted for initial specimen diversion device and SteriPath.

PubMed search strategy: “False-positive blood culture contamination emergency department” or “Blood culture contamination” or “False-positive blood cultures” or “Reduced false-positive blood cultures” or “Best practice collection of blood culture” or “blood specimen diversion device” and “economic” and “cost”.

| Database/other source | Database provider | Database segment/version | Date search conducted | No of results |
|---|---|---|---|---|
| Medline | PubMed | 1.0 | March 16th 2023 | 91 |
| Grey literature | | | | 2 |

The eligibility criteria for including economic studies was as follows:

**Inclusion criteria:**

Population
- People who need a blood culture test within a secondary care setting.

Subgroups of interest include:
- Patients within the ICU setting.
- Patients within the general hospital setting.

Intervention and comparators:
Kurin blood culture collection, including Kurin Lock, ISDD devices
Standard of care: Standard blood culture collection (tubes and container)

Outcomes:
- Economic evaluation:

Summary of cost and hospital outcomes (e.g. bed stay)
  - Model structure and summary
  - Assumptions underpinning resource use
  - Cost drivers
  - Cost-effectiveness estimates
- Cost/ resource use
  - Direct costs
  - Medical costs (e.g. medications, staff, hospitalisation)
  - Indirect costs

- Healthcare resource use

Study design:
- Economic evaluation:
  - Cost-utility analyses
  - Cost-effectiveness analyses
  - Cost-minimisation analyses
  - Cost-benefit analyses
- Cost/ resource use
  - Clinical studies
  - Economic evaluation reporting original cost data

Geography:
No restriction

Publication date:
Studies published in 1998 and later

Language:
English language publications

For the economic evidence, studies were screened at both title and abstract and 60 records were excluded. Following assessment of the remaining 33 full text records, 23 were subsequently excluded. A total of 8 studies were included in the final dataset as relevant to the economic evidence, along with 2 additional posters.

**Company search strategy adverse events**

The company did not detail any search strategy for adverse events.

**EAG search strategy and study selection for clinical and economic evidence**

The EAG conducted a single search for both clinical and economic evidence as directed by the scope. Eleven bibliographic databases were searched to include the period from 1st January 2015 to 12th June 2023, using a range of free text terms and, where appropriate, indexed terms. The searches were not restricted by language of publication. Two clinical trial registries were also searched for ongoing and unpublished trials; the company's website was also searched for additional literature. The MHRA's field safety notices, device safety information and national patient safety alerts and the FDA MAUDE database were searched for adverse events.

| Date | Database Name | Total Number of records retrieved | Total number of records from database after de-duplication |
|---|---|---|---|
| 12/06/23 | Medline ALL (includes Medline In Process & Medline Epub Ahead of Print) | 57 | |
| 12/06/23 | EMBASE | 184 | |
| 12/06/23 | Emcare | 26 | |
| 12/06/23 | Cochrane Library<br>CDSR<br>CENTRAL | <br>0<br>29 | |
| 12/06/23 | CRD<br>(DARE, NHS EED) | 0 | |
| 12/06/23 | INAHTA | 0 | |
| 12/06/23 | PubMed | 7 | |
| 12/06/23 | Web of Science | 43 | |
| 12/06/23 | Scopus | 112 | |
| 12/06/23 | Company website | 10 | |
| 12/06/23 | MHRA | 0 | |
| 12/06/23 | FDA MAUDE | 7 | |
| 12/06/23 | Clinical Trials.gov | 2 | |
| 12/06/23 | ICTRP | 0 | 264 records after manual deduplication |

## EAG Search Strategies

### Ovid MEDLINE(R) ALL <1946 to June 09, 2023>

1 kurin.tw. 2

2 Blood Culture/ 1705

3 Blood Specimen Collection/ 12562

4 (blood adj3 culture*).tw. 39883

5 (blood adj3 collection*).tw. 12019

| | | |
|---|---|---|
| 6 | (blood adj3 specimen*).tw. | 10035 |
| 7 | (blood adj3 contamina*).tw. | 4197 |
| 8 | (blood adj3 "false positive*").tw. | 199 |
| 9 | (blood adj3 (test* or draw* or work* or sample* or sampling)).tw. | 268819 |
| 10 | or/2-9 | 327760 |
| 11 | diversion*.tw. | 22225 |
| 12 | 10 and 11 | 172 |
| 13 | 1 or 12 | 174 |
| 14 | exp animals/ not humans.sh. | 5128705 |
| 15 | 13 not 14 | 156 |
| 16 | limit 15 to yr=2015 -Current | 57 |

**Embase <1974 to 2023 June 09>**

| | | |
|---|---|---|
| 1 | kurin.tw. | 7 |
| 2 | Blood Culture/ | 63855 |
| 3 | blood sampling/ | 266790 |
| 4 | (blood adj3 culture*).tw. | 63388 |
| 5 | (blood adj3 collection*).tw. | 20318 |
| 6 | (blood adj3 specimen*).tw. | 14587 |
| 7 | (blood adj3 contamina*).tw. | 5684 |
| 8 | (blood adj3 "false positive*").tw. | 277 |

| | | |
|---|---|---|
| 9 | (blood adj3 (test* or draw* or work* or sample* or sampling)).tw. | 426942 |
| 10 | or/2-9 | 647700 |
| 11 | diversion*.tw. | 31690 |
| 12 | 10 and 11 | 382 |
| 13 | 1 or 12 | 389 |
| 14 | limit 13 to yr=2015 -Current | 184 |

**Ovid Emcare <1995 to 2023 Week 22>**

| | | |
|---|---|---|
| 1 | kurin.tw. | 1 |
| 2 | Blood Culture/ | 9385 |
| 3 | blood sampling/ | 36029 |
| 4 | (blood adj3 culture*).tw. | 9131 |
| 5 | (blood adj3 collection*).tw. | 3143 |
| 6 | (blood adj3 specimen*).tw. | 2189 |
| 7 | (blood adj3 contamina*).tw. | 1117 |
| 8 | (blood adj3 "false positive*").tw. | 60 |
| 9 | (blood adj3 (test* or draw* or work* or sample* or sampling)).tw. | 67210 |
| 10 | or/2-9 | 96828 |
| 11 | diversion*.tw. | 5410 |
| 12 | 10 and 11 | 54 |

| | | |
|---|---|---|
| 13 | 1 or 12 | 55 |
| 14 | limit 13 to yr=2015 -Current | 26 |

**Cochrane Library**

| | | |
|---|---|---|
| #1 | (kurin):ti,ab,kw | 0 |
| #2 | MeSH descriptor: [Blood Culture] this term only | 99 |
| #3 | MeSH descriptor: [Blood Specimen Collection] this term only | 418 |
| #4 | (blood NEAR/3 culture*):ti,ab,kw | 2393 |
| #5 | (blood NEAR/3 collection*):ti,ab,kw | 3706 |
| #6 | (blood NEAR/3 specimen*):ti,ab,kw | 1327 |
| #7 | (blood NEAR/3 contamina*):ti,ab,kw | 336 |
| #8 | (blood NEAR/3 "false positive"):ti,ab,kw | 9 |
| #9 | (blood NEAR/3 (test* or draw* or work* or sample* or sampling)):ti,ab,kw | 64493 |
| #10 | #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 or #9 | 68907 |
| #11 | (diversion*):ti,ab,kw | 1168 |
| #12 | #10 AND #11 | 42 |
| #13 | #1 OR #12 with Publication Year from 2015 to present, in Trials | 29 |
| #14 | #13 in Cochrane Reviews | 0 |

**CRD**

| | | |
|---|---|---|
| 1 | (kurin) | 0 |

| | | |
|---|---|---|
| 2 | MeSH DESCRIPTOR Blood Culture | 0 |
| 3 | MeSH DESCRIPTOR Blood Specimen Collection | 24 |
| 4 | (blood adj3 culture*) | 110 |
| 5 | (blood adj3 collection*) | 54 |
| 6 | (blood adj3 specimen*) | 41 |
| 7 | (blood adj3 contamina*) | 11 |
| 8 | (blood adj3 "false positive*") | 10 |
| 9 | (blood adj3 (test* or draw* or work* or sample* or sampling)) | 685 |
| 10 | #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 | 836 |
| 11 | (diversion*) | 94 |
| 12 | #10 AND #11 | 2 |
| 13 | #1 OR #12 | 2 |
| 14 | (#13) WHERE LPD FROM 01/01/2015 TO 31/12/2023 | 0 |

---

**INHATA**

((diversion*) AND ((blood AND (test* or draw* or work* or sample* or sampling)) OR (Blood AND "false positive*") OR (Blood AND contamina*) OR (Blood AND specimen*) OR (Blood AND collection*) OR (Blood AND culture*) OR ("Blood Specimen Collection"[mh]) OR ("Blood Culture"[mh]))) OR (kurin)

---

**Scopus**

( ( ( TITLE-ABS-KEY ( blood W/3 ( test* OR draw* OR work* OR sample* OR sampling ) ) ) OR ( TITLE-ABS-KEY ( blood W/3 ( culture* OR collection* OR specimen* OR contamina* OR "false positive*" ) ) ) ) AND ( TITLE-ABS-KEY ( diversion* ) ) ) OR ( TITLE-ABS-KEY ( kurin AND blood ) ) AND PUBYEAR > 2014 AND PUBYEAR < 2023

---

**Web of Science**

| | |
|---|---|
| 1: TS=Kurin | Results: 10 |
| 2: TS=(Blood NEAR/3 Culture*) | Results: 37,595 |
| 3: TS=(Blood NEAR/3 Collection*) | Results: 13,546 |
| 4: TS=(Blood NEAR/3 Specimen*) | Results: 9,491 |
| 5: TS=(Blood NEAR/3 Contamina*) | Results: 4,305 |
| 6: TS=(Blood NEAR/3 "false positive*") | Results: 273 |
| 7: #6 OR #5 OR #4 OR #3 OR #2 | Results: 62,572 |
| 8: TS=Diversion* | Results: 37,500 |
| 9: #8 AND #7 | Results: 104 |
| 10: #9 OR #1 | Results: 114 |
| Timespan: 2015-01-01 to 2023-12-31 | Results: 43 |

---

**PubMed**

“Kurin Lock” = 0 results

Kurin[Title/Abstract] AND blood[Title/Abstract] = 7 results

---

**MHRA**

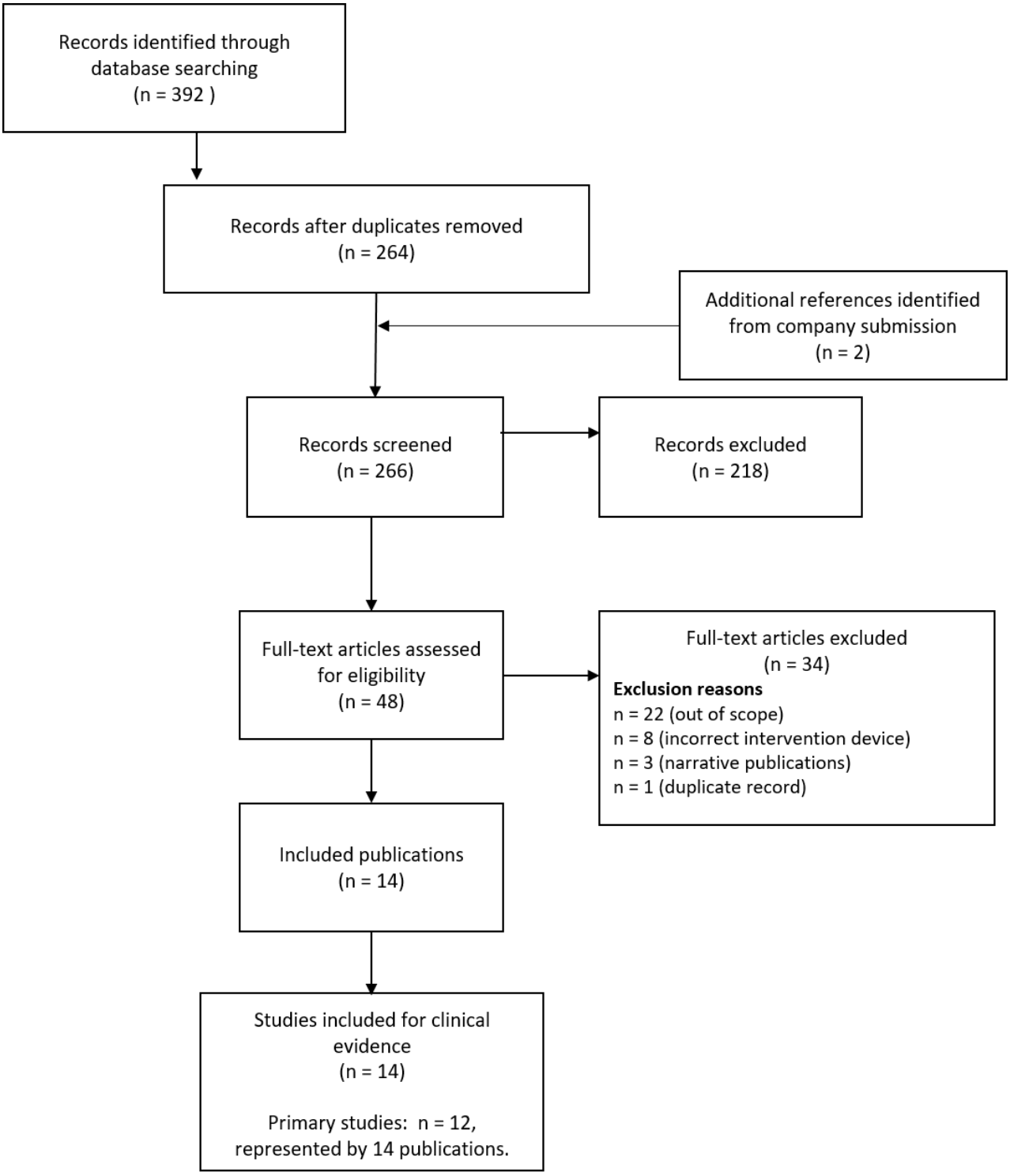
Searched: Kurin – 0 results

---

**MAUDE**

Searched: Kurin Lock, Kurin – 7 results

## EAG Study Selection Flowchart



***Appendix B: Critical appraisal checklists***

# JBI Critical Appraisal Checklist for Case Series

1st reviewer/2nd reviewer: Ayesha Rahim/Susan O'Connell Date: 28/06/2023

Author: Arenas Year: 2021

| | Yes | No | Unclear | Not applicable |
|---|---|---|---|---|
| • Were there clear criteria for inclusion in the case series? | ☐ | ☐ | X | ☐ |
| • Was the condition measured in a standard, reliable way for all participants included in the case series? | ☐ | ☐ | X | ☐ |
| • Were valid methods used for identification of the condition for all participants included in the case series? | X | ☐ | ☐ | ☐ |
| • Did the case series have consecutive inclusion of participants? | ☐ | ☐ | X | ☐ |
| • Did the case series have complete inclusion of participants? | ☐ | ☐ | X | ☐ |
| • Was there clear reporting of the demographics of the participants in the study? | ☐ | X | ☐ | ☐ |
| • Was there clear reporting of clinical information of the participants? | ☐ | X | ☐ | ☐ |
| • Were the outcomes or follow up results of cases clearly reported? | X | ☐ | ☐ | ☐ |
| • Was there clear reporting of the presenting site(s)/clinic(s) demographic information? | ☐ | X | ☐ | ☐ |
| • Was statistical analysis appropriate? | X | ☐ | ☐ | ☐ |

**Comments:**

Overall this is a low quality study. It is not clear which patients were included, and based on what criteria, if any. With respect to identification and measurement of the condition, it is not detailed how the decision to take a blood culture sample is triggered, but the methods used to analyse the blood samples are described. Whether consecutive or complete inclusion of participants was achieved is unclear. There is no demographic or clinical information of any participants. Results are reported relatively clearly and statistical analysis is appropriate. The authors stated that research design may have been limited by 'maturity bias', as the 2 diversion devices were introduced sequentially which meant that the staff had increased familiarity with the second device implemented compared with the first device.

# JBI Critical Appraisal Checklist for Case Series

1st reviewer/2nd reviewer: Ayesha Rahim/Susan O'Connell Date: 28/06/2023

Author: Burnie Year: 2021

| | Yes | No | Unclear | Not applicable |
|---|---|---|---|---|
| • Were there clear criteria for inclusion in the case series? | ☐ | ☐ | X | ☐ |
| • Was the condition measured in a standard, reliable way for all participants included in the case series? | ☐ | ☐ | X | ☐ |
| • Were valid methods used for identification of the condition for all participants included in the case series? | ☐ | ☐ | X | ☐ |
| • Did the case series have consecutive inclusion of participants? | ☐ | ☐ | X | ☐ |
| • Did the case series have complete inclusion of participants? | ☐ | ☐ | X | ☐ |
| • Was there clear reporting of the demographics of the participants in the study? | ☐ | X | ☐ | ☐ |
| • Was there clear reporting of clinical information of the participants? | ☐ | X | ☐ | ☐ |
| • Were the outcomes or follow up results of cases clearly reported? | X | ☐ | ☐ | ☐ |
| • Was there clear reporting of the presenting site(s)/clinic(s) demographic information? | X | ☐ | ☐ | ☐ |
| • Was statistical analysis appropriate? | X | ☐ | ☐ | ☐ |

**Comments:**

Overall this is a low quality study. With respect to identification and measurement of the condition, it is not detailed how the decision to take a blood culture sample is triggered, and the methods used to analyse the blood samples are not described. Inclusion criteria is not explicitly stated and whether consecutive or complete inclusion of participants was achieved is also unclear. There is no demographic or clinical information of any participants reported. Results are reported clearly and statistical analysis is appropriate (descriptive). Information about the presenting site was included, such as historical rates of blood culture contamination and its location in the suburbs of a city.

# JBI Critical Appraisal Checklist for Case Series

1st reviewer/2nd reviewer: Ayesha Rahim/Susan O'Connell Date: 28/06/2023

Author: O'Sullivan Year: 2019

| | Yes | No | Unclear | Not applicable |
|---|---|---|---|---|
| • Were there clear criteria for inclusion in the case series? | X | ☐ | ☐ | ☐ |
| • Was the condition measured in a standard, reliable way for all participants included in the case series? | ☐ | ☐ | X | ☐ |
| • Were valid methods used for identification of the condition for all participants included in the case series? | ☐ | ☐ | X | ☐ |
| • Did the case series have consecutive inclusion of participants? | X | ☐ | ☐ | ☐ |
| • Did the case series have complete inclusion of participants? | X | ☐ | ☐ | ☐ |
| • Was there clear reporting of the demographics of the participants in the study? | ☐ | X | ☐ | ☐ |
| • Was there clear reporting of clinical information of the participants? | ☐ | X | ☐ | ☐ |
| • Were the outcomes or follow up results of cases clearly reported? | X | ☐ | ☐ | ☐ |
| • Was there clear reporting of the presenting site(s)/clinic(s) demographic information? | X | ☐ | ☐ | ☐ |
| • Was statistical analysis appropriate? | X | ☐ | ☐ | ☐ |

**Comments:**

Overall this is a medium quality study. It is clearly stated that the device was used on all patients visiting the Hartford Hospital Emergency Department between April and June, 2017, inclusive. Therefore, the items relating to clear criteria for inclusion, consecutive inclusion and complete inclusion are marked 'yes'. With respect to identification and measurement of the condition, it is not detailed how the decision to take a blood culture sample is triggered, and the methods used to analyse the blood samples are not described. There is no demographic or clinical information of any participants. Outcomes are reported clearly and statistical analysis is appropriate. There is information about the presenting site, which is described as an 869-bed level 1 trauma centre.

# JBI Critical Appraisal Checklist for Case Series

Reviewer: Ayesha Rahim Date: 28/06/2023

Author: Rhew Year: 2021

| | Yes | No | Unclear | Not applicable |
|---|---|---|---|---|
| • Were there clear criteria for inclusion in the case series? | ☐ | ☐ | X | ☐ |
| • Was the condition measured in a standard, reliable way for all participants included in the case series? | ☐ | ☐ | X | ☐ |
| • Were valid methods used for identification of the condition for all participants included in the case series? | ☐ | ☐ | X | ☐ |
| • Did the case series have consecutive inclusion of participants? | ☐ | ☐ | X | ☐ |
| • Did the case series have complete inclusion of participants? | ☐ | ☐ | X | ☐ |
| • Was there clear reporting of the demographics of the participants in the study? | ☐ | X | ☐ | ☐ |
| • Was there clear reporting of clinical information of the participants? | ☐ | X | ☐ | ☐ |
| • Were the outcomes or follow up results of cases clearly reported? | ☐ | X | ☐ | ☐ |
| • Was there clear reporting of the presenting site(s)/clinic(s) demographic information? | X | ☐ | ☐ | ☐ |
| • Was statistical analysis appropriate? | X | ☐ | ☐ | ☐ |

**Comments:**

Overall this is a low quality study. It is not clear which patients were included, and if there was any inclusion criteria. With respect to identification and measurement of the condition, it is not detailed how the decision to take a blood culture sample is triggered, and the methods used to analyse the blood samples are not described. Whether consecutive or complete inclusion of participants was achieved is also unclear. There is no demographic or clinical information of any participants. Detailed results are not reported clearly, with the majority of results only presented in graphs with no corresponding values reported in the text. There is detailed information about the presenting sites/clinics included in the study.

## *Appendix C: Detailed study results*

| Study | Blood culture contamination (BCC) rate | Impact on downstream events (e.g. length of stay, antibiotic usage) | Estimated associated impact on costs* | Staff adherence/satisfaction and implementation |
|---|---|---|---|---|
| **Allain 2018**<br>(USA ED) | • Overall contamination rate from 2013-2016 ranged from 2.1% to 1.6%<br>• Annual average BCC rate pre-Kurin in 2016: 1.6%<br>• BCC rate 3 months post-Kurin Lock in 2017: 0.8%<br><br>Number of samples included in each rate calculation not reported. | N/A | • Where the cost of contamination is assumed to be $5,200 per case, cost savings for the hospital were calculated to be $186,300 if Kurin was implemented.<br>• Above calculated taking into account the number of BCC events observed without Kurin (99) and with Kurin (8) in addition to the cost of the Kurin device. | N/A |

| Study | Blood culture contamination (BCC) rate | Impact on downstream events (e.g. length of stay, antibiotic usage) | Estimated associated impact on costs* | Staff adherence/satisfaction and implementation |
|---|---|---|---|---|
| **Arenas 2021**<br>(USA ED) | 4030 samples included in total.<br>At baseline, the emergency department had contamination rates of 3% to 4.7%.<br><br><u>Device A results</u><br>• BCC rate in control group: 2.2% (761 samples)<br>• BCC rate with device A: 0% (664 samples)<br>• Mean incidence of BCC in the device A group was 0.29 (0.14-0.55) times the incidence of BCC in the control group (based on statistical model prediction)<br><br><u>Device B results</u><br>• BCC rate in control group: 5.2% (1293 samples)<br>• BCC rate with Kurin Lock: 0.3% (1312 samples)<br>• Mean incidence of BCC in the device B group was 0.23 (0.13-0.37) times the incidence of BCC in the control group (based on statistical model prediction) | N/A | N/A | N/A |

| Study | Blood culture contamination (BCC) rate | Impact on downstream events (e.g. length of stay, antibiotic usage) | Estimated associated impact on costs* | Staff adherence/satisfaction and implementation |
|---|---|---|---|---|
| **Arnaout 2021**<br>(USA EDs) | Overall BCC rate (5661 samples)<br>• Standard procedure: 2.9%<br>• With Kurin Lock: 1.9%<br>p = 0.018<br>Emergency department 1 BCC rates (1719 samples)<br>• Standard procedure: 1.4%<br>• With Kurin Lock: 1.1%<br>p = 0.57<br>Emergency department 2 BCC rates (3942 samples)<br>• Pre-Kurin Lock: 3.5%<br>• With Kurin Lock: 2.3%<br>p = 0.024<br><br>BCC rates reduced by 1% overall, with a 34% relative reduction. Significant difference in BCC rate observed overall and at ED 2, but not ED 1. | N/A | N/A | N/A |
| **Atta 2022**<br>(UK A&E) | • Baseline BCC in emergency department: 9% (8.91% in graph)<br>• BCC with Kurin Lock (381 samples included): 3.1% (3.19% stated in graph)<br>• An overall reduction of 65.5% | • Estimated freeing up of 1,444 bed-days in the emergency department and 5,041 bed-days trust-wide. | Based on estimated costs associated with false-positive blood cultures:<br>• Estimated savings of £1.3M in the emergency department alone and £4.6M for the Trust as a whole | • The relationship between adherence with using Kurin Lock and BCC rate was explored; study authors state that the reduction in BCC rate becomes evident when there is 80% adherence in using the device. |

| Study | Blood culture contamination (BCC) rate | Impact on downstream events (e.g. length of stay, antibiotic usage) | Estimated associated impact on costs* | Staff adherence/satisfaction and implementation |
|---|---|---|---|---|
| **Baxter 2020** (USA ED) | • BCC rate without Kurin Lock: 4.93%<br>• BCC rate with Kurin Lock: 1.66%<br>• Overall reduction in BCC rates of 66%. | • Authors state 144 patients spared from receiving unnecessary antibiotics as a result of a false-positive BCC<br>• Based on data from 3 different months, authors calculated that patients with BCC spent an average of 3.97 additional days in hospital | • Authors state results suggest a savings of >$500,000 per year (contaminations on an annual basis fell from 217 to 73), based on an assumed cost of $4,000 per contaminated culture. | • Adherence averaged 70%–75% during the trial period |
| **Burnie 2021** (USA ED) | BCC rate at baseline:<br>• 2.92% in 2018<br>BCC rate with Kurin Lock:<br>• 1.42% in 2019<br>• 1.51% in 2020 (48% improvement from 2018 rate)<br>Introduction at a second site for 6 months (additional data, not associated with the original study period)<br>• BCC rate at baseline:4.96%<br>• BCC rate with Kurin Lock:1.6% | • Study authors report that per BCC, length of stay is increased by 2.65 days (following retrospective analysis of data collected during period of standard care) | • Study authors report cost of admission is increased by $5863 (following retrospective analysis of data collected during period of standard care)<br>• As a result, cost savings associated with the implementation of Kurin Lock device is assumed to be approximately $1.6 million dollars (since project implementation) | N/A |

| Study | Blood culture contamination (BCC) rate | Impact on downstream events (e.g. length of stay, antibiotic usage) | Estimated associated impact on costs* | Staff adherence/satisfaction and implementation |
|---|---|---|---|---|
| **Hodson 2022**<br>(UK A&E) | • BCC rate pre-Kurin Lock: 6% (1343 samples)<br>• BCC rate with Kurin Lock: 1.9% (2% reported in text) (533 samples)<br>p=0.045 (95% CI: 0.29 – 0.98) | N/A | • Based on estimated costs of a false-positive blood culture, cost savings were estimated to be £28,000-72,000 | N/A |
| **Ostwald 2021a**<br>**Ostwald 2021b**<br>(USA Paediatric ED) | Retrospective analysis of BCC rates in department ranged from 0.45 to 5.63%.<br><br><u>First study period:</u><br>Overall BCC rate: 1.5% (stated by authors, figures suggest rate is 1.17%)<br>• 0 instances of contamination observed in 303 samples drawn with Kurin Lock (0%)<br>• 4 instances of contamination observed in 38 samples drawn without Kurin Lock (10.5%)<br>p=0.0001, significant difference in BCC rate observed post-Kurin Lock introduction.<br><br><u>Second study period (modified tubing):</u><br>Overall BCC rate: 0.22%<br>• 0 instances of contamination observed in 872 samples drawn with Kurin Lock (0%)<br>• 2 instances of contamination observed in 33 samples drawn without Kurin Lock (6.06%)<br>p=0.0001, significant difference in BCC rate observed post-Kurin Lock introduction. | • Decreased return visits and decreased unnecessary antibiotic use reported for second study period | • Mean cost of calling a patient back in and/or admission due to FPBC was £1,907 (from administrative records)<br>• An annual cost saving of $71,422 was estimated if Kurin Lock was fully implemented for use with all blood culture draws | Staff satisfaction survey results:<br>• 45% of nurses found the device to be easy to use<br>• 85% of nurses said the device made sense<br><br>Themes identified from the survey included length of tubing was “clumsy, too long, and bulky” for paediatric patients and it was “wasting too much blood” – this influenced the development of the modified device used in the second study period. |

| Study | Blood culture contamination (BCC) rate | Impact on downstream events (e.g. length of stay, antibiotic usage) | Estimated associated impact on costs* | Staff adherence/satisfaction and implementation |
|---|---|---|---|---|
| **O'Sullivan 2019** (USA ED) | BCC rates in 3 most recent months prior to intervention:<br>• March 2017: 1.4%<br>• February 2017: 1.6%<br>• January 2017: 2.1%<br><br>BCC rates in 3 most recent months where Kurin Lock was implemented:<br>• June 2017: 0.4%<br>• May 2017: 0.5%<br>• April 2017: 0.4%<br><br>Significantly lower BCC rate consistently observed with Kurin Lock compared to BCC rates observed without Kurin Lock. Reductions in BCC rate ranged from 65% to 82% ($p<0.05$ for 9 comparisons made).<br><br>Overall, the average BCC rate was 0.44% over the 3 Kurin Lock months compared with the average BCC rate of 1.71% over the 3 non-Kurin Lock months. Average reduction of 74.1%. | N/A | • Where the cost of BCC is assumed to be $5,000 per contamination, annual cost savings from implementing the Kurin Lock device would be more than $900,000, or more than $750,000 after adjusting for device costs.<br>• Above calculated on how many BCC events occurred during 3 months without Kurin Lock and 3 months with Kurin Lock:<br><u>Without Kurin Lock</u><br>– March 2017: 20<br>– February 2017: 24<br>– January 2017: 33<br><u>With Kurin Lock</u><br>– June 2017: 4<br>– May 2017: 5<br>– April 2017: 4 | N/A |

| Study | Blood culture contamination (BCC) rate | Impact on downstream events (e.g. length of stay, antibiotic usage) | Estimated associated impact on costs* | Staff adherence/satisfaction and implementation |
|---|---|---|---|---|
| **Parsons 2023** (UK A&E) | • BCC rate at baseline: 5%<br>• BCC rate with Kurin Lock: 2.6%<br>• Overall reduction of 48% | • Estimated potential to free up 359 bed days in the emergency department, and 1,836 bed days Trust-wide | • Estimated cost avoidance of £1.6M for the Trust as a whole or £327K in emergency department alone | N/A |
| **Rhew 2021** (USA EDs) | *Monthly BCC rates for 4 hospitals not extracted from bar graphs, values not reported in text.*<br><br>Authors state BCC rates fell from 3.1% to 1.3% to 0% when using Kurin Lock over the 5 week trial period. Ultimately, the overall system wide BCC rate fell to less than 2.1%. | N/A | N/A | Authors reported on facilitators to implementation which were:<br>• Visibility of data – for all staff<br>• Visibility of resources<br>• Using workshops, sills fairs and educational material<br>• Clear objectives and expectations<br>• Communications – encouraging collaboration |
| **Sutton 2018a**<br>**Sutton 2018b**<br>(USA ED) | • Pre-intervention BCC rate (1953 samples): 0.025 (2.6%), 95% CI (0.019-0.033)<br>• Post-Kurin Lock BCC rate (2267 samples): 0.012 (1.2%), 95% CI (0.008-0.017)<br><br>Statistically significant difference between 2 rates, $p<0.05$. | N/A | Taking the cost of equipment, cost of cultures, contaminant rate and cost per contaminant (est. $7500) into account:<br>• Costs associated with BCC pre-intervention: $814,512<br>• Costs associated with BCC post-intervention: $440,252 | N/A |

## *Appendix D: Length of stay calculations*

The EAG calculated the following alternative daily costs (after initial admission), as shown in summary Table 23, taken from NHS Cost collection sources listed in Table 24. Methods a and b calculate the difference between the long stay costs and short stay costs to exclude initial admissions costs. This is then divided by either the weighted mean length of stay reported in 2017/18, or the weighted mean length of stay calculated in the model. Method c takes the total long stay cost and divides it by the number of days stay (both as weighted means), however this includes the initial admission in the cost of additional days. All three methods resulted in higher daily costs than the EAG base case, but lower than the submitted model. They are included in the range of the two way sensitivity analysis tables.

**Table 23 Summary of alternative bed day costs**

| | Calculation | Adult | Paediatric |
|---|---|---|---|
| a | (Mean long stay cost – mean short stay cost ) / (mean LOS 2017/18) | £440 | £887 |
| b | (Mean long stay cost – mean short stay cost ) / (mean LOS calculated in model) | £550 | £584 |
| c | Mean long stay cost / mean LOS 2017/18 | £521 | £953 |

**Table 24 Source data for alternative daily costs**

| Parameter | EAG value | Comment |
|---|---|---|
| **Adult** | | |
| Non-elective long stay for adult | £3,432 | HRG groups WJ06A-J and WJ07, 2019/20 inflated to 2021/22 using PSSRU from £3,261 |
| Non-elective short stay for infection (adult) | £970 | HRG groups WJ06A-J and WJ07, 2019/20 inflated to 2021/22 using PSSRU from £921 |
| Weighted mean LOS from NHS cost collection | 6.59 | HRG groups WJ06A-J and WJ07, 2017/18 |
| Weighted mean LOS from model | 5.48 | |
| Daily cost after initial admission using long stay – short stay divided by mean LOS in model | £550 | HRG groups WJ06E-J an WJ07, 2019/20 inflated to 2021/22 using PSSRU, model LOS is calculated as 5.476 days based on SOC rate of contamination in A&E setting |
| Daily cost after initial admission using long stay – short stay divided by weighted mean of LOS from 2017/18 data | £440 | HRG groups WJ06E-J an WJ07, 2019/20 inflated to 2021/22 using PSSRU, model LOS is calculated from reported LOS for NEL in 2017/18 reference costs. |

| Parameter | EAG value | Comment |
|---|---|---|
| **Adult** | | |
| **Paediatric** | | |
| Non-elective long stay for paediatric | £3,763 | HRG groups PW16B - E, 2019/20 inflated to 2021/22 using PSSRU from £3,575 |
| Non-elective short stay for infection (paediatric) | £1,150 | HRG groups PW16B - E, 2019/20 inflated to 2021/22 using PSSRU from £1,093 |
| Weighted mean LOS from NHS cost collection | 3.95 | |
| Weighted mean LOS from model | 5.48 | |
| Daily cost after initial admission using long stay – short stay divided by weighted mean of LOS from 2017/18 data | £887 | HRG groups PW16B - E, 2019/20 inflated to 2021/22 using PSSRU, model LOS is calculated from reported LOS for NEL in 2017/18 reference costs. |
| Daily cost after initial admission using long stay – short stay divided by mean LOS in model | £584 | HRG groups PW16B - E, 2019/20 inflated to 2021/22 using PSSRU, model LOS is calculated as 5.476 days based on SOC rate of contamination in A&E setting |

## *Appendix E: One way sensitivity analysis*

**Table 25: One way sensitivity analysis, EAG base case, parameter variation and results**

| Parameter | Cost saving per patient | |
|---|---|---|
| | Low value | High value |
| Length of stay difference (A&E) (1.00 to 5.00; base case 2.00) | -£14.32 | £74.61 |
| Daily cost of stay in A&E (all) (£301.71 to £800.00; base case £377.14) | -£0.98 | £57.77 |
| Rate of BC contamination (False positives) - SoC (A&E) (2.00% to 10.80%; base case 9.00%) | -£27.83 | £17.10 |
| % reduction of BC contamination with Kurin - in the A&E (0.52 to 0.79; base case 0.66) | -£1.28 | £17.10 |
| Number of cultures drawn with Kurin Lock (1.60 to 2.40; base case 2.00) | £15.71 | £0.11 |
| Duration of empirical antibiotics following identification of False Positive - Hospital (3.00 to 7.00; base case 4.00) | £7.53 | £9.07 |
| Standard of care unit cost (£0.23 to £1.00; base case £0.48) | £7.41 | £8.95 |
| Duration of empirical antibiotics following stopping by culture finalisation - Hospital (1.00 to 4.00; base case 3.00) | £8.46 | £7.64 |
| Number of cultures drawn with Standard of care (1.60 to 2.40; base case 2.00) | £7.72 | £8.10 |
| Probability of empirical antibiotics at culture collection as a precaution - Prior to blood culture results (A&E) (64.00% to 90.00%; base case 71.00%) | £7.99 | £7.69 |
| Vancomycin pack cost (£9.60 to £14.40; base case £12.00) | £7.77 | £8.06 |
| Cost of microbiology test (£6.82 to £10.24; base case £8.53) | £7.81 | £8.01 |
| Adult patients: Patient distribution (0.65 to 0.97; base case 0.81) | £7.85 | £7.98 |
| Cost of a haematology test (£2.37 to £3.55; base case £2.96) | £7.88 | £7.95 |
| Cost of a biochemistry test (£1.24 to £1.86; base case £1.55) | £7.89 | £7.93 |

## *Appendix F: Scenario analysis inputs and results*

Two scenarios were included in the company submission, for intensive care (ICU) and a general hospital setting.

Scenario 1 is based on an ICU setting, where the patient is expected to be more unwell, and the daily costs of care are higher. The clinical inputs are largely taken from a study by Lalezari (2019), in Israel, and blood samples were from patients in general care, rather than specifically ICU. However, the additional length of stay for those patients with a false positive result is similar to that reported in many other studies (largely based in the USA). The ICU scenario is much more robust to changes in baseline BCC rate or changes in length of stay, due to the higher costs of ICU care, compared to hospital care.

**Table 26 Scenario 1: ICU setting, Company and EAG parameters**

| Parameter | Company value | EAG value | Sources & comment |
|---|---|---|---|
| Contamination rate | 2.5% | 2.5% | Souvenir 1998 |
| LOS for patients with a true negative BC | 5.73 days | 5.73 days | Lalezari 2019<br>This study is being used for an ICU setting, but was carried out within a general hospital setting. Despite this, the change in LOS is similar to many other studies, and has not been changed by the EAG |
| LOS for patients with a false-positive BC | 8.08 days | 8.08 days | |
| LOS for patients with a true positive BC | 11.06 days | 11.06 days | |
| **Resulting difference in LOS per BCC** | **2.35** | **2.35** | |
| Duration of empirical antibiotics – stopped by culture finalisation | 1.5 days | 1.5 days | Souvenir 1998 |
| Duration of empirical antibiotics – identification of false positive | 5.0 days | 5.0 days | |
| Duration of empirical antibiotics – confirmed bacteraemia | 6.5 days | 6.5 days | |
| Daily cost of stay in a ward (adult) | £2,389 | £1,897 | |
| Daily cost of stay in a ward (paediatric) | £3,025 | £2,643 | |
| **Resulting daily cost** | **£2,482** | **£2,038** | |

Abbreviations: A&E, accident and emergency; BC, blood culture; LOS, length of stay; ICU, intensive care unit.

**Table 27 Summary of Scenario 1: ICU setting results**

| | Company's results | | | EAG results | | |
|---|---|---|---|---|---|---|
| | Technology | Comparator | Cost saving per patient | Technology | Comparator | Cost saving per patient |
| Device | £39 | £3 | **-£36** | £39 | £1 | **-£38** |
| BC processing | £16 | £16 | **£0** | £13 | £13 | **£0** |
| Confirmation tests | £1 | £2 | **£0** | £1 | £1 | **£0** |
| Antibiotics | £54 | £56 | **£2** | £10 | £10 | **£0** |
| Length of stay | £15,251 | £15,346 | **£96** | £12,520 | £12,598 | **£78** |
| **Total** | **£15,361** | **£15,423** | **£62** | **£12,583** | **£12,624** | **£41** |
| **Avoided events** | | | | | | |
| False positives | 0.01 | 0.03 | **0.02** | 0.01 | 0.03 | **0.02** |
| Days of antibiotics | 1.50 | 1.57 | **0.06** | 1.50 | 1.57 | **0.06** |
| Bed days | 6.14 | 6.18 | **0.04** | 6.14 | 6.18 | **0.04** |

**Table 28 Two way sensitivity analysis of baseline risk of BCC, and difference in bed days between true negative and false positive blood cultures (Scenario 1: ICU setting)**

| | | Baseline risk of BC contamination with SoC (ICU) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | **£41** | 1% | 2% | 3% | 4% | 5% | 6% | 7% | 8% | 9% | 10% |
| Reduction in days in hospital between true negative and false positive results | 1.0 | -£24 | -£11 | £3 | £16 | £30 | £44 | £57 | £71 | £84 | £98 |
| | 1.5 | -£18 | £3 | £23 | £43 | £63 | £84 | £104 | £124 | £144 | £165 |
| | 2.0 | -£11 | £16 | £43 | £70 | £97 | £124 | £151 | £178 | £204 | £231 |
| | 2.5 | -£4 | £29 | £63 | £96 | £130 | £164 | £197 | £231 | £265 | £298 |
| | 3.0 | £2 | £43 | £83 | £123 | £163 | £204 | £244 | £284 | £325 | £365 |
| | 3.5 | £9 | £56 | £103 | £150 | £197 | £244 | £291 | £338 | £385 | £432 |
| | 4.0 | £16 | £69 | £123 | £177 | £230 | £284 | £337 | £391 | £445 | £498 |
| | 5.0 | £29 | £96 | £163 | £230 | £297 | £364 | £431 | £498 | £565 | £632 |
| | 6.0 | £42 | £123 | £203 | £283 | £364 | £444 | £524 | £605 | £685 | £765 |

Scenario 2 is in a general hospital setting. The clinical evidence is taken from Alahmadi (2010) which is based in an NHS general hospital setting in Northern Ireland. The key limitation of this evidence source is that 42% of the BCC samples were from patients in ICU, and the comparator matching process was based on age,

comorbidity and month, but did not include the setting. Therefore, it is probable that patients in the BCC arm had more severe health problems than those in the comparator arm, despite the matching process.

**Table 29 Scenario 2: Hospital setting, Company and EAG parameters**

| Parameter | Company value | EAG value | Sources & comment |
|---|---|---|---|
| Contamination rate | 4.7% | 4.7% | Alahmadi 2010 |
| LOS for patients with a true negative BC | 8.0 days | 8.0 days | Alahamadi 2010<br>The EAG have kept this scenario as it is the only UK based LOS data. The difference in LOS is likely to be exaggerated as 42% of BCC were from ICU, and the comparators were not matched for settings |
| LOS for patients with a false-positive BC | 13.0 days | 13.0 days | |
| LOS for patients with a true positive BC | 13.0 days | 13.0 days | |
| **Resulting difference in LOS per BCC** | **5.0 days** | **5.0 days** | |
| Duration of empirical antibiotics – stopped by culture finalisation | 3.0 days | 3.0 days | Alhamadi 2010<br>The considerations for LOS also apply here, however the model is much less sensitive to the duration of antibiotics. |
| Duration of empirical antibiotics – identification of false positive | 4.0 days | 4.0 days | |
| Duration of empirical antibiotics – confirmed bacteraemia | 10.0 days | 10.0 days | |
| Daily cost of stay in a ward (adult) | £844.13 | £328.88 | The EAG applied the same costs as for A&E, using excess day costs inflated from 2017/18 |
| Daily cost of stay in a ward (paediatric) | £1,091.62 | £584.64 | |
| **Resulting daily cost** | **£880.24** | **£377.14** | |

Abbreviations: A&E, accident and emergency; BC, blood culture; LOS, length of stay; ICU, intensive care unit

The EAG results for Scenario 2 are lower than the company results due to the same changes in daily cost that were described for the base case (Table 30). The additional cost saving seen in the EAG results for this scenario, compared to the EAG base case, is almost entirely due to the larger difference in length of stay per BCC. The two way sensitivity analysis (Table 31) for baseline BCC rate and difference in length of stay is identical to the table for the EAG base case, as the key changes are these two variables.

**Table 30 Summary of Scenario 2: General hospital setting results**

| | Company's results | | | EAG results | | |
|---|---|---|---|---|---|---|
| | Technology | Comparator | Cost saving per patient | Technology | Comparator | Cost saving per patient |
| Device | £39 | £3 | **-£36** | £39 | £1 | **-£38** |
| BC processing | £16 | £16 | **£0** | £13 | £13 | **£0** |
| Confirmation tests | £1 | £2 | **£0** | £1 | £2 | **£0** |
| Antibiotics | £99 | £101 | **£2** | £18 | £18 | **£0** |
| Length of stay | £7,439 | £7,575 | **£135** | £3,814 | £3,872 | **£58** |
| **Total** | **£7,594** | **£7,696** | **£102** | **£3,885** | **£3,906** | **£21** |
| **Avoided events** | | | | | | |
| False positives | 0.02 | 0.05 | **0.03** | 0.02 | 0.05 | **0.03** |
| Days of antibiotics | 2.74 | 2.80 | **0.06** | 2.74 | 2.80 | **0.06** |
| Bed days | 8.45 | 8.61 | **0.15** | 8.45 | 8.61 | **0.15** |

**Table 31 Two way sensitivity analysis of baseline risk of BCC, and difference in bed days between true negative and false positive blood cultures (Scenario 2: general hospital setting)**

| | | Baseline risk of BC contamination with SoC (ICU) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | **£21** | 1% | 2% | 3% | 4% | 5% | 6% | 7% | 8% | 9% | 10% |
| Reduction in days in hospital between true negative and false positive results | 1.0 | -£35 | -£33 | -£30 | -£28 | -£25 | -£22 | -£20 | -£17 | -£14 | -£12 |
| | 1.5 | -£34 | -£30 | -£26 | -£23 | -£19 | -£15 | -£11 | -£7 | -£3 | £1 |
| | 2.0 | -£33 | -£28 | -£23 | -£18 | -£13 | -£7 | -£2 | £3 | £8 | £13 |
| | 2.5 | -£32 | -£25 | -£19 | -£13 | -£6 | £0 | £6 | £13 | £19 | £25 |
| | 3.0 | -£30 | -£23 | -£15 | -£8 | £0 | £7 | £15 | £23 | £30 | £38 |
| | 3.5 | -£29 | -£20 | -£12 | -£3 | £6 | £15 | £24 | £32 | £41 | £50 |
| | 4.0 | -£28 | -£18 | -£8 | £2 | £12 | £22 | £32 | £42 | £52 | £62 |
| | 5.0 | -£26 | -£13 | £0 | £12 | £25 | £37 | £50 | £62 | £75 | £87 |
| | 6.0 | -£23 | -£8 | £7 | £22 | £37 | £52 | £67 | £82 | £97 | £112 |

# GID-MT582 Kurin Lock for blood culture collection

## Draft guidance recommendations

## Medical technologies advisory committee Sep 2023

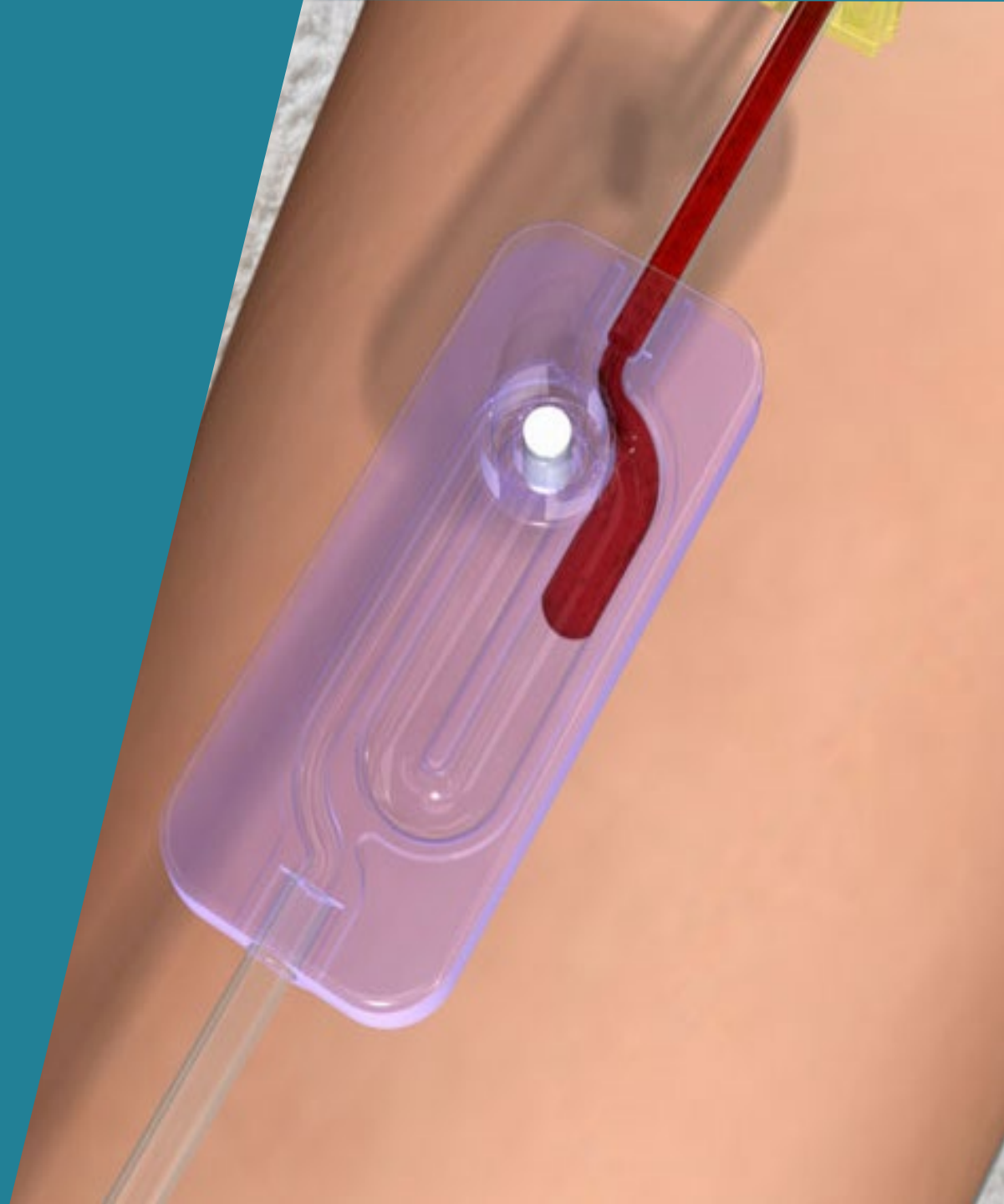
**Committee introducers:** Karen McCutcheon and Stacey Chang-Douglass

**Expert advisers:** Andrew Barton, David Partridge and Jane Hudson

**External assessment group:** Ayesha Rahim and Megan Dale

**Technical team:** Aamer Jawed, Amy Barr and Bernice Dillon

NICE National Institute for Health and Care Excellence



# Kurin Lock for blood culture collection

The following slides provide an overview of the assessment report (AR) for this technology. Not all of the slides will be presented at the committee meeting but the main information in this set of slides will be summarised.

Key documents in this assessment include:

- The final scope - contains the decision problem for the assessment
- The company submission*– presents clinical and economic evidence to support the company's case for adoption
- The expert adviser questionnaires (EAQs)* – clinical expert advice about the potential use of this technology in the NHS
- The assessment report (AR)* - assessment of the company submission by the external assessment group (EAG). The report has a more detailed executive summary which provides an overview of the EAG's work and links to the relevant sections of the report

The slides do not contain any information that has been supplied in confidence

* These documents are in the Committee pack and will be published at consultation

# The technology: Kurin Lock (1)

- Kurin Lock is a device for collecting blood that is then cultured to check for the presence of infections
- The innovative aspect of Kurin Lock is that it collects and isolates the first 0.15 mL of blood before allowing the following blood to flow through the tube into the culture collection bottle
- The aim of Kurin Lock is to avoid contamination of the blood sample by isolating the blood that may contain microbes from the skin at the site of venepuncture, and so reduce the rate of false positive bloodstream infection results
- Kurin Lock is a CE-marked class IIa medical device

# The technology: Kurin Lock (2)

- The Kurin blood culture collection set includes a vasculature connection (a butterfly needle for venepuncture or luer connection to a peripheral catheter), flexible tubing, Kurin Lock (a u-shaped chamber), and blood culture bottle holder
- The Kurin blood culture collection set costs £19.50 per unit (excluding VAT)

# Condition and patient group (1)

- People who are suspected of having a bloodstream infection or sepsis have a blood sample collected. The sample is sent to a laboratory for culturing to detect and potentially identify the infection
- Bloodstream infections account for approximately 40% of emergency admissions, 66% of total hospital deaths and 50% of total bed days, with 100,000 bloodstream infections detected every year in the UK (NHS England, 2022)
- Some people are at an increased risk of infections including:
    - very young people (under 1 year)
    - older people (over 75 years)
    - people who are very frail
    - people who have impaired immune systems because of illness or drugs

# Condition and patient group (2)

- During blood culture collection, blood samples can be contaminated by microbes located on the skin at the site of venepuncture
- Cultures contaminated with skin cells can give false positive results and may lead to inappropriate treatment, increased hospital stays and additional hospital, laboratory and pharmacy costs
- The UK standards for microbiology investigations states that recommended contamination rates are generally below 3%
- In Accident & Emergency departments in the the UK, blood contamination rates have been reported to range between 5% (Bentley, 2016) and 9% (Atta and Mcguire, 2022)

# Current management (1)

- NICE's guideline on the recognition, diagnosis and early management of sepsis (NG51) recommends that all patients with suspected sepsis should have a sample collected for blood culture testing
- Current management involves cleaning the injection site with antiseptic, inserting the needle and collecting blood directly into blood culture collection bottles. Measures, such as appropriate skin and bottle preparation, obtaining cultures from peripheral venepuncture instead of catheters and training can minimise the risk of contamination
- At least 40mL of blood should be cultured for optimum detection of bloodstream infections. This requires at least 2 sets of blood culture samples to be taken within a few hours of each other

# Current management (2)

The UK standards for microbiology investigations notes that the following criteria are used when determining the clinical relevance of a positive result, including whether a sample is contaminated:

- the identity of the organism
- the number of positive sets
- the number of positive bottles within a set
- the quantity of growth
- clinical and laboratory data (including the source of culture).

Samples that are sent for processing and analysis. Preliminary results are usually available within 24-48 hours of incubation, whilst it may take up to 5 days to fully culture a sample to confirm a negative result.

**NICE**

| Decision problem | | |
|---|---|---|
| Population | People who need a blood culture test within a secondary care setting | |
| Subgroups | • People who present with signs or symptoms of infection<br>• People at increased risk of infections such as those who are immunocompromised<br>• People in whom sampling blood can be challenging for example intravenous drug users or children | |
| Interventions | Kurin Blood Culture Collection Set with Kurin Lock technology | |
| Comparator | Standard blood culture collection (tubes and container) | |
| Outcomes | • blood culture contamination rate<br>• length of hospital stay<br>• rates of antimicrobial prescriptions<br>• use of unneeded antibiotic treatment<br>• unnecessary further interventions such as laboratory tests to rule out suspected bacteraemia | • treatment delays<br>• length of hospital stay<br>• rates of hospital acquired infection<br>• patient-reported outcome measures such as health related quality of life<br>• patient-reported experience measures<br>• device-related adverse events |

The company submission proposed a variation to broaden the population to '**people who need a blood culture**'. The EAG did not consider this variation to be valid in the context of this assessment. For the full decision problem see the final scope

# Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

- Infants (under 1 year of age), older people (over 75 years of age), people who are immunocompromised (such a people undergoing cancer treatment) and women who are pregnant, post-partum, or have had a termination of pregnancy or miscarriage in the past six weeks are at an increased risk of developing sepsis
- People with a learning disability or people who have difficulty communicating may also be at an increased risk
- Age, disability and pregnancy and maternity are protected characteristics under the Equality Act (2010)
- No equality issues were identified in relation to Kurin Lock. The company states that Kurin Lock can be used on people of all ages

# Clinical effectiveness

Kurin Lock for blood culture collection

NICE National Institute for Health and Care Excellence

# Clinical evidence summary

- The company included 12 studies in its submission and the EAG did not identify any additional studies from its literature searches. The EAG noted that 2 additional abstracts it identified from the searches provided no further information
- The EAG included 12 studies reported across 14 publications (4 full-texts publications, 5 abstracts and 5 posters)
- Studies included by the EAG consist of 10 before and after studies, a prospective and retrospective trial and a multiphase crossover trial
- Key outcomes reported across studies include blood culture contamination rate (BCC), length of stay, antibiotic use and staff adherence and satisfaction

For more information about the EAG search strategy and evidence selection see section 5.1 and 5.2 of the AR



EAG: external assessment group; AR: external assessment report

# Clinical evidence summary

| Associated publication | Publication type | Company | EAG |
|---|---|---|---|
| Allain 2018 USA | Abstract | ✓ | ✓ |
| **Arenas 2021 USA** | **Full text publication** | ✓ | ✓ |
| Arnaout 2021 USA | Abstract | ✓ | ✓ |
| Atta 2022 UK | Poster from company | ✓ | ✓ |
| Baxter 2020 UK | Abstract | ✓ | ✓ |
| **Burnie 2021 USA** | **Full text publication** | ✓ | ✓ |
| Hodson 2022 UK | Poster from company | ✓ | ✓ |
| Ostwald 2021a USA | Poster with supplementary text | ✓ | ✓ |
| Ostwald 2021b USA | Abstract | ✗ | ✓ |
| **O'Sullivan 2019 USA** | **Full text publication** | ✓ | ✓ |
| Parsons 2023 UK– Unpublished | Poster from company | ✓ | ✓ |
| **Rhew 2021 USA** | **Full text publication** | ✓ | ✓ |
| Sutton 2018a USA | Poster with supplementary text | ✓ | ✓ |
| Sutton 2018b USA | Abstract | ✗ | ✓ |

# Clinical evidence: key studies

| Study and location | Design and intervention | Participants and setting | Outcomes | Quality (JBI Critical Appraisal Checklist ) |
|---|---|---|---|---|
| Arenas 2021, USA<br><br>16 months | Prospective and retrospective trial<br>2 blood diversion devices | Emergency department patients requiring blood culture samples (n=4030) | BCC rate | Low quality |
| Burnie 2021 , USA<br><br>6 months | Before and after study<br>Kurin Lock | Emergency department patients requiring blood culture samples (n=not reported) | BCC rate;<br>Estimated associated impact on costs (cost of admission/cost of blood culture contamination) | Low quality |
| O'Sullivan 2019, USA<br><br>3 months | Before and after study<br>Kurin Lock | Emergency department patients requiring blood culture samples (n=not reported) | BCC rate<br>Estimated impact on associated costs | Medium quality |
| Rhew 2021, USA<br>Assumed 12 months | Implementation study (before and after)<br>Kurin Lock (peripheral IV blood draws) | Emergency department patients requiring blood culture samples (n = not reported) | BCC rate | Low quality |

NICE

3 studies were quality improvement projects which explored the impact of Kurin Lock on BCC rates in UK NHS Trusts (Atta 2022, Hodson 2022, Parsons 2023). These and the other 5 studies were reported in limited detail as abstract and poster publications.

BCC: Blood culture contamination

# Clinical evidence: EAG critique

- The EAG critically appraised the 4 full-text peer reviewed publications using the JBI Case Series critical appraisal checklist. The remaining 10 abstracts and posters were not formally critically appraised due to lack of detail
- The EAG considered Arenas (2021), Burnie (2021) and Rhew (2021) to be of low quality as information on inclusion criteria, patient demographics, results and presenting site were not consistently reported across the studies
- O'Sullivan (2019) was considered medium quality as the inclusion criteria, study setting and outcomes were clearly reported. But, patient demographics were not clearly reported
- It is unclear how participants were selected for blood culture test referral across the studies. Methods of laboratory analysis that may lead to samples being identified as a false positive was reported in detail in Arenas (2021) only
- The EAG noted that variations in practice for referral and laboratory analysis are common and may limit generalisability of the study results

NICE

For further details about the critique of the evidence see section 6.2 and Appendix B of the AR

EAG: external assessment group; AR: assessment report

# Clinical evidence: outcomes – BCC rate

- 4 full-text publications reported BCC rates (all USA based)

| Study and location | BCC rates before Kurin Lock | BCC rates after Kurin Lock |
|---|---|---|
| Arenas 2021, USA ED | 5.2% (n=1293) | 0.3% (n=1312) |
| Burnie 2021 , USA ED | 2.92% | 1.42% and 1.51% per year |
| O'Sullivan 2019, USA ED | 1.4%, 1.6% and 2.1% per month | 0.4%, 0.5% and 0.4% per month |
| Rhew 2021, USA EDs | 3.1% | 0% (5-week trial) |

- 3 studies (poster) reported reduced BCC rates after introducing Kurin Lock in NHS Trusts

| Study and location | BCC rates before Kurin Lock | BCC rates after Kurin Lock |
|---|---|---|
| Atta 2022, UK A&E | 9% | 3.1% |
| Hodson 2022, UK A&E | 6% | 1.9% (Statistically significant p=0.045) |
| Parsons 2023, UK A&E | 5% | 2.6% |

- 5 other studies (abstracts and posters) reported a decrease in BCC rate in the USA with Kurin Lock. 3 of these studies (Arnaout 2021, Ostwald 2021a/2021b, Sutton 2018a/2018b) reported a statistically significant decrease ($p<0.05$)

For further details see section 6.3.1 and table 10 of the AR

NICE



AR: assessment report, BCC: blood culture contamination; ED: emergency department

# Clinical evidence: outcomes – length of stay

Length of stay was not a formal outcome in any of the included studies. But, it is briefly discussed in 4 studies with Atta 2022 and Parsons 2023 UK NHS based whilst Burnie 2021 and Baxter 2022 are USA based

- A poster from (Atta, 2022) reported that implementation of Kurin Lock could release 1,444 bed days in the department the study took place in and 5,041 Trust-wide. The author via correspondence advised that this was calculated by assuming a 5.1 days additional stay per contaminated BC
- Another poster (Parsons, 2023) reported that Kurin Lock would free 359 bed days in the emergency department and 1,836 days Trust-wide. No further details were reported
- Burnie (2021) reported that the average additional length of stay associated with BCC generally is 2.65 days. No comment was made on how implementing Kurin Lock affected the length of stay
- An abstract (Baxter, 2020) reported that patients with BCC spent an average of an additional 3.97 days in hospital. It is unclear if this was calculated during a period of using standard care or Kurin Lock

For further details on length of stay see section 6.3.2 of the AR

NICE



BCC: blood culture contamination; AR: assessment report

# Clinical evidence: outcomes – unnecessary antibiotic use

- Unnecessary antibiotic use is not a formal outcome in any of the studies. But, it is briefly discussed in 3 studies
    - An abstract (Baxter, 2020) reported that 144 patients were spared from receiving unnecessary antibiotic treatment. No further detail is reported on how this is calculated
    - Burnie (2021) stated that nearly 250 patients 'benefitted' from Kurin Lock, including a reduction in unnecessary antibiotic use
    - A study reported by poster and abstract (Ostwald 2021a/2021b) reported that the second trial period of the study led to decrease unnecessary antibiotic use. No further detail was reported

For further details on unnecessary antibiotic use see section 6.3.3 of the AR

NICE



AR: assessment report

# Clinical evidence: outcomes – staff adherence and satisfaction

- Staff adherence and satisfaction are not listed as an outcome in the scope. But, they are discussed briefly in 3 studies
    - A poster (Atta, 2022) reported the relationship between compliance of using Kurin Lock and the BCC rate
    - An abstract (Baxter, 2020) reported that staff adherence ranged between 70% to 75% during a trial use of Kurin Lock
    - A study reported by poster and abstract (Ostwald 2021a/2021b) reported that 45% of nurse found the device 'easy to use' and 85% found that the device 'made sense'
        - The company and clinical experts stated that Kurin Lock would be straightforward to use and would require minimal training

NICE

For further details on staff adherence and satisfaction see section 6.3.4 of the AR

BCC: blood culture contamination; AR: assessment report

# Clinical evidence: adverse events

- The EAG identified 7 medical device reports relating to 5 events on the MAUDE database where Kurin Lock was mentioned in the event description
    - Events were reported between February 2020 and January 2023
- 3 events had manufacturer responses advising that the issue was not related to Kurin Lock
- 2 events were described as the safety needle not fully retracting after blood culture collection, leading to a risk of needlestick injury
    - The event descriptions state that the manufacturer withdrew the batch of devices and provided replacements
    - The EAG sought clarification from the company who stated that they were unaware of product failures in the UK
- No adverse events were reported in the evidence base and clinical experts were unaware of device malfunctions or safety concerns other than standard risks associated with taking blood culture (e.g. bruising)

NICE

For further details about adverse events see section 7 of the AR

EAG: external assessment group; AR: assessment report; MAUDE: manufacturer and user facility device experience

# Clinical evidence: Ongoing studies

- The EAG did not identify any ongoing studies relevant to the decision problem
- The company stated that they are engaging in talks to introduce Kurin Lock to a number of locations across the NHS

For further details about ongoing studies see section 9 of the AR

NICE



EAG: external assessment group; AR: assessment report

# Clinical evidence: EAG overview and interpretation

- The clinical evidence suggests that Kurin Lock is a safe and effective method of reducing BCC rates
- The EAG considers it reasonable to assume the downstream benefits of reducing false-positive blood culture results, may be achieved with the implementation of Kurin Lock. However it noted a significant gap in the evidence linking Kurin Lock with these secondary benefits such as reduced unnecessary antibiotic use and decreased length of stay
    - Some evidence (Skoglund, 2019) links a reduction in false-positive results with secondary benefits in a similar device
    - 1 clinical expert stated that the secondary benefits of Kurin Lock are reasonable, but acknowledged that this evidence was not collected in the trial that took place in their Trust
- Although most of the evidence is non-peer reviewed, the EAG noted that results from posters and abstracts align with those reported in full-text peer reviewed publications
- Most of the included studies (9 out of 12) were done in US-based secondary care settings, which limits generalisability of the results to an NHS setting because of variations in clinical practice

NICE

For further details about the EAG interpretation of the clinical evidence see section 10 of the AR

BCC: blood culture contamination; EAG: external assessment group

# Clinical perspectives

- 4 clinical experts completed and returned EAQs
- 2 clinical experts stated that Kurin Lock would be used in addition to standard of care and 1 stated that it would replace standard of care if benefits are proven
- Clinical experts noted that minimal training is needed to use Kurin Lock, and no or minimal changes in practice would be needed to implement the technology in the NHS
- Clinical experts noted that Kurin Lock may provide the following benefits:
    - reduce the risk of antibiotic resistance (improve antimicrobial stewardship)
    - increasing the quality of care, having a quicker diagnosis
    - reduce staff time managing results
    - reduce the 'emotional stress' for patients
    - reduce false positive results in certain patient groups therefore reducing the incorrect removal of catheters and indwelling lines as suspected causes of infection, and reduction in complications related to unnecessary intravenous cannulation



EAQ: expert adviser questionnaire

# Issues for consideration: Clinical evidence

## Limited evidence base

- The evidence base consists of 12 studies reported across 14 publications (4 full-texts publications, 5 abstracts and 5 posters)
- Only 4 studies are reported as full-text publications, limiting the EAG's ability to critically appraise them due to lack of methodological detail
- Most of the studies are based in the US with only 3 studies reported as posters  based in the NHS
- Evidence suggests Kurin Lock is a safe and effective method of reducing blood culture contamination rates
- None of the included studies reported length of stay, unnecessary antibiotic use or staff adherence as a formal outcome. So, the impact of Kurin Lock on these outcomes is uncertain
- There is evidence related to a similar device that suggests false positive blood cultures are associated with longer hospital stays and higher costs.

# Cost evidence

Kurin Lock for blood culture collection

NICE National Institute for Health and Care Excellence

# Cost evidence: Summary of economic evidence

- No economic analyses directly related to Kurin Lock were identified by the EAG. But, 8 of the studies included in the clinical evidence reported limited data for costs
    - Allain 2018, Atta 2022, Baxter 2020, Burnie 2021, Ostwald 2021a and 2021b, O'Sullivan 2019, Parsons 2023, Sutton 2018a and 2018b
- Length of stay and unnecessary antibiotic use are not formal outcomes in the evidence reporting on the use of Kurin Lock. So, data for these parameters are taken from other sources, based on false positive tests
- Additional studies identified by the EAG (n=9), and the company (n=11) did not include Kurin Lock but provided relevant information about the costs associated with contaminated blood cultures or economic information for similar devices

For further detail of additional economic studies used see table 11 in the AR

NICE



EAG: external assessment group; AR: assessment report

# Cost evidence: Economic evidence (UK)

| Study (setting) | Comparator | Reduction in bed days | Cost per BCC | Baseline contamination |
|---|---|---|---|---|
| Atta 2022 (UK A&E) | Kurin Lock, before and after | Not reported | *£5,000 assumed | 9% (reduced to 3.1%) |
| Parsons 2023 (UK A&E) | Kurin Lock, before and after | 5 assumed | *£5,000 assumed | 5% (reduced to 2.6%) |

- Both Atta 2022 and Parsons 2023 based their projected cost savings on the results from Alahmadi 2010 which investigated the costs associated with false-positive blood cultures in a general hospital in Northern Ireland between July 2007 to July 2008
- Kurin Lock is not used in this study, but the findings provide evidence to estimate cost savings
    - length of hospital stay difference is 5.4 days [95% confidence interval: 2.8–8.1 days; P < 0.001]
    - total costs difference is £5,001.5 [95% confidence interval: £3,283.9 to £6,719.1; P < 0.001]
- The EAG and experts considered that the £5,000 assumed cost saving may be driven by the 42% population were in ICU (controls were not matched to setting)
    - Patients may be expected to have longer stays and higher daily stay costs in ICU compared to other settings



BCC: blood culture contamination, ICU: intensive care unit

# Cost evidence: Economic evidence (non-UK)

The following clinical studies were before and after studies involving Kurin Lock

| Study (setting) | Reduction in bed days | Cost per BCC | Baseline BCC | Comments |
|---|---|---|---|---|
| Allain 2018 (USA ED) | - | $5,200 assumed | 1.6% | Based on applying cost saving to number of BCC, minus device cost |
| Baxter 2020 (USA ED) | 3.97 extra days per BCC | $4,000 assumed | 4.93% | Based on applying cost saving to number of BCC. Appears not to include device cost |
| Burnie 2021 (USA ED) | 2.65 extra days per BCC | $5,863 per BCC from data | 2.92 – 4.96% | Data collected and analysed over 1 month pre introduction. No cost analysis post introduction |
| Ostwald 2021 (USA Paediatric ED) | - | Mean cost of calling a patient back in and/or admission due to BCC was £1,907 | 0.45 – 5.63% | Data was taken from administrative records |
| O'Sullivan 2019 (USA ED) | - | $5,000 assumed | 1.4 – 2.1% | Costs calculated based on this assumption and including device costs, but method unclear |
| Sutton 2018a Sutton 2018b (USA ED) | - | $7,500 assumed | 2.6% | Reports including cost of equipment, cultures and BCC, no details given |



BCC: blood culture contamination; ED: emergency department

# Cost evidence: Company and EAG model structure

A decision tree was submitted by the company comparing the use of Kurin Lock compared with standard care in an Accident & Emergency setting using a mixed population setting. The EAG stated that this was appropriate. Additional scenarios were provided for general hospital settings and the intensive care unit

**Population: Mixed adult and children in A&E** (85% 12 years and over & 15% under 12 years)*

**Time horizon:** Duration of hospital stay

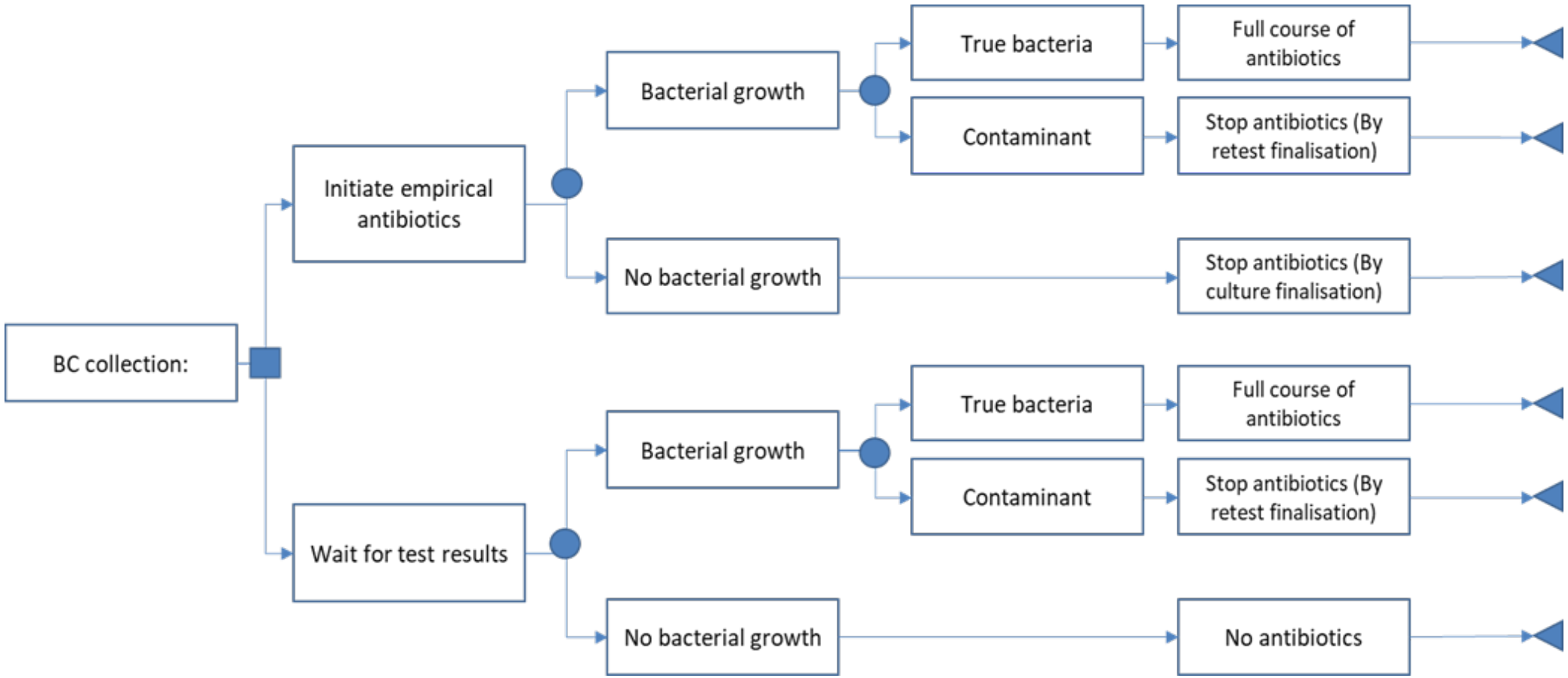
**Discount rate:** Not applicable

* The EAG updated the paediatric population to people who are under 18 years rather than under 12 years old



A&E: accident and emergency; EAG: external assessment group

# Cost evidence: Decision tree model structure




The EAG stated that the company model structure reflected the scope and the clinical pathway appropriately. The structure is the same for blood culture collection by either Kurin Lock or standard care

BC: blood culture; EAG: external assessment group

# Cost evidence: company model overview (1)

- Following blood culture collection, empirical antibiotic treatment is started in a proportion of the population based on clinical suspicion of bacteraemia
- People with an initial positive result undergo further testing of the sample to confirm if the result was a contaminant (false positive) or true infection
- When empirical treatment has been started
    - a negative blood culture confirmation would result in stopping antibiotics for people who have a false-positive (contaminant)
    - a positive blood culture would result in continuing treatment (or starting if not already started)

# Cost evidence: company model overview (2)

- A length of hospital stay is assumed for every person that has a blood culture taken
  - For people with true negative and true positive blood cultures, the length of stay reflects the respective care setting and will be the same in both arms of the model
  - For people with false positive (contaminated) blood cultures, there will be an unnecessary increased length of stay which will be bigger than that of true negative patients and less than that of true positive patients
- Reducing false positive (contaminated) blood cultures, will result in reduced costs by reducing length of stay, unnecessary antibiotic treatment and confirmatory testing

For further details of the company model structure see section 11.2 of the AR

NICE



AR: assessment report

# Cost evidence: Company model assumptions

The EAG agreed with the choice of clinical parameters apart from the choice of antibiotic

- Blood culture collection involves taking  2 blood samples from 2 sites which utilises 2 blood culture collection sets and 4 bottles
- Baseline contamination rate for standard care is 9% in an A&E setting based on UK data (Atta, 2022)
- Reduction of BCC rate for Kurin Lock is 65.5% based on UK data (Atta, 2022)
- Treatment for confirmed or suspected bacteraemia is vancomycin (Skoglund, 2019). The model assumes no adverse effects from vancomycin treatment (Patel, 2022). Despite serum assays being recommended for vancomycin this was conservatively excluded from the company base case
- The economic or resource impact for people that are a false negative is not considered in the model
- The economic or resource impact of hospital acquired infections and associated mortality is not considered within the model
- Underlying baseline bacteraemia risk is 7.4% (Rupp, 2017)

NICE

For further details see table 14 on pages 55 to 56 of the AR

AR: assessment report; BCC: blood culture contamination

# Cost evidence: Additional assumptions identified by EAG

- Company assumption: Blood culture collection only occurs at 1 point for any single patient
  - The EAG noted that patients may require more than 1 set of blood cultures if a false positive or negative is suspected. This would reduce the cost savings of Kurin Lock and is explored in the sensitivity analysis
- Company assumption: All false positive results (contaminated results) would have an impact on treatment
  - The EAG noted that the evidence for Kurin Lock is based on the reduction of false positives (contamination), but there is no direct evidence to suggest that all false positive results have an impact on treatment as consequences may not always be realised
- Company assumption: All patients with a blood culture taken would be admitted from A&E
  - Clinical experts noted that only a small number would not be admitted, and this may result in additional appointments in hospital rather than an increase in length of stay in hospital

NICE

For further details see table 15 in the AR

AR: assessment report; A&E: accident and emergency; EAG: external assessment group

# Cost evidence: Clinical parameters (1)

| Parameters used | Value | Study | EAG changes? | Further details |
|---|---|---|---|---|
| **Bacteraemia and contamination rates** | | | | |
| Baseline risk of bacteraemia | 7.4% | Rupp 2017 (USA) | No | Taken from single centre A&E with 904 patients (1808 samples) |
| Baseline contamination rate for standard of care | 9% | Atta 2022 (UK, A&E) | No | Reported in graph as 8.91%. Experts advised that this may be up to 10% in NHS A&E. Lower values observed in USA studies |
| Reduction of BCC by using Kurin Lock | 65.5% | Atta 2022 (UK, A&E) | No | Reported range of 32.3% to 86.4% in included studies |
| Length of Stay (LOS) | | | | |
| LOS for a patient with a true negative BC in A&E | 5.0 | Skoglund 2019 (USA, ED) | No | The EAG accept this as based in an ED setting although USA based. Alahmadi (2010) reported 8 days LOS for true negative and 13 days for false positive across all settings in a general hospital in Northern Ireland (rather than A&E). 42% of contaminated samples were from ICU which may influence and explain the longer LOS |
| LOS for a patient with a false positive BC in A&E | 7.0 | As above | No | As above |
| LOS for a patient with a true positive BC in A&E | 9.0 | As above | No | As above |

A&E: accident and emergency; BC: blood culture; BCC: blood culture contamination; EAG: external assessment group; ED: emergency department; LOS: length of stay

# Cost evidence: Clinical parameters (2)

| Parameters | Value | Study | EAG changes? | Further details |
|---|---|---|---|---|
| **Antibiotic use** | | | | |
| Probability of starting treatment after a positive BC | 100% | Assumption | No | EAG and experts accept this is a reasonable assumption |
| Probability of starting antibiotic prior to receiving BC results | 71% | Skoglund 2019 (USA, ED) | No | For people who have a BC taken, 71% will be given antibiotics at the same time point. Expert opinion stated that this may be up to 90% in an NHS setting. |
| Days of treatment given for a true negative patient in A&E | 3.0 | As above | No | The experts stated that some initial results may be received from 24 hours, but cultures would continue until 5 days for certainty. |
| Days of treatment given to a false positive (contaminated) patient in A&E | 4.0 | As above | No | The EAG accepted this is reasonable given the comment above |
| Days of treatment given to a true positive (bacteraemia) patient in A&E | 10.0 | As above | No | Same as above |



A&E: accident and emergency; BC: blood culture; EAG: external assessment group; ED: emergency department

# Cost evidence: Cost and resource parameters summary

- The daily hospital costs in the company base (£844 for adults and £1,092 for children) case is for A&E and uses a daily cost of a short stay that is derived from patient level data for 1 NHS Trust. The EAG considered the costs to be high compared to similar economic models
- The EAG used an alternative approach to calculate hospital stay costs. A non-elective short stay cost was applied for the first day of admission. For subsequent days of admission excess stay costs were calculated. This is in line with approaches used previously in NICE assessment reports
    - The EAG chose Healthcare Resource Groups that included sepsis with no intervention, or single or multiple interventions with, or without complications, or fever of unknown origin
    - There were no changes to clinical parameters therefore LOS was identical in both models

For further details see table 17 in the AR



A&E: accident and emergency; AR: assessment report; EAG: external assessment group; LOS: length of stay

# Cost evidence: Cost and resource parameters (1)

| | First day cost | Excess day cost | Source | Total cost over 5.36[d] days (base case) |
|---|---|---|---|---|
| Company (adult) | £844 | £844 | 2020-21 National Cost Collection PLICS data | |
| EAG (adult) | £970[a] | £329[b] | [a] 2019-2020 PSSRU & [b] 2017-2018 PSSRU - inflated to 2021/2022 | |
| Company (child) | £1,092 | £1,092 | 2021-22 National Cost Collection TFC | |
| EAG (child) | £1,150[a] | £585[b] | [a] 2019-2020 PSSRU & [b] 2017-2018 PSSRU - inflated to 2021/2022 | |
| Company ([c] base case population) | £881 | £881 | These are the weighted values used for the base case | **£4,716** |
| EAG ([c] base case population) | £1,044 | £377 | These are the weighted values used for the base case | **£2,647** |

[a] This is the EAG value for initial admission. This year was used to avoid any impact of Covid-19; [b] This is the EAG value for additional days. This year was the last point this cost was reported; [c] The base case population comprises of 85% adults and 15% children; [d] The length of stay is slightly under 5.36 therefore calculated costs may differ slightly



EAG: external assessment group

# Cost evidence: Cost and resource parameters (3)

| Parameter | Company value | EAG value | Source | Comments |
|---|---|---|---|---|
| Kurin Lock | £19.50 | £19.50 | Company | |
| Standard of Care | £1.50 | £0.48 | NICE MIB | EAG value from NHS supply chain 2023 |
| Number of blood cultures per patient | 2 | 2 | | The EAG have considered the possibility of 50% with a positive blood culture having an additional test in sensitivity |
| Collection and process of blood culture | £15.66 | £13.04 | 2020-21 National Cost Collection Direct Access Pathology | EAG value from 2021-222 National Cost Collection Direct Access Pathology. These costs comprise of microbiology, biochemistry and haematology test. A second processing cost is applied to all positive BC to confirm true positives |
| Vancomycin (cost per vial) | £11.25 | N/A | BNF 2023 | Alternative treatment regimen is considered for the EAG model based on clinical expert advice |
| Gentamycin (cost per vial) | N/A | £1.20 | BNF 2023 | Alternative treatment regimen is considered for the EAG model based on clinical expert advice |
| Cost per day per patient treated | £35.99 | £6.52 | | The cost difference is due to the selection of different antibiotic regimens (see above) |

EAG: external assessment group

# Cost evidence: Base case results

| Costs | Company results | | | EAG results | | |
|---|---|---|---|---|---|---|
| | Kurin Lock | Comparator | Cost saving per person | Kurin Lock | Comparator | Cost saving per patient |
| Device | £39 | £3 | -£36 | £39 | £1 | -£38 |
| BC processing | £16 | £16 | £0 | £13 | £13 | £0 |
| Confirmation tests | £2 | £3 | £1 | £1 | £2 | £1 |
| Antibiotics | £100 | £104 | £4 | £18 | £19 | £1 |
| Length of stay | £4,716 | £4,820 | £104 | £2,647 | £2,692 | £44 |
| Total | **£4,872** | **£4,945** | **£73** | **£2,719** | **£2,727** | **£8** |
| Avoided events | | | | | | |
| False positives | 0.03 | 0.09 | 0.06 | 0.03 | 0.09 | 0.06 |
| Days of antibiotics | 2.77 | 2.88 | 0.11 | 2.77 | 2.88 | 0.11 |
| Bed days | 5.36 | 5.48 | 0.12 | 5.36 | 5.48 | 0.12 |

- The EAG model has a cost saving of £8 rather than £73 in the company model
- This is due to the significant impact of the lower hospital stay cost used in the EAG model



BC: blood culture; EAG: external assessment group

# Cost evidence: Additional analyses

- One-way sensitivity analysis done by the EAG showed the length and cost of stay, rate of BCC at baseline and the reduction due to Kurin Lock all have the potential to mean Kurin Lock is cost incurring, or cost neutral
- Two-way SA tables compare baseline contamination with reduction in contamination by using Kurin Lock (the effectiveness of Kurin Lock), the difference in length of stay between people that have true negative and false positive BC results, and the cost of an additional day in hospital
- The company submitted scenario analysis which were updated by the EAG
    - For adult and paediatric populations (this changed the treatment dose and cost, and the daily cost of hospital stay)
    - Alternative settings in intensive care unit (ICU) and general hospital (this changed the baseline contamination rate, length of stay, duration of antibiotics and a higher daily hospitalisation cost for people in ICU



BC: blood culture; BCC: blood culture contamination; EAG: external assessment group; SA: sensitivity analysis

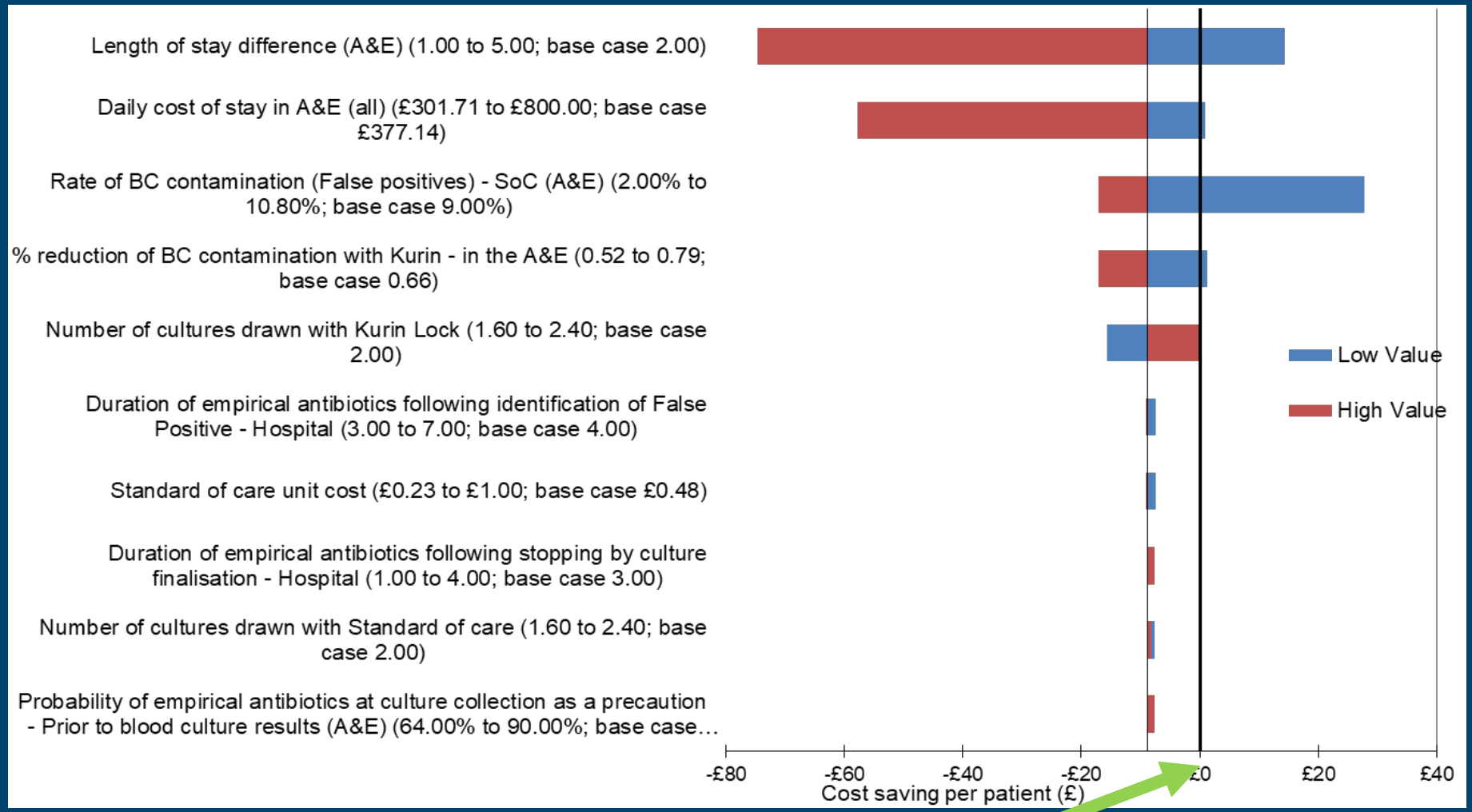
# Cost evidence: Sensitivity analysis results

- The EAG re-ran the one-way sensitivity analysis and probabilistic sensitivity analysis (PSA) for the EAG base case, and used an increased 20% variation for all PSA variables and those one-way variables that were not determined separately
- One-way sensitivity analysis using the reduced cost saving in the EAG base case and the 10% variation included in the company submission, length of stay is the only variable resulting in Kurin Lock becoming cost incurring
- EAG adjustments to sensitivity ranges results in more uncertainty in the results
    - The length and cost of stay, rate of BCC at baseline and reduction in rate of BCC by Kurin Lock all have the potential to make Kurin Lock is cost incurring or cost neutral



BCC: blood culture contamination; EAG: external assessment group

# Cost evidence: One-way sensitivity analysis




NICE Anything to the right hand side of this line indicates Kurin Lock is cost incurring

# Cost evidence: Two-way and probabilistic sensitivity analysis

- The probabilistic sensitivity analysis (PSA) using a 20% variance on the EAG base case showed a 62% probability of Kurin Lock being cost saving which indicates uncertainty on the cost saving potential of Kurin Lock
- The results from the two-way sensitivity analysis can be generalised as;
    - Baseline contamination rates of less than 3%, there is low probability of Kurin Lock being cost-saving whilst contamination rates of more than 9% have a high probability of Kurin Lock being cost-saving. For baseline contamination rates in between there is less certainty, although a break-even point of around 7% is expected
    - Kurin Lock is more likely to be cost saving when the daily cost of hospital stay is higher, the reduction of contamination with Kurin Lock is higher and when there is greater reduction in hospital stay between true negative and false positive results
- The ICU setting shows a higher cost saving per person (despite there being a lower baseline contamination rate). This is driven by the much higher daily costs incurred in ICU



EAG: external assessment group; ICU: intensive care unit

# Cost evidence: Two-way sensitivity analysis

| Daily cost of hospital stay | Baseline risk of BC contamination with SoC (ED | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 3% | 4% | 5% | 6% | 7% | 8% | 9% | 10% |
| £200 | -£30 | -£27 | -£24 | -£21 | -£18 | -£16 | -£13 | -£10 |
| £300 | -£26 | -£22 | -£18 | -£13 | -£9 | -£5 | -£1 | £3 |
| £400 | -£22 | -£16 | -£11 | -£6 | £0 | £5 | £11 | £16 |
| £500 | -£18 | -£11 | -£4 | £2 | £9 | £16 | £22 | £29 |
| £600 | -£14 | -£6 | £2 | £10 | £18 | £26 | £34 | £42 |
| £700 | -£10 | -£1 | £9 | £18 | £27 | £37 | £46 | £55 |
| £800 | -£6 | £5 | £15 | £26 | £36 | £47 | £58 | £69 |
| £900 | -£2 | £10 | £22 | £34 | £46 | £58 | £70 | £82 |
| £1,000 | £2 | £15 | £28 | £42 | £55 | £68 | £81 | £95 |

| Reduction in days in hospital between true negative and false positive results | Baseline risk of BC contamination with SoC (ED) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | £8 | 3% | 4% | 5% | 6% | 7% | 8% | 9% | 10% |
| 1.0 | -£30 | -£28 | -£25 | -£22 | -£20 | -£17 | -£14 | -£12 |
| 1.5 | -£26 | -£23 | -£19 | -£15 | -£11 | -£7 | -£3 | £1 |
| 2.0 | -£23 | -£18 | -£13 | -£7 | -£2 | £3 | £8 | £13 |
| 2.5 | -£19 | -£13 | -£6 | £0 | £6 | £13 | £19 | £25 |
| 3.0 | -£15 | -£8 | £0 | £7 | £15 | £23 | £30 | £38 |
| 3.5 | -£12 | -£3 | £6 | £15 | £24 | £32 | £41 | £50 |
| 4.0 | -£8 | £2 | £12 | £22 | £32 | £42 | £52 | £62 |
| 5.0 | £0 | £12 | £25 | £37 | £50 | £62 | £75 | £87 |
| 6.0 | £7 | £22 | £37 | £52 | £67 | £82 | £97 | £112 |

| % reduction of BC contamination with Kurin | Baseline risk of BC contamination with SoC (ED) | | | | | |
|---|---|---|---|---|---|---|
| | 5% | 6% | 7% | 8% | 9% | 10% |
| 10.0% | -£34 | -£33 | -£33 | -£32 | -£31 | -£30 |
| 20.0% | -£30 | -£29 | -£27 | -£26 | -£24 | -£22 |
| 30.0% | -£26 | -£24 | -£22 | -£19 | -£17 | -£15 |
| 40.0% | -£22 | -£19 | -£16 | -£13 | -£10 | -£7 |
| 50.0% | -£19 | -£15 | -£11 | -£7 | -£3 | £1 |
| 60.0% | -£15 | -£10 | -£5 | -£1 | £4 | £9 |
| 65.5% | -£13 | -£7 | -£2 | £3 | £8 | £13 |
| 70.0% | -£11 | -£5 | £0 | £6 | £11 | £17 |
| 80.0% | -£7 | -£1 | £6 | £12 | £18 | £24 |
| 90.0% | -£3 | £4 | £11 | £18 | £25 | £32 |
| 100.0% | £1 | £9 | £17 | £24 | £32 | £40 |

- Where the text is green, this indicates Kurin Lock is cost saving, whilst red is cost incurring
- The circled text highlights the values used for the base case scenario

For further details about see section 11.3 of the AR



AR: assessment report; BC: blood culture; ED: emergency department; SoC: standard of care

# EAG changes to model and their impact

- The key drivers are length of hospital stay, daily cost of hospital stay, the baseline BCC rate and the reduction in BCC due to Kurin Lock
- The main driver for the model is the length of stay difference and the associated stay cost
    - The lower daily stay cost in A&E and hospital setting weighted at £377 per day has the most significant impact on the results as this leads to a large reduction in cost saving for Kurin Lock
- Other changes to the model have a small or negligible impact on the cost saving of Kurin Lock including
    - Change of antibiotic regimen (very small reduction in cost saving)
    - Reduction of blood culture processing cost (negligible reduction in cost saving)
    - Reduction of comparator costs (small reduction in cost saving)
    - Change to adult/paediatric weighting to reflect NHS cost collection definition of paediatric as 18 or under
    - Reduction in ICU daily cost (small reduction in the ICU scenario only)

For further details see table 15 in the AR



A&E: accident and emergency; AR: assessment report; BCC: blood culture contamination; ICU: intensive care unit

# Issues for consideration: Economic considerations

## Uncertainty in the cost savings

- The base case results and sensitivity analysis indicate there is uncertainty around whether Kurin Lock is cost saving or cost incurring
    - As the unit cost of Kurin Lock compared to the standard of care is high, there's a high potential resource impact
- The lack of clinical outcomes data for Kurin Lock means the economic model is built on resource consequences from other studies exploring the impact of a false positive result
    - The length of stay cost and the reduction of length of stay by using Kurin Lock are the key drivers of the model results. There is no data for the reduction in the length of stay or change in antibiotic use for Kurin Lock.
    - Where there is a higher hospital stay cost (such as in ICU), or a greater reduction in hospital stay using Kurin Lock, the more likely that Kurin Lock is cost saving

# Issues for consideration: Clinical evidence

## Limited evidence base

- The evidence base consists of 12 studies reported across 14 publications (4 full-texts publications, 5 abstracts and 5 posters)
- Only 4 studies are reported as full-text publications, limiting the EAG's ability to critically appraise them due to lack of methodological detail
- Most of the studies are based in the US with only 3 studies reported as posters  based in the NHS.
- Evidence suggests Kurin Lock is a safe and effective method of reducing blood culture contamination rates
- None of the included studies reported length of stay, unnecessary antibiotic use or staff adherence as a formal outcome. So, the impact of Kurin Lock on these outcomes is uncertain
- There is evidence related to a similar device that suggests false positive blood cultures are associated with longer hospital stays and higher costs.

NICE National Institute for Health and Care Excellence

# Thank you.

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Medical technology guidance scope

# Kurin Lock for reducing blood culture contamination

# Final scope

## 1 Technology

### 1.1 Description of the technology

Kurin Lock (Kurin Inc.) is a device for collecting blood that is then cultured to check for the presence of infections. The Kurin blood culture collection set includes a vasculature connection (a butterfly needle for venepuncture or luer connection to a peripheral catheter), flexible tubing, Kurin Lock, and blood culture bottle holder. The Kurin Lock is a u-shaped chamber that collects, isolates and shows the first 0.15 ml of blood. After separating the initial blood sample, Kurin Lock automatically sends the blood through the tube into the culture collection bottle.

### 1.2 Relevant diseases and conditions

The Kurin Lock is intended for collecting blood samples for culture tests. Blood culture is a laboratory test to detect infections when people show signs or symptoms of a systemic infection such as sepsis.

Infections place a huge strain on the health system. Emergency departments often provide the initial management and investigations for people who present with suspected infections to hospitals. About 40% of emergency admissions are due to bacterial infections, and 33% of patients admitted to hospitals are on antibiotics at any one time. Infections also account for 66% of all hospital deaths and 50% of all bed days. In the UK, 100,000 bloodstream infections are found every year. (NHS England, 2022).

Blood culture is the primary diagnostic procedure to find bloodstream infections. It identifies the type of pathogens that cause infections and informs antimicrobial treatments. During collection, blood samples can be contaminated. Blood cultures contaminated with skin commensals or other non-pathogenic bacteria provide false positive results, resulting in people having unnecessary treatments such as antibiotics. The American Society for Microbiology (ASM) and the Clinical Laboratory Standards Institute (CLSI) recommend no more than a 2 to 3% contamination rate. In the UK blood culture contamination rates have been reported to range from 5% (Bentley et al. 2016) to 7% (Raja et al. 2009).

Blood culture contamination or false positive blood culture results complicate interpretation and can have detrimental effects on the patient and health service. For example, people may have unnecessary treatments and may have to extend their hospital stays. Additional financial burdens include laboratory testing costs on health services (Alahmadi et al. 2011).

The company notes that over 3 million blood cultures are done every year in the NHS for testing causes of blood stream infections.

## 1.3 Current management

The standard way to collect a blood sample for culture involves putting a tight band (tourniquet) around a person's arm. The needle injection site is cleaned with an antiseptic, for example, 2% w/v chlorhexidine gluconate in 70% isopropyl alcohol. The needle is then inserted, and the blood is drawn directly into blood culture collection bottles. At least 2 blood culture sets should be obtained within a few hours of each other to optimise the detection of pathogens. NHS England has recently published a report on improving and standardising a pre-analytical phase of the blood culture pathway across the NHS. The standardisation of practice will help reduce variations in service delivery to improve antimicrobial stewardship and patient outcomes.

UK Standards for Microbiology Investigations notes that several criteria are used when determining the clinical relevance of a positive result and when deciding whether a sample is contaminated or indeed has bacteraemia. These

include the identity of the organism, the number of positive sets, the number of positive bottles within a set, the quantity of growth, and clinical and laboratory data (including the source of culture). Some measures such as appropriate skin and bottle preparation, obtaining cultures from peripheral venepuncture instead of vascular catheters, and training can minimise the risk of contamination.

The following guidelines have been identified as relevant to this care pathway:

- NICE guideline on sepsis: recognition, diagnosis and early management
- NICE guideline on healthcare-associated infections: prevention and control in primary and community care
- NICE guideline on healthcare-associated infections: prevention and control
- ANTT clinical guideline on blood culture collection

## 1.4 Regulatory status

Kurin Lock is a CE marked class IIa medical device.

## 1.5 Claimed benefits

The benefits to patients claimed by the company are:

- Improved rates of detection of people with blood stream infections (BSI)
- Reduced rates of false positive blood culture because blood samples are unlikely to be contaminated by skin organisms around injection sites
- Reduced use of unneeded antibiotic treatment
- Reduced unnecessary further interventions such as laboratory tests to rule out suspected bacteraemia
- Avoiding treatment delays
- Reduced length of hospital stay

The benefits to the healthcare system claimed by the company are:

- Reduced blood culture contamination rates

- Improved patient management using appropriate use of antibiotics
- Improved efficiency in the use of resources such as staff and laboratory tests
- Reduced risk of hospital-acquired infections and associated costs and resource use associated with management.

# 2 Decision problem

| | |
|---|---|
| Population | People who need a blood culture test within a secondary care setting |
| Subgroups | • People who present with signs or symptoms of infection<br>• People at increased risk of infections such as those who are immunocompromised<br>• People in whom sampling blood can be challenging for example intravenous drug users or children |
| Intervention | Kurin blood culture collection including Kurin Lock |
| Comparator(s) | Standard blood culture collection (tubes and container) |
| Outcomes | The outcome measures to consider include:<br>• Blood culture contamination rate<br>• Positive and negative predictive values<br>• Rates of antimicrobial prescriptions<br>• Use of unneeded antibiotic treatment<br>• Unnecessary further interventions such as laboratory tests to rule out suspected bacteraemia<br>• Treatment delays<br>• Length of hospital stay<br>• Rates of hospital acquired infection<br>• Patient-reported outcome measures such as health related quality of life<br>• Patient-reported experience measures<br>• Device-related adverse events. |
| Economic analysis | A health economic decision model will be developed comprising a cost-comparison analysis.<br>The time horizon should be long enough to reflect all important differences in costs or outcomes between the technologies being compared.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>Sensitivity analysis and appropriate scenario analysis should be undertaken to address the relative effect of parameter or structural uncertainty on the cost-comparison estimates. |
| .Other considerations | No |

| | |
|---|---|
| Special considerations, specifically related to equality | Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic? No |
| | Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality? No |
| | Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance? No |
| Any other special considerations | Not applicable |

# 3 Stakeholders

## 3.1 Healthcare professional organisations

The following healthcare professional organisations have been invited to register as stakeholders for this guidance development:

- Association for Clinical Biochemistry and Laboratory Medicine
- Academy of Medical Sciences
- The Association of Clinical Microbiologists and Biochemists (ACMB)
- Academy of Medical Royal Colleges
- Association for Paediatric Emergency Medicine
- Association of Clinical Pathologists
- Association of Clinical Scientists
- British Association of Emergency Medicine
- British infection association
- British Trauma Society
- British Association of Critical Care Nurses
- Healthcare Infection Society
- Infection Prevention Society
- Institute of Biomedical Science
- Intensive care society
- Neuro-Anaesthesia and Critical Care Society of Great Britain and Ireland
- NHS Blood and Transplant

- Paediatric Intensive Care Society
- Royal College of Emergency Medicine
- Royal College of General Practitioners
- Royal College of Nursing
- Royal Society for Public Health (RSPH)
- Society for Acute Medicine
- Society for General Microbiology
- The UK sepsis trust

## 3.2 Patient and carer organisations

NICE's Public Involvement Programme contacted the following patient and carer organisations and invited them to register as stakeholders for this guidance development:

- Action Cancer - NI
- African Caribbean Leukaemia Trust (ACLT)
- Anthony Nolan
- Blood Cancer UK
- BME cancer communities
- Cancer Black Care
- Cancer Research UK
- Cancer Support UK
- Cancer52
- Children's Cancer and Leukaemia Group
- Chronic Lymphocytic Leukaemia Support Association (CLLSA)
- Chronic Myeloid Leukaemia Support Group (CML Support)
- Critical Care Patient Liaison Committee
- Diabetes Research & Wellness Foundation
- Diabetes UK
- DKMS
- DWIB Leukaemia Trust
- Follicular Lymphoma Foundation
- Foot in Diabetes UK (FDUK)

- Friends of the Cancer Centre (NI)
- Helen Rollason Cancer Charity
- ICU Steps
- Independent Cancer Patients' Voice
- InDependent Diabetes Trust
- Juvenile Diabetes Research Foundation (JDRF)
- Leukaemia Cancer Society
- Leukaemia Care
- Leukaemia UK
- Lymphoedema support network
- Lymphoma Action
- Macmillan Cancer Support
- Maggie's Centres
- MDS UK Patient Support Group
- MPN Voice
- Myeloma UK
- Penny Brohn Cancer Care
- Pernicious Anaemia Society (PAS)
- Primary Sclerosing Cholangitis Support (PSC Support)
- Sickle Cell Society
- The Aplastic Anaemia Trust (AAT)
- The Haemophilia Society
- The ITP Support Association
- The Rik Basra Leukaemia Campaign
- Trauma Care
- Tenovus Cancer Care
- UK Thalassaemia Society
- WMUK
- World Cancer Research Fund (WCRF UK)
- XLH UK

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

# Medical technologies guidance

# GID-MT582 Kurin Lock

# Company evidence submission

**Company name: ISKUS HEALTH UK LTD**

**Submission date:** 06-06-2023

**Regulatory documents attached:**

All regulatory documents are listed below and attached

1_GMED_EC Certificate, II.3_35591-1_exp052624

2_Declaration of Conformity, TF-01, Rev 2_030620

3_IFU 920 KUR-4000_F_EU-IFU_DFT3.1

6_MHRA_UK Certificate of Verification_Kurin

**Contains confidential information:** No

## Instructions for companies

This is the template for submission of evidence to NICE as part of the medical technologies evaluations process. Note that the information requirements for evidence submissions are summarised in this template; **full details of the requirements are in the user guide for company evidence submissions**

Please keep evidence submissions (including any supporting evidence) as succinct as possible by avoiding unnecessary repetition and keeping text relevant and focussed. If it is too long it will not be accepted.

Companies making evidence submissions to NICE should also refer to NICE health technology evaluations: the manual.



# Contents





# 1 Decision problem, the technology and clinical context

## 1.1 Decision problem

**Table 1: The decision problem**

| Part of decision problem | Scope issued by NICE | Variation from scope (if applicable) | Rationale for variation |
|---|---|---|---|
| **Population** | People who need a blood culture test within a secondary care setting | People who need a blood culture | Whilst the vast majority of blood cultures are taken in the secondary care setting with more patients being managed and treated in the community, this may not always be the case. Therefore, it is applicable to any patient who may require a blood culture to be taken dependent on their clinical presentation. |
| **Subgroups to be considered** | • People who present with signs or symptoms of infection<br>• People at increased risk of infections such as those who are immunocompromised<br>• People in whom sampling blood can be challenging for example intravenous drug users or children. | Blood cultures are taken to identify patients with bacteraemia. There are many signs and symptoms in a patient which may suggest bacteraemia and clinical judgement is required,<br>but the following indicators should be taken into account when assessing a patient for signs of bacteraemia or sepsis:<br>• core temperature out of normal range;<br>• focal signs of infection;<br>• abnormal heart rate (raised), blood pressure (low or | Improved clarification of why a clinician will have a blood culture taken on a patient. |

| Part of decision problem | Scope issued by NICE | Variation from scope (if applicable) | Rationale for variation |
|---|---|---|---|
| | | raised) or respiratory rate (raised);<br>• chills or rigors;<br>• raised or very low white blood cell count; and<br>• new or worsening confusion.<br>• Could it be Sepsis? | |
| **Intervention** | Kurin blood culture collection including Kurin Lock | Kurin® Blood Culture Collection Set with Kurin Lock® Technology | Clarification of exact terms. |
| **Comparator(s)** | Standard blood culture collection (tubes and container) | Standard blood culture collection methods including standard winged butterfly sets with tubes and adaptor caps (closed system). Also, standard safety needle and syringe method (open system) for collecting a blood culture is common practice. | Clarification of variation in methods of blood culture collection. |
| **Outcomes** | The outcome measures to consider include:<br>• Blood culture contamination rate<br>• Positive and negative predictive values<br>• Rates of antimicrobial prescriptions<br>• Use of unneeded antibiotic treatment<br>• Unnecessary further interventions such as laboratory tests to rule out suspected bacteraemia<br>• Treatment delays<br>• Length of hospital stay | All of these are relevant, but for clarification the main outcome is by significantly lowering the rates of contaminated blood cultures clinicians improve the clinical value and accuracy of blood cultures. Essential the diagnostic value is more accurate, and therefore the knock-on consequences to the patient and healthcare system as detailed are avoided. | Clarification of the outcomes being measured and assessed. |

| Part of decision problem | Scope issued by NICE | Variation from scope (if applicable) | Rationale for variation |
|---|---|---|---|
| | • Rates of hospital-acquired infection<br>• Patient-reported outcome measures such as health-related quality of life<br>• Patient-reported experience measures<br>• Device-related adverse events | | |
| **Economic analysis** | A health economic decision model will be developed comprising a cost-comparison analysis.<br>The time horizon should be long enough to reflect all important differences in costs or outcomes between the technologies being compared.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>Sensitivity analysis and appropriate scenario analysis should be undertaken to address the relative effect of parameter or structural uncertainty on the cost-comparison estimates. | Enter text. | Enter text. |
| **Other considerations, including issues related to equality** | No | Enter text. | Enter text. |

## 1.2 The technology

*Give the brand name, approved name and details of any different versions of the same device (including future versions in development and due to launch). Provide links to (or send copies of) the instructions for use for each version of the device.*

**Brand name:** Kurin®

**Approved name:** Kurin® Blood Culture Collection Set with Kurin Lock® Technology

**Any alternative names for technology (e.g. in the literature):** Blood culture collection division device

**UKCA/CE-mark class and date of authorisation:** Class IIA and Class 1A – 10th April 2020

**Indications and any restriction(s) as described in the labelling or instructions for use (IFU):**

**INDICATIONS FOR USE:** The Kurin Blood Culture Collection Set is intended to obtain blood samples through the patient's vasculature via venepuncture or Peripheral IV (PIV) access. As it enters the Kurin Lock, blood initially fills a side channel then flows into the sample collection device (syringe or bottle) via an adjoining sampling channel to reduce blood culture contamination rates[1].

When supplied with a pressured-rated extension set, the pressured-rated extension set is intended to be utilized separately with infusions systems to administer IV fluids, medications, blood and blood products into the patient's vascular system and may be safely used with power injectors at pressures up to 325 psi.

**CONTRAINDICATIONS:** The Kurin Blood Culture Collection Set is to be used for blood collection only. It is not to be used for infusion, IV administration, or transfusion except when supplied with a pressured-rated extension set and the pressure-rated extension set is detached and used separately.

[1] The Kurin Blood Collection System is for use as a blood collection system and its Kurin Lock allows the specimen of blood from the patient to be sidelined prior to the collection of the test sample to reduce the frequency of blood culture contamination when contaminates are present in the initial blood sample compared to blood cultures drawn using standard practice without the Kurin Lock.

**INSTRUCTIONS FOR USE**

1. Visually inspect the device and packaging to confirm there is no damage (device is not cracked or broken). If the packaging appears to be damaged (punctured, torn) do not use the device.
2. Remove device from its packaging.
3. Ensure that the blood culture bottle holder, when supplied, and other connections are secure before use. If needed, remove the holder by twisting and pulling the holder to collect the blood specimen using a syringe.
4. Vasculature Access

   4.1 FOR VENEPUNCTURE SETS:

   Remove needle cover. Perform disinfection and venepuncture per hospital protocol.

   *Caution: Care should be taken to avoid touching the needle.*

   4.2 FOR PERIPHERAL IV (PIV) SETS:

   Perform disinfection and catheter access per hospital protocol. Attach the set's luer connector to the freshly placed short peripheral catheter.
5. Observe the flow of blood into the Kurin Lock side channel. Once blood flow has stopped, the set is ready for blood sample acquisition.

   *Caution: Do NOT connect the collection vial or culture bottle to the blood culture bottle holder before flow has stopped.*
6. Perform blood collection using collection vials or culture bottle per hospital protocol. For blood culture bottle holders that include an insert, it can be removed, if necessary, by grasping the outside of the holder with one hand and pulling on the upper rim with the other hand. The insert will separate from the holder.

   *Caution: Avoid touching the sampling needle in the blood culture bottle holder.*
7. Completion of Sample Acquisition

   7.1 FOR STANDARD NEEDLE SETS:

   Withdraw the patient needle by grasping the translucent safety shield grip area with the thumb and index finger.

   With opposite hand, grasp tubing between thumb and index finger while pushing the safety shield forward until a click is heard indicating the needle is completely retracted and the safety shield is locked in place.

   7.2 FOR PUSH BUTTON NEEDLE SETS:

   Depress the button. The needle will slide out of the venepuncture site and lock into place (Do not impede device retraction).

   7.3 FOR PERIPHERAL IV (PIV) SETS WITH PRESSURED-RATED EXTENSION SET:

Clamp the extension line with the slide clamp, disconnect the blood culture collection set from the extension set, and then proceed with the setup of the IV line per hospital protocol. Completely prime the extension set by connecting to a primed IV administration set or syringe. Flush the device after each use with flushing syringe.

Replace the IV line per hospital protocol.

8. After use, dispose of set per hospital protocol.
9. Per hospital protocol, use the provided package lid form to track collections.

A List of the different versions of the Kurin device are presented in Table 2.

**Table 2: Different versions of the same device**

| Item code | Item description & features | UK launch date |
|---|---|---|
| D11221 | KURIN w BD VACUTAINER & SAFETY SLIDE NEEDLE 21G | January 2021 |
| D11223 | KURIN w BD VACUTAINER & SAFETY SLIDE NEEDLE 23G | January 2021 |
| D21221 | KURIN w BD VACUTAINER PUSH BUTTON NEEDLE 21G | January 2021 |
| D21223 | KURIN w BD VACUTAINER PUSH BUTTON NEEDLE 23G | January 2021 |
| DPIV12 | KURIN w BD VACUTAINER PERIPHERAL IV LUER CONNECT | January 2021 |
| DPIV18 | KURIN w BD VACUTAINER PERIPHIERAL IV LUER CONNECT w6" EXTENSION TUBE | January 2021 |
| M11221 | KURIN w BIOM VACUTAINER & SAFETY SLIDE NEEDLE 21G | January 2021 |
| M11223 | KURIN w BIOM VACUTAINER & SAFETY SLIDE NEEDLE 23G | January 2021 |
| M21221 | KURIN w BIOM VACUTAINER PUSH BUTTON NEEDLE 21G | January 2021 |
| M21223 | KURIN w BIOM VACUTAINER PUSH BUTTON NEEDLE 23G | January 2021 |
| MPIV12 | KURIN w BIOM VACUTAINER PERIPHERAL IV LUER CONNECT | January 2021 |
| MPIV18 | KURIN w BIOM VACUTAINER PERIPHIERAL IV LUER CONNECT w6" EXTENSION TUBE | January 2021 |
| S-PIV10 | KURIN, 10" EXTENSION SET DUAL IV LUER CONNECT FOR LOW VOLUME BLOOD DRAWS | January 2021 |
| S-PIV4 | KURIN, 4" WITH DUAL IV LUER CONNECT FOR LOW VOLUME BLOOD DRAWS | January 2021 |

Kurin has multiple product configurations which allow compatibility with the different blood culture bottle manufacturers and varying collection methods, as presented in Figure 1.

**Figure 1: Multiple product configurations of Kurin**

Kurin for Venepuncture

BD Bactec® and Thermo Fisher
VersaTREK® REDOX™ EZ DRAW™

| | 21 GAUGE | 23 GAUGE |
|---|---|---|
| Safety Slide | D-11221 | D-11223 |
| Push Button | D-21221 | D-21223 |

bioMérieux
BacT/Alert®

| | 21 GAUGE | 23 GAUGE |
|---|---|---|
| Safety Slide | M-11221 | M-11223 |
| Push Button | M-21221 | M-21223 |

BD

bioMerieux

Kurin for Peripheral IV Collection

| | BD BACTEC® & THERMO FISHER VERSATREK® EZ DRAW® | BIOMÉRIEUX BACT/ALERT® |
|---|---|---|
| 12-inch set | D-PIV12 | M-PIV12 |
| 12-inch set + 6-inch extension | D-PIV18 | M-PIV18 |

BD

bioMerieux

Kurin for Low Volume Blood Draws with a syringe

| OPTIONS | CATALOG NUMBER |
| --- | --- |
| 4-inch set | S-PIV4 |
| 4-inch set + 6-inch extension | S-PIV10 |

Abbreviations: IV, intravenous.

*What are the key claimed benefits of using the technology for patients and the NHS?*

Key claimed benefits of using the technology for patients and the NHS are presented in Table 3.

**Table 3: Key benefits of Kurin for patients and the NHS**

| Type of benefit | Description of benefit<br>The benefits to patients claimed by the company are: | Supporting evidence | Rationale |
|---|---|---|---|
| **Patient** | Improved rates of detection of people with BSIs | Skoglund et al., 2019<br><br>CDC, 2023<br><br>CLSI, 2007<br><br>Bentley et al<br><br>Nannan et al. | Blood culture is considered the 'gold standard' method of investigation for the detection of microorganisms in the blood that lead to the diagnosis of serious infections. However, blood cultures continue to be a source of frustration to clinicians and microbiologists and a burden to health care systems due to erroneous results caused by contaminated samples. The universally "acceptable" BCC rate is currently quoted as 3%.[1] However, the CDC and Clinical Laboratory Standard Institute have identified the feasibility, and pursuit of 1%. Studies from both North America and Europe illustrate widely varying contamination rates between institutions, from as little as 0.6% to >10%.[2] For a blood culture test to be revered as the 'gold standard' it needs to be upheld as having the lowest possible error rate and negative effects on both patients and hospitals.<br>Essentially, the diagnostic value is more accurate by the avoidance of contaminated blood cultures, and therefore the knock-on consequences to the patient and healthcare system as detailed are avoided, which includes improving BSI diagnostic accuracy.<br>'The investigators further demonstrated that the observed prevalence of true bacteraemia was not affected by use of the ISDD (7.2%) compared with conventional techniques (7.6%, p=0.41)'. |
| **Patient** | Reduced rates of false positive blood culture because blood samples are unlikely to be contaminated by skin organisms around injection sites | Doern GV et al. (2020)<br><br>All References detailed in section: 2.2 Table1.<br><br>Hodson et al (Sept 2022)<br><br>Atta M, Mcguire R. (April 2022).<br><br>Parson K & Webb D (2023). | The principal source of contaminants is commensal bacteria that colonise the skin. Primarily coagulase-negative staphylococci.[3]<br>Kurin is proven to significantly reduce the rates of contaminated blood cultures (false positives) as captured in the supporting references by its mechanism of action in side-lining the first 0.15 ml of blood where potential skin contaminants may reside. |

| Type of benefit | Description of benefit<br>The benefits to patients claimed by the company are: | Supporting evidence | Rationale |
|---|---|---|---|
| **Patient** | Reduced use of unneeded antibiotic treatment | NHS England B0686-improving-the-blood-culture-pathway--executive-summary.pdf (england.nhs.uk)<br><br>Dargère et al., 2018<br><br>Bates et al., 1991<br><br>Klucher et al., 2022<br><br>Nielsen et al., 2022 | According to NHS England (June 2022) Optimising the blood culture pathway is essential in ensuring the best outcomes for patients with sepsis and in providing the most effective antimicrobial stewardship programs.<br>According to Dargére, unnecessary antibiotics are prescribed in 40–50% of cases of BCC and needless use of antibiotics for patients' conflicts with the efforts to combat and improve global antimicrobial stewardship.[4]<br>While antimicrobial stewardship is recognised by many clinicians as a key factor to the future of healthcare, false-positive blood culture results misguide clinicians and microbiologists. Blood culture contamination is a leading cause of unnecessary prescription of broad-spectrum antibiotics which subsequently undermines the antimicrobial stewardship effort.<br>By reducing the rates of blood culture contamination with Kurin the use of unnecessary antibiotics can support antimicrobial stewardships efforts.<br>Bates, via Doern: 'There are several untoward clinical consequences of contaminated blood cultures, the most obvious of which is increased antibiotic exposure. Bates et al. found that intravenous antibiotic charges were 39% higher for contaminant blood culture episodes than among culture-negative patient'.[3, 5]<br>Kluchler: BCC associated with a 16.4% increase in Vancomycin administration compared with true negative results.[6]<br>Nielsen et al, found that the adoption of a diversion device resulted in a 31.4% decrease of vancomycin days of treatment.[7] |
| **Patient** | Reduced unnecessary further interventions such as laboratory tests to rule out suspected bacteraemia | Skoglund et al., 2019)<br><br>Michaelidis et al., 2014<br><br>Waltzman & Harper, 2001<br><br>Hughes, J A et al. 2018 | Blood culture is a critical tool for health care staff as it allows for both the identification and the subsequent targeting of specific microorganisms. However, contaminated samples producing incorrect results compromise the integrity of blood cultures as a diagnostic tool and place patients at risk of misinformed prognoses and incorrect targeted therapies. In cases where blood culture is used to diagnose bacteraemia, which has a significant morbidity and a mortality rate of up to 37%, any delay in treatment due to identifying more than one causative organism could be fatal for patients.[8]<br>Skoglund via Michaelidis 2014, Waltzman 2001:<br>Published observational data was utilised to estimate the probabilistic cost of 146 additional diagnostic or therapeutic interventions as a result of a positive blood culture, including central line placement/removal ($1,272), bone |

| Type of benefit | Description of benefit<br>The benefits to patients claimed by the company are: | Supporting evidence | Rationale |
|---|---|---|---|
| | | | scan ($980), echocardiogram ($1 ,254), additional laboratory assays 148 ($130), and diagnostic imaging ($1,700), with a final point estimate of $1,100 of additional 149 diagnostic/procedural cost due to a positive blood culture.[9-11] |
| **Patient** | Avoiding treatment delays | Doern et al., 2020 | Improvements in the diagnostic accuracy of the blood culture result help to ensure the patient gets the right treatment in the fastest possible time frame. Avoiding the risk of a contaminated sample is essential to this outcome.<br>Doern et al: 'Initial focus on the blood culture result as the aetiology of the patient's presenting clinical syndrome may result in "anchoring bias (a form of cognitive bias in which one leans too heavily on an initial piece of information when making subsequent decisions). This can lead to a delay in obtaining the correct diagnosis and a delay in initiating appropriate therapy'.[3] |
| **Patient** | Reduced length of hospital stay | Skoglund et al. 2019<br><br>Alahmadi et al. 2011<br><br>Atta & McGuire. 2022<br><br>Burnie & Vining. 2021<br><br>Arnaout et al. 2021<br><br>Baxter et al. 2020<br><br>Allain. 2018 | Skoglund et al (2019) identified six studies which assessed total length of stay in patients with false-positive blood cultures, of which 5 were compared versus negative cultures. Lengths of stay ranged from 1–22 days for patients with contaminated cultures and 1–17 days for negative cultures.[9]<br>Alahmadi et al (2011) stated an average of 5 extra days per patient with a contaminated blood culture.[12] Atta et al (2022) at Kings College NHS Trust London applied these 5 extra bed days per blood culture contamination and determined Kurin adoption could potentially free up 1,444 bed-days at the PRUH, and 5,041 trust-wide.[13]<br>Burnie and Vining showed an average extended length of stay of 2.65 days.[14]<br>Arnaout reported an increased length of stay of 1.3 days for contaminated cultures, which translates to 343 avoided hospital days per year for their organisation.[15]<br>Baxter et al. (2020) estimated that patients with a contaminated culture had an extended stay of almost 4 days compared with those with true negatives.[16]<br>Allain (2018) reported an increased length of stay of 3.2 days associated with false positive blood cultures.[17]<br>BCC results in a cascade of additional treatments and increases the length of stay of patients in hospital. Those patients with negative blood cultures, i.e non-contaminated or true negatives are subject to short hospital stays.<br>Kurin being proven to reduce contaminated blood cultures will in turn result in reduced length of stay for patients. |

| Type of benefit | Description of benefit<br>The benefits to patients claimed by the company are: | Supporting evidence | Rationale |
|---|---|---|---|
| **System** | Reduced blood culture contamination rates | Hodson et al., 2021<br><br>Atta & McGuire, 2022<br><br>Parson K & Webb D (Jan 2023)[27]<br><br>Arenas et al., 2021<br><br>O'Sullivan & Steere, 2019<br><br>Burnie & Vining, 2021<br><br>Arnaout et al., 2021<br><br>Ostwald & Whitsell, 2021<br><br>Baxter et al., 2020<br><br>Allain, 2018<br><br>Sutton et al., 2018 | Kurin has consistently demonstrated its ability to reduce Blood culture contamination rates from the baseline rates identified at each hospital that has evaluated Kurin:<br>• Guys & St Thomas': 66% reduction[18]<br>• Kings College: 65.5% reduction[13]<br>• Shrewsbury & Telford: 48% reduction[27]<br>• Arenas et al: 63-86% lower than control[19]<br>• O'Sullivan and Steere: 74% reduction[20]<br>• Burnie and Vining: 51% at first site, more than 70% reduction at secondary site[14]<br>• Arnaout: 63% reduction of the observational rate[15]<br>• Ostwald: 97% reduction[21]<br>• Baxter: 67% reduction[16]<br>• Allain: 50-57% reduction[17]<br>• Sutton: 53% reduction[22] |
| **System** | Improved patient management using appropriate use of antibiotics | NHS England B0686-improving-the-blood-culture-pathway--executive-summary.pdf (england.nhs.uk)<br><br>Klucher et al., 2022 | Antibiotic resistance amongst pathogens (particularly Gram-negative bacteria) is the most frequent cause of ineffective empirical treatment in bloodstream infection. Early identification and antibiotic susceptibility results for blood culture isolates provide valuable diagnostic information on which appropriate antimicrobial therapy can be based, so helping to reduce morbidity and mortality, improve patient care and reduce healthcare costs. Decreasing turnaround times at each stage of the process from transportation of samples to reporting of results is therefore recommended.[23]<br>Additionally, Klucher et. al. (2022) demonstrated findings that included unnecessary exposure to antibiotics (1.3 days of treatment) and procedures, development of antibiotic-associated adverse events, and higher hospital charges.[6] |
| **System** | Improved efficiency in the use of resources such as staff and laboratory tests | Doern GV et al. (2020)<br><br>Souvenir et al., 1998 | Blood culture contamination directly affects analytical testing and laboratory efficiency.<br>Workup of contaminated blood cultures increases technologists' workloads at a time when many microbiology laboratories are |

| Type of benefit | Description of benefit<br>The benefits to patients claimed by the company are: | Supporting evidence | Rationale |
|---|---|---|---|
| | | Gander et al., 2009<br><br>Skoglund et al., 2019 | experiencing staffing shortages. In addition, contaminated cultures divert technologist efforts away from other critical samples. There is also the issue of increased time spent in trying to reach staff about false-positive blood cultures and the critical action required to address the problem. This is disruptive not only to the laboratory but also to recipients of phone calls, e.g., nurses, physicians, and other health care providers.<br>Skoglund: The clinical uncertainty created by contaminated blood cultures decreases the diagnostic value of an initial report of positive growth and often results in detrimental downstream effects, such as increased diagnostic evaluations, unnecessary antibiotic exposure, increased hospital length of stay, increased risk of nosocomial infections, and increased strain on microbiology labs.[9]<br>Souvenir, et al via Doern: Contaminated blood cultures also result in financial consequences to the laboratory, as they lead directly to unnecessary and costly additional laboratory testing. Examples include repeat blood cultures, cultures of ancillary sites, and non-microbiologic studies such as therapeutic drug monitoring for agents such as vancomycin, basic metabolic panels, and CBC.[3, 24]<br>Gander et al: Microbiology laboratories may use more media, perform additional organism identification procedures, and conduct unnecessary antimicrobial susceptibility tests.<br>Therefore, reducing the rates of contaminated blood cultures will help address the challenges detailed and improve efficiency with laboratories and already stretched NHS staff time.[25] |
| **System** | Reduced risk of hospital-acquired infections and associated costs and resource use associated with management. | Doern et al., 2020<br><br>Klucher et al., 2022<br><br>Skoglund et al., 2019 | 'Increased antibiotic exposure is associated with several potential adverse events, including allergic reactions, drug-drug interactions, antibiotic resistance emergence, and disruption of the host microbiome that can lead to Clostridioides difficile infection as well as other adverse consequences. Unfortunately, limited data exist to quantify the burden of the adverse events that are specifically associated with contaminated blood cultures'.[3]<br>Additionally, Klucher et. al. published the largest known study evaluating the clinical and financial impact of BCC with inclusion of 1,102 cases and 11,266 controls during a 5-year period.[6] The study is the first reporting increased mortality associated with BCC. It also shows a correlation with increased length of stay (2 days), unnecessary exposure to antibiotics (1.3 days of treatment) and procedures, development of |

| Type of benefit | Description of benefit<br>The benefits to patients claimed by the company are: | Supporting evidence | Rationale |
|---|---|---|---|
| | | | antibiotic-associated adverse events, and higher hospital charges.[6]<br>Clinical outcome measures were significantly higher in patients with false positive test results.<br>Vancomycin days of therapy increased by 40%, length of stay increased by 24%, in-hospital mortality nearly doubles, increasing from 4.6% to 8% for those patients admitted with BCC. Contamination was also found to increase the need for ID consultation and increased the incidence of acute kidney injury.<br>Skoglund:" The cost -benefit analysis also showed that routine ISDD implementation was associated with a reduction in 219 antibiotic usage, adverse drug reactions and hospital-acquired infections'.[9]<br>The risk of a hospital-acquired infection was modelled using an incremental 1.37% risk per hospital (Via Kilgore ML, Ghosh K, Beavers CM, Wong DY, Hymel PA, Jr., Brossette SE. 2008. The costs of 380 nosocomial infections. Med Care 46:101-4).[26] |
| **Sustainability** | A compact, elegant design offers space-efficient storage, minimal packaging, and convenient disposal in standard medical waste receptacles. | Enter text. | The Kurin device is made from materials that are safe for the intended use. The device is designed using the smallest possible material footprint to minimise waste. There are no hazardous materials, no special handling or waste considerations required. The device can be disposed of in the same manner as most hospital/medical supplies/sharps. |

Abbreviations: BCC, blood culture contamination; BSI, blood stream infection; CBC, complete blood count; NHS, National Health Service.

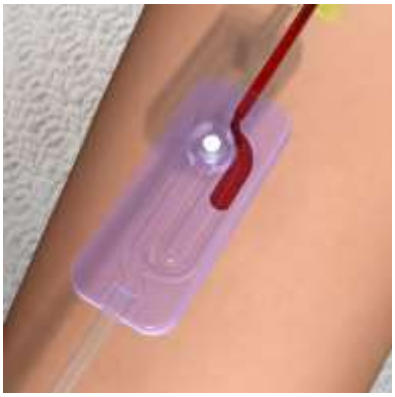
*Briefly describe the technology (no more than 1,000 words). Include details on how the technology works, any innovative features, and if the technology must be used alongside another treatment or technology.*

**How does The Kurin Blood Culture Collection Set work?**

The Kurin Lock® with Flash Technology automatically side-lines the initial flash of blood from an accessed vein to reduce skin contaminants that enter into the blood culture sample bottle.

Kurin requires only about 0.15 ml of precious blood, making the device ideal for paediatric and patients at risk for hypovolemic anaemia.

With venous access, the initial flash of blood and any contaminants within, fills a U-shaped side channel until it reaches a white porous plug. Kurin Lock serves as a flash chamber to provide visual confirmation of proper needle placement in the vein:



Approximately 0.15 ml of the initial blood flow is captured in the U-shaped Kurin Lock®:

Once the side channel is full, blood will flow a variable distance into the adjoining sampling channel before stopping. This indicates that the set is ready for specimen collection. When a vacuum is applied, blood then passes from the vein into the collection device through the sampling channel.

Kurin requires no change in patient experience or caregiver practice, enabling caregivers to continue using familiar, proven venepuncture technique.

*Provide an assessment of whether the use of this technology is likely to raise any equality issues.*

There are no equality issues with this technology. Kurin can be used on any patient from neonatal to the very elderly.

*Briefly describe the environmental impact of the technology and any sustainability considerations (no more than 1,000 words).*

The Kurin device is made from materials that are safe for the intended use. The device is designed using the smallest possible material footprint to minimise waste. There are no hazardous materials, no special handling or waste considerations required. The device can be disposed of in the same manner as most hospital/medical supplies/sharps.

## 1.3 Clinical context

*Describe the current use of the technology in the NHS (e.g. number of hospitals using technology)*

One large leading NHS Hospital has now fully implemented Kurin as a key product for the collection of all their peripheral blood cultures. This follows the successful evaluation and impact in reducing blood culture contamination rates by >66% (Hodson et al, 2022) in their A&E department (4_GSTT Hospital Policy for Peripheral Blood Culture is attached).[18]

As of March 2023, one UK-based Private Hospital Group has also initiated the implementation of Kurin as part of its infection prevention measures to improve blood culture collection procedures and reduce the risk and consequences of contaminated blood cultures.

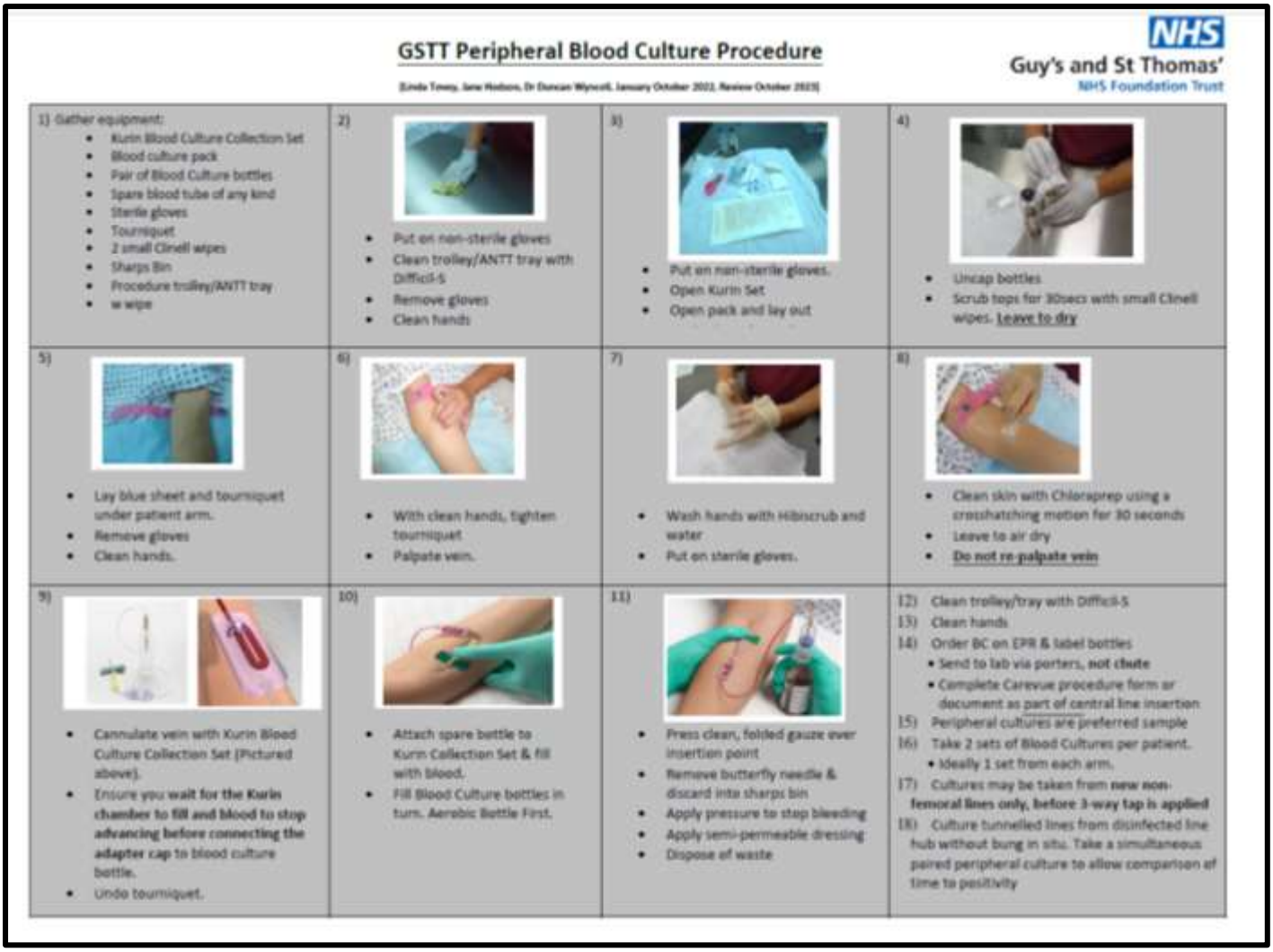
Kurin has been successfully evaluated in three NHS Hospital Trusts to date in assessing the impact it has had in reducing blood culture contamination rates. Multiple other NHS Trusts have expressed serious interest in Kurin in their desire to reduce the significant burden of contaminated blood cultures.

Kurin was developed and launched in 2017 in the US. To date, several hundred US hospitals are using Kurin as their blood culture collection device of choice and there have been several millions of units that have been used safely and effectively in that market during that time.

*Describe the clinical care pathway(s) that includes the proposed use of the technology, ideally using a diagram or flowchart. Provide source(s) for any relevant pathways.*

An example of where Kurin is used (Step 9–11) within the Guys & St Thomas' NHS Trust blood culture collection procedure is presented in Figure 2, and Figure 3.[18]

**Figure 2: Example use of Kurin within the Guys & St Thomas' NHS Trust blood culture collection procedure**

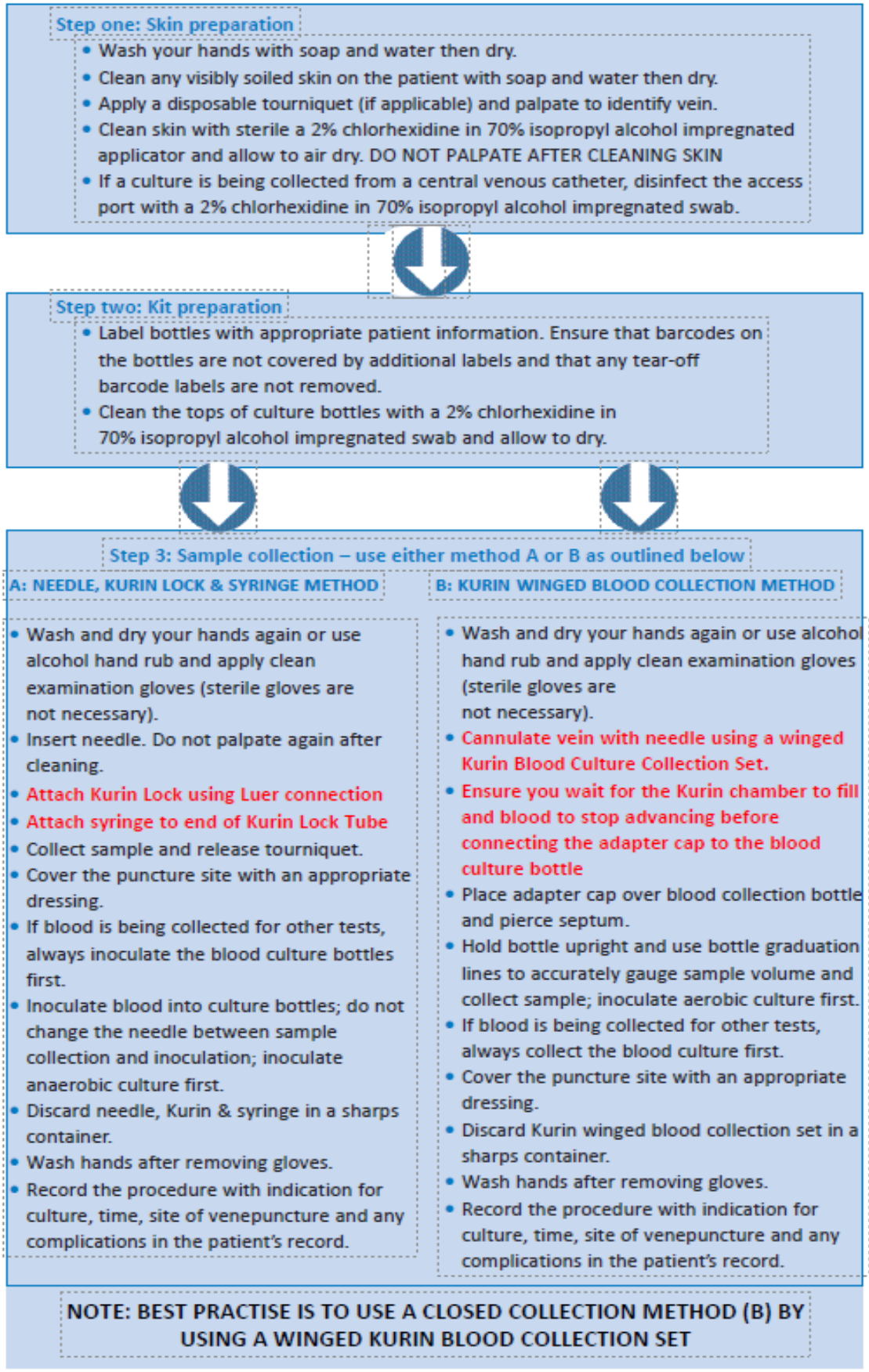



Abbreviations:

The Guys & St Thomas' NHS Trust hospital policy including the use of Kurin is attached for more information (4_GSTT Hospital Policy for Peripheral Blood Culture and 5_GSTT_Infection_Prevention__Control_Chapter_14_Guideline_for_Taking_Blood_for_Culture_v8.0).

The use of Kurin Lock in the blood culture collection procedure is presented in Figure 3.

**Figure 3: Example use of Kurin in a blood culture collection procedure**



*Describe any training (for healthcare professionals and patients) and system changes that would be needed if the NHS were to adopt the technology.*

Kurin requires no change in patient experience or caregiver practice, enabling caregivers to continue using familiar, proven venepuncture technique. The Kurin Lock® with Flash Technology automatically side-lines the initial flash of blood from an accessed vein to reduce skin contaminants that enter into the blood culture sample bottle.

As a company we provide comprehensive blood culture procedural training and product support. We are on a quest to help NHS Hospitals achieve and eradicate avoidable blood culture contamination (Figure 4):

- https://www.youtube.com/watch?v=y9VYSJdz768
- https://www.youtube.com/watch?v=-LkLU5zjneE

**Figure 4: Example demonstration of Kurin**

# 2 Clinical effectiveness evidence

## 2.1 Identification and selection of studies

*Complete the following information about the number of studies identified.*

*Report in full transparent and reproducible detail the search methods as used for all search resources, and provide a detailed list of any excluded studies, in appendix A. Number of studies reported below should be after any duplicates have been removed.*

A targeted literature search was conducted to identify relevant published clinical effectiveness evidence on the use of Kurin for blood culture collection in a hospital setting.

Searches were conducted using Medline (PubMed) and https://www.kurin.com/studies/ and were limited to publications from 2017 to 2023. Search terms related to “Kurin”, “Kurin Lock Blood Culture collection” and “Initial Specimen Diversion Device”

The full search strategy is presented in Appendix A. The database search identified 12 studies potentially relevant to blood culture collection with Kurin in a hospital setting, along with an additional 7 posters which were identified as relevant to this submission.

| Study selection | Number of records |
|---|---|
| Number of studies identified in a systematic search. | 12 |
| Number of studies identified as being relevant (i.e. directly relevant to the decision problem by ensuring it fits the eligibility criteria outlined in the scope) | 12 |
| Of the relevant studies identified, the number of published, peer-reviewed full-text studies | 4 |
| Of the relevant studies identified, the number of conference abstracts. | 3 in UK and 4 in the US |
| Of the relevant studies identified, the number of unpublished (without peer-review) studies | 3 posters in UK and 6 in the US |

Abbreviations: UK, United Kingdom; US, United Kingdom.

## 2.2 List of relevant clinical effectiveness studies

*In Table 4 give* brief *details of all studies identified as relevant (consider the decision problem, particularly the eligibility criteria of studies).*

*For any unpublished studies, please provide a structured abstract in appendix A. If a structured abstract is not available, you must provide a statement from the authors to verify the data.*

*Any data that is submitted in confidence must be correctly highlighted. See section 1 of the user guide for how to highlight confidential information. Include any confidential information in appendix F. Please provide details as to how the systematic reviews have been carried out, including the number of reviewers.*

**Table 4: Summary of all clinical effectiveness studies (published full text, abstracts and unpublished) identified as being relevant (i.e. directly relevant to the decision problem by ensuring it fits the eligibility criteria outlined in the scope)**

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| Hodson et al (Sept 2022)[18]<br>Guys & St Thomas' NHS Hospital, London, UK<br>Poster Presentation at AVA, USA in Sept 2022<br>Hospital delivered, but product provided free of charged.<br>☑ | Before & After Intervention study<br>Kurin lock was used to take blood cultures as the new intervention in place of standard collection methods.<br>Compared with current practise where baseline blood culture contamination rate was stated as being consistently around 6% of all blood cultures taken.<br>The project ran over a 5-month period from May to September 2021. | Any patient requiring a blood culture to be taken and it was recorded that Kurin was used to collect that sample.<br>In Adult Accident & emergency at St Thomas' NHS Hospital, London.<br>A total of 533 patients blood culture samples where Kurin was recorded as being used were captured and analysed. | There was a significant reduction from a baseline of 6% to 2% in the number of contaminated blood cultures when using Kurin Lock. A 66% reduction in contamination rates. Statistical significance was proven using Fishers exact test that returned a p value of 0.045 with odds ratio of 0.53 with 95% CI 0.29 –0.98.<br>Regular training on use of the device was provided though no change in practice was required.<br>The ISSD was found to be equally effective in reducing contamination rates when taking blood cultures from a cannula versus standard phlebotomy thereby mitigating risk when a cannula is used.<br>The ISSD was extremely easy to use, and the positive results of the trial encouraged staff participation<br>Based on the estimated costs of a false – positive blood culture savings are estimated to be £28–£72K for this initial sample | This is real life evidence that Kurin, when used in a busy NHS Hospital reduces the rates of blood culture contamination significantly.<br>Confidence that Kurin impacts clinical results<br>Improve patient care and outcomes, delivers significant savings and efficiencies to the hospital economy.<br>Staff found the device very easy to use and training requirement was minimal.<br>Guy's and St Thomas' NHS Foundation Trust has now fully adopted Kurin as part of their standard blood culture taking procedure. Ongoing training and support is being provided.<br>Not published in a journal at time of submission for peer review. |

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| Atta M, MacGuire R (2022)[13]<br>Kings College Hospital, London, UK<br>Poster Presentations delivered at:<br>National Infusion and Vascular Access Society (NIVAS), June 2022.<br>Infection Prevention Society (IPS) Annual Conference, October 2022.<br>Hospital delivered, but product provided free of charged.<br>☑ | Before & After Intervention study<br>Kurin lock was used to take blood cultures as the new intervention in place of standard collection methods.<br>Compared with current practise where baseline blood culture contamination rate was stated as being consistently around 9% of all blood cultures taken.<br>The project ran over a 3-month period from August till October 2021. | Any patient requiring a blood culture to be taken and it was recorded that Kurin was used to collect that sample.<br>In Adult Accident & emergency at Kings College NHS Trust, PRUH Site, London.<br>A total of 381 patients blood culture samples where Kurin was recorded as being used were captured and analysed. | The results demonstrated a decrease in blood culture contamination to 3.1% from a pre intervention baseline of 9%.<br>A reduction of 65.5% vs the baseline.<br>There was no change to current practice, and staff found the Kurin device easy and simple to use. Using Kurin mitigates the increased risk of contamination, and the demonstrated decrease in numbers of false positives encouraged the ED staff to follow best practice.<br>Kurin as a stand-alone item is expensive, however, based on the estimated cost of false-positive blood cultures, savings are estimated to be £4.6M for the Trust as a whole and £1.3M in PRUH ED.<br>Additionally, adoption could potentially free up 1,444 bed-days at the PRUH, and 5,041 trust-wide. The reduction in contamination rates becomes evident when there is 80% compliance utilising the device. | This is real life evidence that Kurin when used in a busy NHS Hospital reduces the rates of blood culture contamination significantly.<br>Confidence that Kurin impacts clinical results.<br>Demonstrates the relationship between compliance with using the device for blood culture collection and lowering of contamination rates. I.e., the more it is used the lower the contamination rates.<br>Improve patient care and outcomes, delivers significant savings and efficiencies to the hospital economy.<br>Not published in a journal at time of submission for peer review. |

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| Parson K & Webb D (Jan 2023)[27]<br>Princess Royal NHS Hospital, Telford, Shropshire, UK<br>Hospital delivered and funded.<br>☑ | Before & After Intervention study<br>Kurin lock was used to take blood cultures as the new intervention in place of standard collection methods.<br>Compared with current practise where baseline blood culture contamination rate was stated as being consistently around 5% of all blood cultures taken.<br>The project ran over a 3-month period from April – June 2022. | Any patient requiring a blood culture to be taken and it was recorded that Kurin was used to collect that sample.<br>In Adult Accident & emergency at Princess Royal NHS Hospital, Telford, Shropshire.<br>A total of 464 patients blood culture samples where Kurin was recorded as being used were captured and analysed. | The base line contamination rate in PRUH ED was 5%<br>When using Kurin the contamination rate reduced to 2.6%<br>An overall reduction of 48%<br>Cost avoidance is estimated to be £1.6M for Shrewsbury & Telford NHS Trust as a whole and £327K in PRUH ED alone.<br>The Trust has an opportunity to free 359 bed days from PRUH ED and 1,836 bed days trust wide.<br>The decrease in false positives encouraged ED staff to follow best practice. | This is real life evidence that Kurin when used in a busy NHS Hospital reduces the rates of blood culture contamination significantly.<br>Confidence that Kurin impacts clinical results.<br>Improve patient care and outcomes, delivers significant savings and efficiencies to the hospital economy.<br>Not published in a journal at time of submission for peer review. |

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| Arenas M, et al. (2021)[19]<br>Central Texas Veterans Health Care System, Texas, USA<br>Published / Peer reviewed Journal<br>☑ | Prospectively, 2 different blood culture-diversion devices were made available in the unit supplies to ED clinicians at a single site during 2 different periods of time as a follow-up strategy to an ongoing quality improvement project. Blood samples were collected in the emergency department over a period of 16 months.<br>A retrospective record review study was conducted comparing the use of the 2 specimen-diversion devices with no device (control group) for blood culture contamination rates. The main outcome of monthly blood culture contamination per device was tested using a Bayesian Poisson multilevel regression model. | A total of 4,030 blood samples were collected and analysed from November 2017 to February 2019. | The model estimated that the mean incidence of contaminated blood cultures in the device A group was 0.29 (0.14–0.55) times the incidence of contaminated draws in the control group. The mean incidence of contaminated blood draws in the device B group was 0.23 (0.13–0.37) times the incidence of contaminated draws in the control group, suggesting that initial-diversion methods reduced blood culture contamination.<br>Initial specimen-diversion devices supplement present standard phlebotomy protocols to bring down the blood culture contamination rate. | Arenas and colleagues recommended that initial specimen diversion devices be adopted as part of a bundle of interventions for sustained reduction of blood culture contaminations in emergency clinical practice. |

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| O'Sullivan DM et al. (2019)[20]<br>Hartford Hospital, Connecticut Medicine, USA.<br>Published / Peer reviewed Journal<br>Financial Sources/Disclosures: This study was supported by an investigator-initiated grant from Kurin, Inc. (San Diego, CA). However, neither the company nor any of its personnel had any influence in the design or the analysis of the study, nor drafting of the manuscript. None of the authors has any disclosures.<br>☑ | Before & After Intervention study<br>Kurin lock was used to take blood cultures as the new intervention in place of standard collection methods.<br>Blood samples were sent to the Microbiology laboratory for standard analysis. The false-positive rate (FPR) for each month is a standard report, providing the number of blood samples analysed and the number of false positive findings. | Blood culture was collected using the Kurin Lock device on all patients visiting the Hartford Hospital Emergency Department between April and June, 2017, inclusive, from whom blood cultures were ordered. | There was a statistically significant lower rate of FPR, with reductions ranging from 65% to 82%, in all nine comparisons. For the three most recent months in which the Kurin Lock was used, the false-positive rate was 0.44%, compared with an average false-positive rate of 1.71% for the three most recent months during which the Kurin Lock device was not used, an average reduction of 74.1%. This reduction in the absolute risk also yields a number needed to treat (NNT) equal to eight, meaning that use/implementation of the device would save one person from the ramifications of a FPBC for every eight times the diversion device was used.<br>Kurin Lock device would result in a yearly savings of more than $900 000, or more than $750 000 after adjusting for device costs | Using Kurin significantly lowers blood culture contamination rates in the ED.<br>A <1% contamination rate is achievable using Kurin.<br>Financial savings were achieved by the lowering of BCC. |

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| Burnie J and Vining S (2021)[14]<br>TriHealth Healthcare<br>Published/Peer Reviewed Journal<br>Financial Sources/Disclosures: None to report<br>☑ | Before and after intervention study<br>Kurin Lock was added to an evidence-based blood culture collection bundle established by the shared leadership committee (SLC) to determine the effectiveness of Kurin Lock on further lowering the contamination rate. Kurin was the only changed variable for the length of the trial.<br>Blood culture collections were sent to the facility microbiology lab for standard processing and analysis. A blood culture contamination report was provided monthly, providing the number of blood cultures collected and the number of false positive results.<br>The SLC also performed a cost analysis and increase length of stay analysis for patients that experienced a contaminated blood culture. The facility found a cost of $5,863 with each contamination and increased length of stay by 2.65 days. | All clinicians collecting blood cultures the in the emergency department were trained how to use Kurin Lock for every blood culture collection on every patient in the emergency department. Super users were identified to support the addition of Kurin Lock to the blood culture collection workflow. Each shift had at least one super user available to act as a resource and aid in monitoring compliance to best practice and utilization. | The average contamination rate in 2018 before Kurin implementation was 2.92, just below the recommended 3% benchmark. After Kurin implementation starting in January 2019, the contamination rate decreased to 1.42%. The facility maintained rates of 1.5% or less for the following calendar year of 2020.<br>250 patients benefitted from the introduction of Kurin by experiencing a decreased risk of an extended length of stay, exposure to unnecessary treatment and antibiotics and increased risk of healthcare acquired conditions.<br>The facility demonstrated a cost savings of $1.6 million, which justified an expansion the additional three hospitals within the TriHealth System. The system blood culture contamination average decreased from 4.96% to 1.6% as a result, experiencing ~$2+ million savings annually. | The financial cost of contaminated blood cultures has long been studied and often difficult for facilities to pinpoint costs directly related to them. This facility found it necessary to justify the cost of Kurin by determining the cost of a contamination to their health system. The facility studied patient records with the same diagnostic related group code cost and similar co-morbidities. The SLC concluded a financial cost difference of $5,863 and an average extended length of stay by 2.65 days for patients with a contaminated blood culture. Their findings are consistent with the ranges demonstrated in published literature. |

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| Ostwald C & Whitsell K. (2021)[21]<br>John R. Oishei Children's Hospital, Buffalo, NY, USA<br>Poster and Oral Presentation Association Infection Prevention and Control (APIC) National Conference 2021, USA<br>Hospital delivered and funded.<br>☑ | Before and after intervention study<br>A paediatric emergency department experienced a wide range of blood culture contamination rates (1.7% to 11%) and found the lower rates correlated with time frames after education and re-education on proper blood culture collection was provided.<br>With a desire to sustain low rates and not rely on constant education, the emergency department sought to implement Kurin alongside education and study longevity of decreased rates before education was required again. | All nurses collecting blood cultures were educated with direct 1:1 and hands on education of the Kurin Lock device and were made aware they were expected to utilize Kurin with every blood culture collection for the duration of the study period of two months.<br>The finance department performed a retroactive cost analysis of blood culture contamination using 2017 data and the infection prevention team provided a cost analysis of using Kurin to decrease contamination rates and received approval to study Kurin's impact.<br>After the initial study period, the nurses were given a simple 5 question satisfaction survey. 85% of clinicians found using Kurin Lock and decreasing blood culture contamination to "make sense" while 45% desired a device with shorter tubing, yielding less waste for the vulnerable pediatric population. The Kurin team received this feedback and produced a shorter tubing with Kurin Lock integrated and launched a second study period. | Adding results of the two study periods together, the emergency department performed 1175 blood cultures with the Kurin Lock device and had 0 contaminations, as opposed to 6 contaminations across 71 collections without the Kurin Lock device. Using Fisher's exact test, the results are statistically significant with a p-value of 0.0001.<br>The finance department determined the implantation of the Kurin Lock device would yield a cost savings of $71,422 annually.<br>Non-quantified measures impacted were the decreased frequency of physician call back times, lost time for the patient and their guardians for return follow up tests for false positives, increased staff productivity and workflow and overall increased patient and family satisfaction. | This is one of very few studies which looks at the issue of BCC in paediatric patients and demonstrates Kurin is equally effective in this patient population.<br>With any process that impacts patient safety and outcomes, it is imperative processes and tools cand be standardized across all patient populations. The Kurin Lock device has demonstrated effectiveness across the adult population and through this study, the paediatric population. The ease of use combined with low blood waste allows for a standard of care regardless of who is performing the blood culture collection and which patient population is requiring the intervention. |

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| Sutton J et. al 2018[22]<br>Bayfront Health St. Petersburg, USA<br>Poster Presentation Association for Professionals in Infection Control (APIC) National Conference 2018<br>Hospital delivered and funded<br>☑ | Pre- and post-intervention study<br>After attempting to rely on education and a blood culture collection kit that included a sterilized waste tube to discard the initial sample of blood, a facility continued to struggle to maintain low blood culture contamination rates. They then implemented the Kurin Lock device and studied the impact to their overall contamination rate. | All clinicians collecting blood cultures in the emergency department were educated and on blood culture collection and the Kurin Lock device. The expectation was to use Kurin Lock butterfly on all blood cultures collected via butterfly venepuncture. At the time of the study, the peripheral IV adaptation of Kurin was not available. The standard practice of the emergency department was to collect the first set of blood cultures upon fresh peripheral IV insertion and the second set with a winged butterfly needle set and attached transfer adapter. | The pre-intervention contamination rate was 2.6%. After Kurin implementation, the contamination rate decreased to 1.2%, yielding a 54% decrease. Using a chi-square statistical analysis, the results were found to be statistically significant with a p-value less than 0.05. Given the standard practice at the time, Kurin was utilized only 50% of blood culture collections. It would be expected to see a lower contamination rate if the device was used 100% of the time. Out of 9 collections where the Kurin Lock was not used, 8 collections were found to be contaminated. | Finding standard practice in several emergency departments is for clinicians to collect blood cultures via fresh peripheral IV insertion, the organization found it necessary to produce an adaption for freshly placed peripheral IV. This facility quickly adopted the additional offering and has continued to maintain low contamination rates. This addition continues to support the Kurin product portfolio as an appropriate standard of care for all patient populations and scenarios. |
| Allain, M. (2018)[17]<br>Abstract from 2018 National Association of Clinical Nurse Specialists Annual Conference: Not Your ‘‘Average’’ ED: A CNS-Led Project That Reduced Blood Culture Contaminations in One Emergency Department to Below Expected Levels. Clin Nurs Specialist 2018 May/June; E1-2<br>Crouse Hospital, Syracuse, NY<br>Hospital funded.<br>☑ | Retrospective quasi-experimental<br>Before & After Intervention study<br>Introduction of the Kurin Lock, concurrent with product and process education. | Any patient requiring a blood culture to be taken and it was recorded that Kurin was used to collect that sample in a single Emergency Department. | During the study period, the use of Kurin resulted in a significant reduction of contamination rates, falling to 0.8%, which was 50% below the facility's previous best performance and 57% below their mean performance. 7 out of 9 contaminations during the study period occurred when Kurin was not used. Based on a cost estimate of $5,200 per contaminated culture, Allain calculated that the hospital could save over $185,000 per year. The study also revealed an increase in length of stay of 3.2 days associated with false positive blood cultures. | This study shows the impact of utilising a combination of strategies, including department-wide education, compliance monitoring, but most importantly the use of the Kurin blood collection device. The study demonstrates the effectiveness of process improvements, aided by technology in reducing blood culture contamination rates and highlights the potential benefits of implementing similar interventions in other healthcare settings. |

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| Arnaout, et al. (2021)[15]<br>UMass Memorial Medical Center, Worcester, MA, USA<br>Abstract, ID Week, Sept/Oct 2021<br>Hospital funded<br>☑ | Prospective crossover pre-and post-design<br>This trial compared the use of the Kurin Lock device with standard equipment in two emergency departments. Each phase lasted for 10 weeks, with the device being used initially in one ED and then in the other after a washout period. Contaminants were identified and evaluated by three independent infectious disease physicians before statistical analysis. An intention-to-treat analysis was conducted, and Chi-square tests were used to compare contaminant rates between the two methods. | Two emergency department settings. 5,675 blood samples were obtained with 5,661 samples analysed after 14 were deemed inconclusive by the ID physician review. There were 1,719 samples obtained at Memorial ED and 3,942 at University ED, with 2,836 samples collected during diversion device periods and 2,825 during standard equipment periods. | Kurin was able to significantly lower blood culture contamination rates overall by 1% at the institution's two EDs (34% relative reduction). The "observed" contamination rate, when Kurin was used, showed a reduction from 3% to 1.1%, a 63% decrease. | UMass used a cost of $7,000 per contaminated culture, yielding a cost savings calculation of $1.8M in the "observed" rate.<br>They reported an increased LOS of 1.3 days for contaminated cultures, which translates to 343 avoided hospital days per year. All while compliance was relatively poor averaging 50–60%. |

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| Rhew (2021)[28]<br>Cone Health, Greensboro, NC, USA.<br>Nur Primary Care. 2021; 5(3): 1-6<br>Hospital funded<br>☑ | Retrospective quasi-experimental<br>Before & After Intervention study<br>Enacted a multidisciplinary approach to standardize blood culture collection. Including policy, procedural and practical reviews. Along with the introduction of a product and implementing education feedback loops.<br>Kurin lock was introduced and used to take blood cultures as the new intervention in place of standard collection methods. | Blood culture was collected using the Kurin Lock device on patients presenting to the ED identified as needing blood cultures collected. The hospital system consists of four hospitals with five 24-hour emergency departments located in the southeastern region of the United States. (1 Free standing ED not included in study).<br>• A community 238-bed community facility with 58 ED beds.<br>• A rural community-based facility and has 110 acute care beds with 23 ED beds<br>• The flagship – 510-bed teaching hospital and referral centre with a level II trauma adult ED with 60 beds and the paediatric ED with 11 beds.<br>• A community acute-care facility and offers 175 private beds with 55 ED beds | The device has shown to decrease our contamination rates from 3.1% to 1.3% to 0% when using the diversion product during our five-week controlled trial. Ultimately, the overall ED system wide contamination rate fell to <2.1%, which factors a real-world blended rate.<br>The key outcome is that withdrawing off a fresh peripheral IV stick using the device did not increase our contamination rates but helped decrease IV contamination rates by side-lining the first flash of blood prior to collecting the blood culture sample. Using the kit helped decrease the skin contaminants being the source of the blood culture contaminant, causing a false-positive result.” | Before the introduction of Kurin, this facility experienced BCC rates above the old 3% benchmark in 4/5 EDs. Upon completion were able to sustain a real-world, or blended, rate of 2.1% which accounts for variance in properly trained staff, and overall product compliance. |

| Study name, location, status and funding | Design and intervention(s) | Participants and setting | Main outcomes | Company comments |
|---|---|---|---|---|
| Baxter et al (2020)[16]<br>Passive Engineering Controls Result in Sustained 66% Reduction in Blood Culture Contamination.<br>St. Mary's Regional Medical Center, Russellville AR<br>Abstract, Global Solutions to Antibiotic Resistance in Healthcare. Infection Control & Hospital Epidemiology Volume 41, Issue S1: October 2020, pp.s342-s343.<br>Hospital funded<br>☑ | Retrospective<br>quasi-experimental<br>The intervention involved implementing a "novel specimen diversion device" (Kurin lock), following education of laboratory and emergency department (ED) staff on the proper use of the device. In addition, daily safety huddles were implemented to monitor contaminations and provide quick feedback to specific clinical staff. | Community hospital, Emergency Department | In analysing data for 3 different months, patients with contaminated cultures spent an average of 3.97 additional days in the facility. In conclusion, the implementation of this specimen diversion device significantly lowered our contamination rates from 4.93% to 1.66%, a 66% reduction. | St. Mary's, they previously struggled with high contamination, with a historical average above 6%. This was reduced to around 5% with staff education. However, after implementing Kurin, contamination rates significantly reduced from 4.93% to 1.66%, indicating a 66% reduction. St. Mary's reported a compliance rate of 70-75% for Kurin use. Additionally, the use of Kurin prevented over 140 patients from experiencing the potential complications of a contaminated blood culture. St. Mary's also estimated that patients with a contaminated culture experienced an extended stay of almost 4 days compared to those with true negatives, which results in significant cost savings. Based on an estimated cost of $4,000 per contamination, St. Mary's estimated annual savings of over $500,000. |

Key: ☑ aspect of study in scope; ☒ aspect of study in scope ☑☒ aspect of study partially in scope, or elements of this are not in scope.
Abbreviations: BCC, Blood culture contamination; ED, Emergency Department;

## 2.3 Critical appraisal of the clinical effectiveness studies

*In appendix B, provide the complete quality assessment for each included study using an appropriate and validated tool specific to the study design. See the user guide for further details of the information required. ROBIS-A or another relevant tool is recommended for quality assurance of systematic reviews and meta-analyses, which will be needed if the company has presented such a review or analysis instead of presenting its own de novo review or analysis.*

*Summarise the relevance of each of the included studies to the decision problem in Table 5.*

**Table 5: Critical appraisal summary for the clinical effectiveness studies**

| Study | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the economic model? | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|
| Hodson et all (2022)[18] | Real world evidence that Kurin reduces the number of contaminated blood cultures in a major NHS Hospital Trust | Yes, that by using Kurin for blood culture collection the rates of contaminated samples are significantly reduced (66% reduction) | Yes, in relation to assumptions that can be applied in blood culture contamination reduction by using Kurin | Only available in poster presentation currently. Not a peer reviewed study. | Hospital delivered, but product provided free of charged. |
| Atta et all (2022)[13] | Real world evidence that Kurin reduces the number of contaminated blood cultures in a major NHS Hospital Trust | Yes, that by using Kurin for blood culture collection the rates of contaminated samples are significantly reduced (65% reduction) | Yes, data is used for health economic model and scenario analyses in relation to assumptions that can be applied in blood culture contamination reduction by using Kurin | Only available in poster presentation currently. Not a peer reviewed study. | Hospital delivered, but product provided free of charged. |
| Parson K & Webb D (2023)[27] | Real world evidence that Kurin reduces the number of contaminated blood cultures in a major NHS Hospital Trust | Yes, that by using Kurin for blood culture collection the rates of contaminated samples are significantly reduced (48% reduction) | No | Only available in poster presentation currently. Not a peer reviewed study. | Hospital delivered and funded. |
| Arenas M, et al. (2021)[19] | Real-world evidence that ISDD such as Kurin reduces the number of contaminated blood cultures in an acute hospital setting. | Yes, that by using a ISDD (Kurin) for blood culture collection the rates of contaminated samples are significantly reduced. Initial specimen-diversion devices supplement present standard phlebotomy protocols to bring down the blood culture contamination rate | No | Overall demonstrates the effectiveness of ISDD's in reducing blood culture contamination. Does not officially state which device was A&B, although we are fully aware Device B is Kurin and they continue to use it to this day… | Hospital delivered and funded. |

| Study | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the economic model? | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|
| O'Sullivan DM et al. (2019)[20] | Real-world evidence that Kurin reduces the number of contaminated blood cultures in an acute hospital emergency department setting. | Yes, that by using Kurin for blood culture collection the rates of contaminated samples are significantly reduced by on average 74%. | No | Single centre study | Hospital delivered. This study was supported by an investigator-initiated grant from Kurin, Inc. (San Diego, CA). However, neither the company nor any of its personnel had any influence in the design or the analysis of the study, nor drafting of the manuscript. |
| Burnie J and Vining S (2021)[14] | Real-world evidence that Kurin reduces the number of contaminated blood cultures in an acute hospital emergency department setting. | Yes, that by using Kurin for blood culture collection the rates of contaminated samples are significantly reduced by on average 74%.<br>The average contamination rate in 2018 before Kurin implementation was 2.92, just below the recommended 3% benchmark. After Kurin implementation starting in January 2019, the contamination rate decreased to 1.42%. The facility-maintained rates of ≤1.5% for the following calendar year of 2020. | No | Single centre study | Hospital delivered and funded. |

| Study | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the economic model? | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|
| Ostwald C & Whitsell K. (2021)[21] | Real-world evidence that Kurin reduces the number of contaminated blood cultures in an acute hospital emergency department setting. | Adding results of the two study periods together, the emergency department performed 1,175 blood cultures with the Kurin Lock device and had 0 contaminations, as opposed to 6 contaminations across 71 collections without the Kurin Lock device. Using Fisher's exact test, the results are statistically significant (p=0.0001).<br>Non-quantified measures impacted were the decreased frequency of physician call back times, lost time for the patient and their guardians for return follow up tests for false positives, increased staff productivity and workflow and overall increased patient and family satisfaction. | No | Poster presentation and not currently journal-published | Hospital delivered and funded. |
| Sutton J et. Al. (2018)[22] | Real world evidence that Kurin reduces the number of contaminated blood cultures in an acute hospital emergency department setting. | Yes, that by using Kurin for blood culture collection the rates of contaminated samples are significantly reduced by on average 54%. | No | Single centre study | Hospital delivered and funded. |

| Study | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the economic model? | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|
| Arnaout, et al. (2021)[15] | Real world evidence that Kurin reduces the number of contaminated blood cultures in an acute hospital emergency department setting. | Yes, Kurin was able to significantly lower blood culture contamination rates by 63%. | No | | Hospital delivered and funded. |
| Allain, M. (2018)[17] | Real world evidence that Kurin reduces the number of contaminated blood cultures in an acute hospital emergency department setting. | During the study period, the use of Kurin resulted in a significant reduction of contamination rates, falling to 0.8%, which was 50% below the facility's previous best performance.<br>Based on a cost estimate of $5,200 per contaminated culture, Allain calculated that the hospital could save over $185,000 per year.<br>The study also revealed an increase in length of stay of 3.2 days associated with false positive blood cultures. | No | | Hospital delivered and funded. |
| Rhew (2021)[28] | Real world evidence that Kurin reduces the number of contaminated blood cultures in an acute hospital emergency department setting. | Yes, Kurin lowered contamination rates from 3.1% to 1.3% to 0% when using the diversion product during a five-week controlled trial. Ultimately, the overall ED system wide contamination rate fell to <2.1%, which factors a real-world blended rate. | No | | Hospital delivered and funded. |

| Study | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the economic model? | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|
| Baxter et al (2020)[16] | Real world evidence that Kurin reduces the number of contaminated blood cultures in an acute hospital emergency department setting. | Blood culture contamination reduced by 66% when using Kurin.<br>Patients with a contaminated culture experienced an extended stay of almost 4 extra days compared to those with true negatives. | No | Poster presentation so limited data | Hospital delivered and funded. |

Abbreviations: BCC, Blood Culture Contamination; ED, Emergency Department

## 2.4 Results from the clinical evidence base

*For each study identified in Section 2.2 as relevant to your submission, provide results for all outcomes specified in the NICE scope and those used to inform the decision model.*

*Summarise the results in an appropriate format, such as by study design, quality, other study characteristic or by outcome. Use a table, if most of the studies can be captured succinctly in a single table, for ease of comparison. Alternatively, present results with separate sections and subsections, for example for each key outcome across all relevant studies, using descriptive text, tables, or both.*

*Comment below Table 6 if any of the key outcomes are a surrogate endpoint; see the NICE health technology evaluations: the manual (see sections 4.6.6 to 4.6.10) – discuss what level of evidence (1-3) supports the surrogate relationship for decision making, and comment whether the surrogate endpoint is considered validated.*

**Table 6: Key results from the clinical evidence base**

| Study | Outcome 1 | Outcome 2 | Outcome 3 | Outcome 4 | Outcome 5 |
|---|---|---|---|---|---|
| Hodson et al, (2022)[18] | Reduced blood culture contamination by 66%.<br>From a baseline of 6% to 2%.<br>Statistical significance was proven using Fishers exact test that returned a p-value of 0.045 with odds ratio of 0.53 with 95% CI 0.29–0.98. | Effectiveness of Kurin was achieved when Blood cultures were taken using the Peripheral IV Connect version | Based on the estimated costs of a false – positive blood culture savings are estimated to be £28–£72K for this initial sample. | Kurin was easy to use and positive results encourage staff participation | Infection Control Committee approved Kurin for full implementation throughout the Trust |
| Atta M & MacGuire R (2022)[13] | Decreased in blood culture contamination to 3.1% from a pre intervention baseline of 9%.<br>A reduction of 65.5% versus baseline.<br>There was no change to current practice, and staff found the Kurin device easy and simple to use | Savings are estimated to be £4.6M for the Trust as a whole and £1.3M in PRUH ED. | Potentially free up 1,444 bed-days at the PRUH, and 5,041 for Kings College NHS Trust. The reduction in contamination rates becomes evident when there is 80% compliance utilising the device. | The reduction in contamination rates becomes evident when there is 80% compliance utilising the device. | There was no change to current practice, and staff found the Kurin device easy and simple to use. |
| Parson K & Webb D (2023)[27] | Decreased in blood culture contamination to 2.6% from a pre intervention baseline of 5%. An overall reduction of 48% from baseline. | Cost avoidance is estimated to be £1.6M for Shrewsbury & Telford NHS Trust as a whole and £327K in PRH ED alone. | The decrease in false positives encouraged ED staff to follow best practice. | The Trust has an opportunity to free 359 bed days from PRUH ED and 1,836 bed days trust wide | Enter text. |
| Arenas M, et al. (2021)[19] | The model estimated that the mean incidence of contaminated blood cultures in the device A group was 0.29 (0.14–0.55) times the incidence of contaminated draws in the control group. suggesting that initial-diversion methods | The mean incidence of contaminated blood draws in the device B group was 0.23 (0.13–0.37) times the incidence of contaminated draws in the control group. | Initial-diversion methods reduced blood culture contamination. | Enter text. | Enter text. |

| Study | Outcome 1 | Outcome 2 | Outcome 3 | Outcome 4 | Outcome 5 |
|---|---|---|---|---|---|
| | reduced blood culture contamination. | | | | |
| O'Sullivan DM et al. (2019)[20] | There was a statistically significant lower rate of FPR, with reductions ranging from 65% to 82%, in all nine comparisons. For the three most recent months in which the Kurin Lock was used, the false-positive rate was 0.44%, compared with an average false-positive rate of 1.71% for the three most recent months during which the Kurin Lock device was not used, an average reduction of 74.1%. | A 74% reduction in the absolute risk also yields a number needed to treat (NNT) equal to eight, meaning that use/implementation of the device would save one person from the ramifications of a FPBC for every eight times the diversion device was used. | Kurin Lock device would result in a yearly savings of more than $900,000, or more than $750,000 after adjusting for device costs. | Enter text. | Enter text. |
| Burnie J and Vining S (2021)[14] | Over the course of the study period BCC was reduced by 51% in the first facility and achieved >70% reduction in the secondary facility. | An internal analysis of the financial cost of BCC resulted in an estimated average of $5863, which amounted to more than $2 Million USD saved during the study period. | An internal review returned an estimated length of stay increase of 2.65 days for those patients with BCC, and it is estimated that nearly 250 patients benefitted from the use of Kurin. | Enter text. | Enter text. |
| Ostwald C & Whitsell K. (2021)[21] | The first study analysing the PIV configuration, as well as the use of Kurin in a paediatric population. Of the 1,175 cultures collected using Kurin, the zero were contaminated, while the study observed 6 contaminations during this period when the Kurin Lock was not utilised, | | | | |

| Study | Outcome 1 | Outcome 2 | Outcome 3 | Outcome 4 | Outcome 5 |
|---|---|---|---|---|---|
| | reflecting a statistical significance of p=0.0001. | | | | |
| Sutton J et. al (2018)[22] | The study showed a statistically significant reduction in contamination rates from 0.025 to 0.012. | After accounting for the cost of the Kurin product used during the study period, it is estimated that Kurin would save the hospital more than $500k USD per annum, based the hospitals estimated cost of BCC ($7500) | | | |
| Arnaout, et al. (2021)[15] | The observed contamination rate when Kurin was used showed a reduction equivalent to 63%. | The hospital estimated a BCC cost of $7,000 per event, amounting to a cost savings of 1.8 million USD in the observed rate. | Arnaout reported an increased length of stay of 1.3 days per event, which translates to 343 avoided hospital bed days per year for the hospital. | | |
| Allain, M. (2018)[17] | With the use of Kurin, rates fell to 0.8%, which is 50% below the hospitals best performance, and 57% below their mean BCC rate. | Allain estimated the cost of BCC to be $5200 per event, calculating that the hospital stood to save more than $185,000 per year. | Allain reported an increase in length of stay of 3.2 days associated with BCC events. | | |
| Rhew (2021)[28] | Rates across multiple sites fell from 3.1% to 1.3% to 0% with introduction of the Kurin Lock. | The key outcome is that withdrawing off a fresh peripheral IV stick using the device did not increase our contamination rates but helped decrease IV contamination rates. | | | |

| Study | Outcome 1 | Outcome 2 | Outcome 3 | Outcome 4 | Outcome 5 |
|---|---|---|---|---|---|
| Baxter et al (2020)[16] | The use of Kurin resulted in a significant decrease in contamination rates, falling from 4.93% to 1.66%, a 66% reduction overall. | More than 140 patients benefitted from the implementation, avoiding the potential complications associated with BCC. | The authors estimated that patients who experienced BCC had an extended length of stay of nearly 4 days, compared with those patients with true negatives. | With an approximated cost of $4,000 per event, the hospital estimated that savings per year would be greater than $500k USD. | |

Abbreviations: BCC, Blood Culture Contamination; ED, Emergency Department; NHS, National Health Service; IV Intravenous; USD, United States Dollars

## 2.5 Adverse events

*Describe any adverse events and outcomes associated with the technology recorded in national regulatory databases such as those maintained by the Medicines and Healthcare products Regulatory Agency (MHRA) and the US Food and Drug Administration (FDA; the MAUDE, manufacturer and user facility device database). Provide links and references. If appropriate, do a systematic review and provide details in appendix C.*

There are no recorded adverse events relating to Kurin lock. The product is highly effective and safe to use.

*Describe any adverse events and outcomes associated with the technology in the clinical evidence.*

There are no documented adverse events.

## 2.6 Evidence synthesis and meta-analysis

*Although evidence synthesis and meta-analyses are not mandatory for a submission to be accepted, they are strongly encouraged if data is available to support such an approach. If an evidence synthesis is not considered appropriate, instead complete the section on qualitative review. If a quantitative evidence synthesis is appropriate, describe the methods used along with a rationale for the studies selected. The description of methods and any assumptions or calculations used should be clear and detailed such that the EAG can reproduce the analysis, see the example text in the table below and user guide for more information on what to include.*

The core studies as referenced in section 2 capture the primary end points in the rates of contaminated blood cultures (Table 7).

**Table 7: Evidence synthesis description of outcomes, sources and other relevant details**

| Study | Outcome | Intervention | Comparator | Comments |
|---|---|---|---|---|
| Hodson et al[18] | Blood Culture Contamination Rate Reduction 66% | Kurin 2% BCCR | Current Practise 6% baseline BCCR | 533 Patients had Kurin. Over 60% of Patients had a blood culture drawn from a Peripheral IV and used Kurin. |
| Atta M, MacGuire R (2022)[13] | Blood Culture Contamination Rate Reduction 65.6% | Kurin 3.1% BCCR | Current Practise 9% baseline. BCCR | 381 Patients had Kurin. High compliance with Kurin achieved the lowest BCC rates in weekly measures. |
| Parson K & Webb D (2023)[27] | Blood Culture Contamination Rate Reduction 48% | Kurin 2.6% BCCR | Current Practice 5% baseline BCCR | |
| Arenas M, et al. (2021)[19] | Blood Culture Contamination Rate Reduction 87% | Kurin 0.3% BCCR | Current Practice 2.2% baseline BCCR | 1,312 Kurin blood culture samples with a contamination rate of 0.3%. |
| O'Sullivan DM et al. (2019)[20] | Blood Culture Contamination Rate Reduction 74.3% | Kurin 0.4% BCCR | Current Practice 1.7% baseline BCCR | |
| Burnie J and Vining S (2021)[14] | Blood Culture Contamination Rate Reduction 51.4% | Kurin 1.4% BCCR | Current Practice 2.9% baseline BCCR | Second ED site BCC went from 5% to 1.6% with Kurin |
| Ostwald C & Whitsell K. (2021)[21] | Blood Culture Contamination Rate Reduction 97% | Kurin 0.2% BCCR | Current Practice 6.6% baseline BCCR | Zero BCC were seen in 874 Kurin BC samples |
| Sutton J et. al 2018[22] | Blood Culture Contamination Rate Reduction 53.8% | Kurin 1.2% BCCR | Current Practice 2.6% baseline BCCR | The post-intervention period included 2267 cultures and a contamination rate of 0.012, 95% CI |
| Arnaout, et al. (2021)[15] | Blood Culture Contamination Rate Reduction 63.3% | Kurin 1.1% BCCR | Current Practice 3.0% baseline BCCR | |

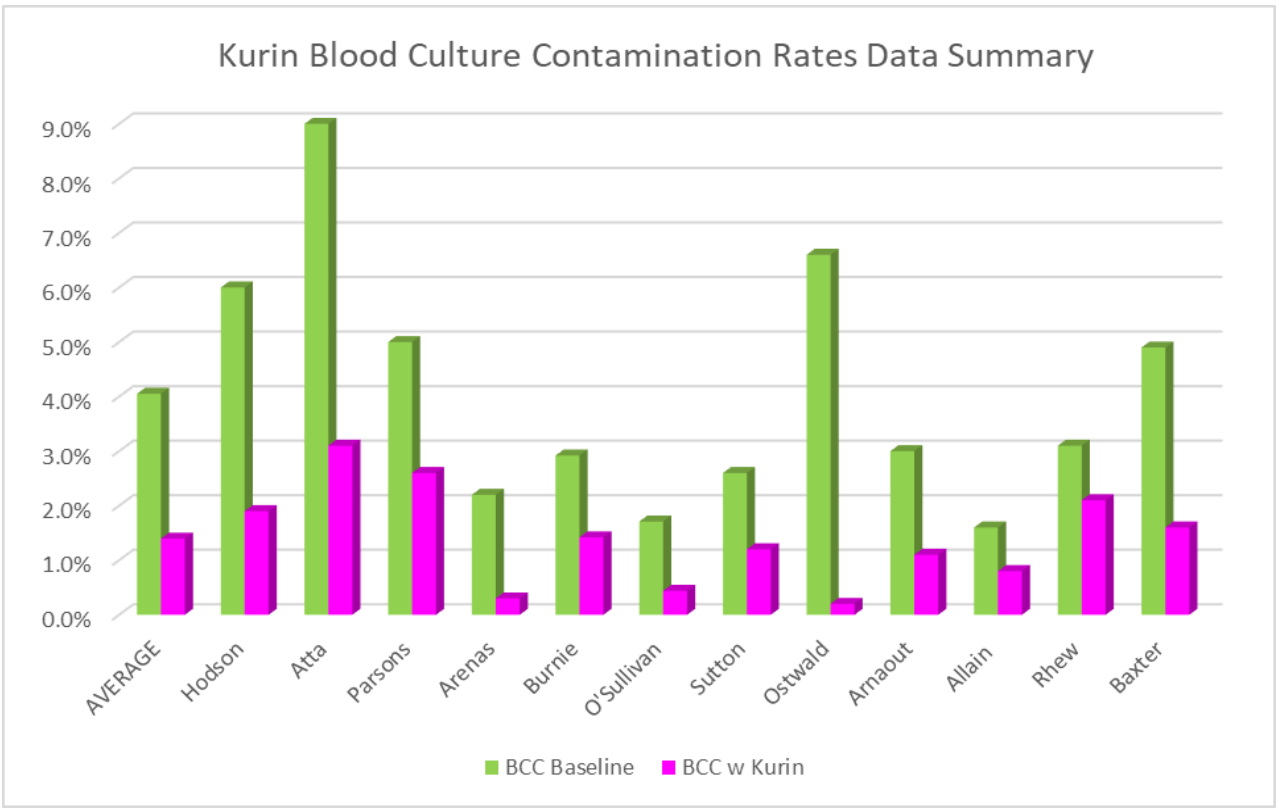
| Study | Outcome | Intervention | Comparator | Comments |
|---|---|---|---|---|
| Allain, M. (2018)[17] | Blood Culture Contamination Rate Reduction 50% | Kurin 0.8% BCCR | Current Practice 1.6% baseline BCCR | |
| Rhew (2021)[28] | Blood Culture Contamination Rate Reduction 32.3% | Kurin 2.1% BCCR | Current Practice 3.1% baseline BCCR | |
| Baxter et al (2020)[16] | Blood Culture Contamination Rate Reduction 67.3% | Kurin 1.6% BCCR | Current Practice 4.9% baseline BCCR | |

Abbreviations: BCCR, Blood culture contamination rate; BC, Blood Culture; ED, Emergency Department

*Report all relevant results, including diagrams if appropriate. Provide the results in an appropriate format (i.e. so it is accessible and can clearly be followed by an EAG so they can quality assure the analyses). See the user guide for more information on what to present here.*

Summary of key outcomes from Kurin impact studies

| EVIDENCE SYNTHESIS | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| YEAR | | 2022 | 2022 | 2023 | 2021 | 2021 | 2019 | 2018 | 2021 | 2021 | 2018 | 2021 | 2020 |
| COUNTRY | | UK | UK | UK | USA | USA | USA | USA | USA | USA | USA | USA | USA |
| HOSPITAL NAME | | Guys & St Thomas NHS Trust, London | Kings College NHS Trust, London | Shrewsbury & Telford NHS Trust | Central Texas Veterans Health Care System | TriHealth and Bethesda North Hospital, Cincinnati, Ohio. | Hartford Hospital, Connecticut | Bayfront Health St. Petersburg, FL | Oishei Children Hospital | University of Massachusetts Chan Medical School | Crouse Hospital | Cone Health, Greensboro, NC | St. Mary's Regional Medical Center, Russellville AR |
| Author | AVERAGE | Hodson | Atta | Parsons | Arenas | Burnie | O'Sullivan | Sutton | Ostwald | Arnaout | Allain | Rhew | Baxter |
| Kurin Blood Culture No.s | | 533 | 381 | 464 | 1,312 | | 250 | 2267 | 905 | | | | |
| BCC Baseline | 4.1% | 6.0% | 9.0% | 5.0% | 2.2% | 2.9% | 1.7% | 2.6% | 6.6% | 3.0% | 1.6% | 3.1% | 4.9% |
| BCC w Kurin | 1.4% | 1.9% | 3.1% | 2.6% | 0.3% | 1.4% | 0.4% | 1.2% | 0.2% | 1.1% | 0.8% | 2.1% | 1.6% |
| % Reduction | 65.5% | 68.3% | 65.6% | 48.0% | 86.4% | 51.4% | 74.3% | 53.8% | 97.0% | 63.3% | 50.0% | 32.3% | 67.3% |



*Explain the main findings and conclusions drawn from the evidence synthesis.*

The summary of the published data on the impact Kurin has on reducing blood culture contamination is extremely clear. The combined average reduction in blood culture contamination rates is 67.5% across all the available studies detailed above.

Observationally blood culture contamination rates in the USA are generally lower than the UK, but with the adoption of best practise clinical procedures it is possible to achieve a sub 1% contamination rate and even zero!

## 2.7 Summary and interpretation of clinical evidence

*Summarise the main clinical evidence, highlighting the clinical benefit and any risks relating to adverse events from the technology.*

The main clinical evidence consistently aims to assess if blood culture contamination rates are reduced from the respective hospitals baseline by the introduction of the Kurin Lock blood culture collection system. Consistently Kurin has reduced (48–66%) blood culture contamination rates in all UK NHS Hospitals where it has been introduced. In published studies from the US, reductions of >50% have been consistently recorded. This evidence supports the primary outcome measure achieved in that Kurin significantly reduces the risk of blood culture contamination. This in turn improves the outcomes for patients.

The outcome benefits of reducing blood culture contamination rates are well documented in the literature:

1. Improving diagnostic accuracy so the patient can be treated appropriately.
2. Avoidance of unnecessary antibiotics for patients and so contributing positively towards antimicrobial stewardship priorities in addressing antimicrobial resistance.
3. Reducing unnecessary further interventions, such as lines being removed and further diagnostic tests on patients.
4. Decreasing length of stay (LOS) for an already overstretched NHS healthcare system.
5. Improving efficiencies within the healthcare system (physician time, laboratory time, patient management etc.) with wide-reaching costs to be avoided downstream.



Kurin is simple and a highly effective quality improvement measure for NHS Hospitals to utilise in improving patient care.

No adverse events have been reported with Kurin to date. It is a simple and elegant device that is safe to use on patients by healthcare providers.

*Briefly discuss the relevance of the evidence base to the scope. This should focus on the key claimed benefits described in the scope and the quality and quantity of the included studies.*

All the evidence associated with Kurin is focused on measuring the rates of blood culture contamination pre-and post-intervention. Kurin consistently achieves the primary end point in all studies by reducing significantly blood culture contamination rates. As detailed in the evidence, the downstream benefits of reducing blood culture contamination are listed in the scope:

1. Improving diagnostic accuracy so the patient can be treated appropriately.
2. Avoidance of unnecessary antibiotics for patients and so contributing positively towards antimicrobial stewardship priorities in addressing antimicrobial resistance.
3. Reducing unnecessary further interventions, such as lines being removed and further diagnostic tests on patients.
4. Decreasing length of stay (LOS) for an already overstretched NHS healthcare system.
5. Improving efficiencies within the healthcare system (physician time, laboratory time, patient management etc.) with wide-reaching costs to be avoided downstream.

All the clinical studies/posters (12 in total) on Kurin to date are real life product interventions in a simple before and after intervention design. Most are centred around the Emergency Department as this is the biggest source of blood culture contamination within the acute hospital setting.



*Identify any factors which might be different between the patients in the submitted studies and patients having routine care in the NHS. Provide appropriate references, including clinical experts who you consulted, to identify these differences.*

The clinical experience of Kurin within NHS Hospitals (as documented in the 3 product evaluation studies submitted by; Hodson et al, Atta et al and Parson et al) are real world busy NHS emergency department scenarios. Kurin was evaluated in these hospitals during the COVID19 pandemic when departments were often stretched with excess patients and dealing with staff shortages. Kurin helped these hospitals during these evaluations reduce the burden and consequences of managing patients who had a contaminated blood culture.

*Describe any criteria that would be used in clinical practice to select patients for whom the technology would be most appropriate. Provide appropriate references, including clinical experts who you consulted, to identify these criteria.*

Blood culture is considered to be the “gold standard” method of investigation for the detection of microorganisms in the blood that lead to the diagnosis of serious infections. Kurin Lock should be used on any patient that the clinician has decided needs peripheral blood culture taken.

Hodson et al, Atta et al and Parson et al are all NHS testaments to the impact Kurin has on reducing blood culture contamination and supporting NHS England[23] initiatives for adopting best practise in blood culture collection.

*Briefly summarise the strengths and limitations of the clinical evidence for the technology.*

There are multiple journal publications which detail the clinical and economic impact of contaminated blood cultures. As stated, the published clinical evidence (12 studies in total) on Kurin is focused around assessing its impact in lowering the primary end point of blood culture contamination. The benefits of this are well evidenced in multiple journal publications detailing the consequences of blood culture contamination.

As Kurin is a device that prevents the consequences of contaminated blood cultures it is often an assumption that the consequences have actually been prevented.



## 2.8 Ongoing studies

*Provide details of all relevant ongoing or planned studies using the technology. See the user guide for full details of the information required and suggested table format.*

There are additional UK-based product evaluations underway which we expect to report results on within the next 6 months, for example another NHS Trust is in the midst of a Kurin intervention product evaluation to assess its effects on lowering the rates of blood culture contamination within their hospital.

# 3 Published economic evidence

## 3.1 Identification and selection of studies

*Economic evidence in this section refers to economic evidence specifically on the use of the intervention technology. Unpublished economic evidence is not normally accepted unless there is justification provided why it has not been published and the study considered particularly important and relevant. Complete the following information about the number of studies identified.*

*Report in full transparent and reproducible detail the search methods as used for all search resources, and provide a detailed list of any excluded studies, in appendix D. Number of studies reported below should be after any duplicates have been removed.*

A targeted literature search was conducted to identify relevant published health economic studies on the contamination rate following blood culture sample collection in a hospital setting.

Searches were conducted using Medline (PubMed) and were limited to publications from 1983 to 2003. Search terms related to “blood culture contamination” and “false-positive” results. The full search strategy is presented in Appendix D. The database search identified 91 published records potentially relevant to blood culture contamination in a hospital setting, along with an additional 2 posters which were identified through a grey literature search. Following screening and assessment of both title and abstract, 60 records were excluded. Following assessment of the remaining 33 full-text records, 23 were subsequently excluded. A total of 8 studies were included in the final dataset, along with 2 additional posters (Table 8).

**Table 8. Study selection process for the targeted literature search**

| Study selection | Number of records |
|---|---|
| Number of studies identified in a systematic search | 91 |
| Number of studies identified as relevant (i.e. directly relevant to the decision problem by ensuring it aligns with the eligibility criteria outlined in the scope) | 8 |
| Additional articles identified through manual bibliography review | 2 |
| Of the relevant studies identified, the number of published, peer reviewed studies | 8 |
| Of the relevant studies identified, the number of posters | 2 |

## 3.2 List of relevant economic studies

*In Table 9, provide brief details of any published economic studies or abstracts identified as being relevant (i.e. directly relevant to the decision problem by ensuring it fits the eligibility criteria outlined in the scope).*

A summary of relevant economic studies that assessed cost are presented in Table 9.

**Table 9: Summary of relevant economic studies**

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| Lalezari A et al. 2020. Israel, Work was supported by internal departmental funding[29] | N/A as the study was a randomised, parallel assignment, open label trial | 756 patients were enrolled, aged <18 years, in Hadassah-Hebrew University Medical Centre, Israel | **Intervention:** Regular vacuum specimen tubes for ISDT (intervention) **Comparator:** commercially available sterile diversion devices (comparator) | **Costs (NIS):**<br>• Blood culture collection and processing: 100 NIS<br>• Organism identification and antimicrobial susceptibility testing: 98 NIS<br>• Daily antibiotic therapy: 286 NIS<br>• Serum vancomycin assay: 218 NIS<br>• Daily non-intensive care unit (floor): 2,292 NIS<br><br>**Resource use:**<br>Administration of intravenous vancomycin upon receipt of a positive blood culture result: | N/A as the study was an open trial. From the open trial, the overall contamination rate with the ISDT was 1.7% compared with 5% with the standard method. Per-patient costs associated with a contaminated blood culture was 5,791 NIS more than for patients with negative cultures. The mean length of stay for patients with contaminated blood cultures was 2.35 days longer than for patients with a negative culture | N/A |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | | | | • Negative blood culture: 2%<br>• Contaminated blood culture: 30%<br>• True bacteraemia: 10%<br>Drawing an additional set of blood cultures upon receipt of a positive blood culture result:<br>• Negative blood culture: 24%<br>• Contaminated blood culture: 73%<br>• True bacteraemia: 60%<br>Hospital length of stay (days):<br>• Negative blood culture: 5.73<br>• Contaminated blood culture: 8.08<br>• True bacteraemia: 11.06 | | |
| Skoglung et al. 2019. USA, project was supported by a research grant from Magnolia Medical Technologies, Inc., Seattle, WA[9] | A decision analysis model was developed to identify the cost benefit of the use of an ISDD device in the ED.<br>A decision analysis model was built using TreeAge software | Patients comprised of all patients in the ED with an order for blood culture collection.<br>Patients were excluded if they did not have two blood culture sets drawn. | **Intervention**: An initial specimen diversion device (SteriPath)<br>**Comparator**: Collection by a nurse or phlebotomist via venepuncture with a clean, but nonsterile, | **Unit costs ($, 2019):**<br>• Blood culture collection and processing: $36<br>• Organism identification and AST with RDT: $300 | The routine implementation of an ISDD for blood culture collection in the ED was cost beneficial compared to conventional blood culture collection methods. | The sensitivity analysis confirmed the robustness of the model to a range of base-base parameter values.<br>The most influential parameters in the model for the |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | (TreeAge Software, Inc., Williamstown, MA). The structure was modified from a previously published model assessing the cost implications of blood culture contamination in the ED. The model was developed to perform a cost-benefit analysis comparing the routine use of an ISDD for blood culture collection in the ED compared to the use of conventional practices without an ISDD | In total, 28 patient encounters were observed, in which a contaminated blood culture was collected in the ED | technique using 2% chlorohexidine in 70% isopropanol as the antiseptic or similar | • Organism identification and AST without RDT: $104<br>• Daily antibiotic therapy: $75 (a composite daily pharmacy cost of antibiotic provision was constructed using institutional purchasing data for several broad-spectrum intravenous antibiotics at standard daily doses that are commonly administered as empirical therapy in patients with suspected blood stream infections)<br>• Serum vancomycin assay (laboratory): $68<br>• Serum vancomycin assay (pharmacy): $41<br>• Non-IC (floor) (per day): $1,500<br>• Follow-up tests and procedures: $1,100<br>• Hospital-acquired infection: $5,000 | Using a baseline contamination rate of 6%, the total expected cost of a blood culture patient episode was $8,893 using an ISDD and $9,165 with conventional methods in hospital utilising RDT, resulting in a cost saving of $272 per blood culture collection.<br>In hospital, not utilising RDT, the total expected cost of a blood culture patient episode was $8,868 with an ISDD and $9,130 with conventional methods, resulting in a cost saving of $261 per blood culture collection.<br>In addition, considering only direct microbiology and pharmacy costs, the expected cost savings were $28 in hospital using RDT and $16 not using RDT. | intervention was the duration of antibiotics with negative culture if discontinued by culture finalisation, unit cost of SteriPath for two sets of blood cultures and microbiology workup cost of positive blood culture with RDT.<br>The most influential parameters in the model for the comparator was the baseline blood culture contamination rate, duration of antibiotics with negative culture if discontinued by culture finalisation, and microbiology workup cost of positive blood culture with RDT.<br>A one-and two-way sensitivity analyses were performed considering only direct purchasing and labour costs within the pharmacy and microbiology departments. The |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | | | | • Adverse drug reaction: $150<br><br>**Resource use:**<br>• Duration of inpatient antibiotics with negative blood culture (days)<br>• Empirical antibiotics, stopped by culture finalisation: 3<br>• Empirical antibiotics, not stopped by culture finalisation: 9<br>• No empirical antibiotics: 0<br>• Duration of inpatient antibiotics with contaminated culture (days):<br>• Empirical antibiotics, stopped by culture finalisation: 4<br>• Empirical antibiotics, not stopped by culture finalisation: 10<br>• No empirical antibiotics, stopped by culture finalisation: 1.5<br>• No empirical antibiotics, not | Implementation with an ISDD was associated with a 1.7% absolute reduction in number of patients receiving at least one dose of vancomycin after blood culture collection in the ED every month, with ISDD associated with the complete avoidance of vancomycin administration in 6 additional patients per month | threshold values for the unit cost of an ISDD at which the strategy of routine ISDD use was equal in direct costs to the conventional BC collection strategy were $28 with RDT and $16 without RDT. Using a two-was sensitivity analysis of the expected per culture direct cost of routine ISDD use versus SoC in a hospital with RDT demonstrated that the use of an ISDD was the least costly strategy at an ISDD cost of $30 over a range of baseline blood culture contamination rates above 6% |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | | | | stopped by culture finalisation<br>• Duration of inpatient antibiotics with true bacteraemia (days): 10<br>• Hospital length of stay (days):<br>• Negative blood culture: 5<br>• Contaminated blood culture: 7<br>• True bacteraemia: 9 | | |
| Dempsey et al. 2019[30] | N/A, as the study was a systematic review | Adult and paediatric population, in the emergency department and inpatient setting | N/A | N/R | Up to 59% of patients received vancomycin unnecessarily as a result of blood culture contamination, resulting in increased pharmacy charges between $2,397 and $11,152 per patient. Hospital LOS ranged from 1-22 days | N/A |
| Alahmadi et al. 2011. Northern Ireland. No funding[12] | N/A, the study was a retrospective case-control study (from July 2007 to July 2008) | Patients were matched for age by two categories: 19-64 years and >64 years. The study was carried out in Antrim Area Hospital in Northern Ireland, a 426-bedded district general teaching | N/R | **Costs (£, 2017):**<br>• Antibiotic: £157 (false positive); £14 (true negative)<br>• Microbiology test: £120 (false positive); £32 (true negative) | Differences in medians, between cases and controls, for the LOS and the total costs were 5.4 days and £5,001.5, respectively.<br>Considering 254 false-positive blood cultures that had | N/R |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | | hospital serving a population of around 420,000. A total of 142 patients who had false-positive blood culture cases were matched and compared with patients who had true-negative blood culture (controls) | | • Radiology test: £0 (false positive); £14 (true negative)<br>• Biochemistry test: £16 (false positive); £14 (true negative)<br>• Hotel costs: £5,060 (false positive); £1,890 (true negative)<br><br>**LOS:**<br>• In hospital from admission to sample taken in days: 1 (false positive); 1 (true negative)<br>• In hospital from admission to discharge: 13 (false positive); 8 (true negative) | occurred in the study, patients with false-positive blood cultures added 1,372 extra hospital days and incurred additional hospital costs of £1,270,381 per year | |
| Waltzman, M and Harper, M, 2001. USA[11] | N/A, a retrospective review of microbiology and medical records was performed | All patients who were treated in the ED from 1 January 1993 to 31 December 1996, aged 3-36 months who had a rectal temperature of >39 degrees Celsius at the time of triage were included. A total of 11,908 eligible | **Intervention**: Standard practice (included the use of three separate clean preparation pads that were saturated with 70% isopropyl alcohol for skin preparation) | Note: Charges rather than costs were reported, as they reflect the actual dollar amounts at the time of the study and were not adjusted for inflation.<br><br>**Inpatient charges included:** | An average of $3.4 additional cost per patient charge was incurred as a result of a false-positive blood culture test.<br><br>A lower rate of false-positive charges was obtained in the study: 0.9% | N/R |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | | patients were included | | • Hospitalisation: $1,200 per charge<br>• Treatment with IV antibiotics: $188.60 per charge<br>• Chemistry tests: $56 per charge<br>• Hepatic transaminase determination: $32 per charge<br>• Prothrombin time/ partial thromboplastin time determination: £30 per charge<br>• Erythrocyte sedimentation rate: $15 per charge<br>• Bone scan: $977 per charge<br>• Primary care physician visit: $56.25 per charge<br>• Emergency department visit: $175 per charge<br>• Complete blood count: $50 per charge<br>• Repeated blood culture test: $76 per charge | | |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | | | | • Urine analysis/ culture test: $42 per charge<br>• CSF analysis test: $147 per charge<br>• Chest radiography: $175 per charge<br>• Antibiotic treatment with Amox/clav: $85 per charge<br>• Antibiotic treatment with amoxicillin: $18 per charge<br>• Antibiotic treatment with ceftriaxone: $35 per charge | | |
| Zwang, O and Albert, R. 2006. USA[31] | N/A, as the study was a retrospective analysis of 939 sets of cultures drawn | Denver Health Medical Centre, a 400-bed university-affiliated public safety net hospital | **Intervention**: A single venepuncture, regardless of the number of bottles sent for culturing | **Laboratory charges for blood cultures in July 2005 ($):**<br>• True negative cultures-<br>• Phlebotomy: $13.25 per charge<br>• Microbiology: $147.50 per charge<br>• False positive cultures:<br>• Phlebotomy: $13.25 per charge<br>• Microbiology: $147.50 per charge | Patients with false-positive blood cultures added 145–220 extra hospital days and accrued additional charges of $4,305,000 and costs of $1,808,100 | N/R |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | | | | • Identification: $60.75 per charge<br>  • Sensitivity: $89.75 per charge<br><br>**Resource use:**<br>• Hospital LOS True negative: 5 days<br>• LOS false-positive: 8 days | | |
| Geisler et al. 2019. USA[32] | N/A, as the study was a retrospective matched survival analysis | 135 patients identified as having a false-positive blood culture were matched with a patient with a true-negative blood culture<br><br>For the hospital perspective, a typical, medium-sized hospital with 250–400 beds and an annual volume of 10,000 blood cultures was assumed | Implementation of dedicated phlebotomists and a device-based treatment (ISDD, SteriPath) were chosen as comparators | • Additional blood culture set (1.3 unit): $10<br>• Gram strain, identification/ speciation, and subculture with susceptibility resistance: (1 unit): $103<br>• Additional length of stay (2.35 days): $1,361<br>Antibiotic treatment<br>• Empiric treatment of gram-positive cocci (3 days of treatment): $61<br>• Empiric treatment of gram-positive rods (3 days): $73 | • Patients with blood culture contamination experienced a mean increase in LOS of 2.35 days.<br>• Avoiding blood culture contamination would decrease costs by $6,463 ($4,818 spent during hospitalisation).<br>• Typically, a 250-400-bed hospital could save $1.3 million. An ISDD is estimated to save $1.9 million | A sensitivity analysis was performed by varying the inputs by +/-30%, the interquartile range for primary data, and a 2-8% false-positive rate |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | | | | • Definite composite inpatient treatment (1 day): $47<br>• Definite composite outpatient treatment (10 days): $61<br>• Outpatient parenteral antibiotic therapy (10 days): $385<br>• Additional inpatient blood tests and imaging: $625<br>• Hospitalisation-associated adverse events (CDI), 32.6 incidence: $8,560<br>• Venous thromboembolism (0.4 incidence): $8,138<br>• Hospital-acquired pneumonia (1.3 incidence): $16,527<br>• Catheter-related UTI (18.2 incidence): $1,009<br>• Fall (14.9 incidence): $332<br>• Delirium (311.1 incidence): $4,051<br>• LOS for true-negative: 6.67 days | | |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | | | | • LOS for false-positive: 9.02 days | | |
| Sheppard, C. et al. 2008. USA[33] | N/A | 2,986 blood cultures were collected in the ED | **Intervention**: Phlebotomist **Comparator**: Non phlebotomist | • Phlebotomist cost per hour: $13.49<br>• Medical technologists per hour: $24.44 | • Contamination was reduced for phlebotomist collection versus baseline (1.1% and 5%)<br>• Cost-savings: $445,523.80 | N/R |
| Arenas, M. et al. 2020. USA[19] | N/A, as the study was a retrospective record review study | 4,030 blood samples were collected and analysed from November 2017 to February 2019, in a single-centre ED in an urban 146-bed teaching hospital | **Intervention**: Two blood culture-diversion devices. **Comparator**: No device.<br>One device (Magnolia Medical Technologies) is manually triggered vein-to-bottle closed system that isolates the first 1 mL to 2 mL of blood from the rest. The other diversion device, Kurin, passively diverts less than 0.15 mL of blood into a U-shaped flash chamber. | • Gram-positive and gram-negative culture and sensitivity tests: $20 and $40, respectively.<br>• Rapid BC identification: $136 | False-positive BC ranges from $4,500 to $10,000 | N/R |
| Klutcher, J. et al. 2022. USA[6] | N/A, as the study was a single-centre, retrospective case-control risk factor and | 13,782 blood cultures in a 509-bed tertiary-care university | **Intervention**: Patients with a positive blood culture revealing microbial | N/R | • 7.3% were contaminated blood cultures (cases) and | N/R |

| Author, year, location, status and funding | Summary of decision model | Patient population and setting | Intervention and comparator | Unit costs and resource use | Decision model outputs | Description of Sensitivity or scenario analyses |
|---|---|---|---|---|---|---|
| | clinical outcome analysis | hospital ED from 2014 to 2018 | contaminants were considered cases<br>**Comparator**: Patients with negative blood cultures were considered controls | | 81.7% were negative (controls)<br>• LOS for cases: 7.9 days<br>• LOS for controls: 6.6 days<br>• Antibiotic length of treatment case 6.2 days<br>• Antibiotic length of treatment for controls: 5.2 days<br>• Hospital charges for cases: $36,008<br>• Hospital charges for controls: $28,875<br>• Vancomycin was ordered more frequently: 81% versus 65% and administered for longer: 3.5 days versus 2.5 days | |

Abbreviations: AST, antimicrobial susceptibility testing; CSF, cerebrospinal fluid; ED, emergency department; ISDD, initial specimen diversion device; ISDT, initial specimen diversion technique; LOS, length of stay; N/A, not applicable; N/R, not reported; NIS, New Israeli Shekel; RDT, rapid diagnostic testing; SoC, standard of care; USA, United States of America.

## 3.3 Critical appraisal of relevant economic studies

*In Appendix E, provide the complete quality assessment for each included study using an appropriate and validated tool: a table is provided in Appendix E based on the NICE economic evaluations appraisal checklist (2019). See the user guide for the information required.*

*Summarise the relevance of each of the included studies to the decision problem in Table 10.*

**Table 10. Critical appraisal summary for economic evidence**

| Study | What are the main differences in resource use and clinical outcomes between the technologies? | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the decision model? | Which cost analysis was done in the study? Explain the results. | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|---|---|
| Lalezari, A et al. 2020[29] | The differences in utilisation of resources connected to blood culture and LOS were assessed between the groups of patients with true bacteraemia, contaminated blood cultures and randomly matched patients with negative blood cultures | The study demonstrates that ISDT through altered order of test tube versus current blood culture sampling significantly reduces contamination of blood cultures. It demonstrates that blood culture contamination results in additional procedures and increased hospitalisations. It illustrates that diversion of blood significantly | It supports the claims that hospital LOS and administration of vancomycin is increased with contaminated blood cultures | Yes, the hospital LOS will be included within the ICU subgroup setting | The cost analysis was from the hospital perspective. Differences in utilisation of resources associated with the contaminated blood culture and LOS were assessed between the group of patients with true bacteraemia, contaminated blood cultures and group of randomly matched patients with negative blood cultures. The per- | The study was conducted in Israel, and therefore medical practices and hospital costs may vary. Furthermore, the cost analysis did not include all services | Unfunded investigator-initiated study |

| Study | What are the main differences in resource use and clinical outcomes between the technologies? | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the decision model? | Which cost analysis was done in the study? Explain the results. | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|---|---|
| | | reduces contamination | | | patient hospital expenditures associated with a contaminated blood culture were calculated from previously published parameters. Pricing was based on the 2018 Israel Ministry of Health formal price list. Furthermore, blood cultures were drawn by staff from several disciplines. The number of blood cultures drawn were too small to stratify the contamination rate according to the personnel. Therefore, the impact of ISDT may differ in places where only a phlebotomist takes blood cultures | | |

| Study | What are the main differences in resource use and clinical outcomes between the technologies? | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the decision model? | Which cost analysis was done in the study? Explain the results. | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|---|---|
| Skoglung, E et al. 2019[9] | Contamination rate without an ISDD was 1.78%, which decreased to 0.22% using an ISDD. ISDD resulted in shorter LOS, and fewer antibiotic administrations | The results demonstrate that the routine implementation of an ISDD for blood culture collection in the ED is cost beneficial compared to conventional care (collection by a nurse or phlebotomist via a venepuncture with a clean technique using 2% chlorohexidine in 70% isopropanol) | It supports the claims that when implementing an ISDD in a hospital setting, with a baseline contamination rate of 6%, that it is associated with a cost saving of $272 per blood culture in terms of overall hospital costs, of which $28 are direct costs | Yes, specifically:<br>• Probability of stopping antibiotics by culture finalisation<br>• Probability of empirical antibiotics at culture collection (71%, with a negative or contaminated blood culture)<br>• Duration of inpatient antibiotics with negative blood culture days<br>• Hospital LOS and,<br>• Duration of inpatient antibiotics with contaminated culture days | The cost analysis was from the hospital perspective. The indirect costs included those related to an increased hospital LOS, additional procedures, adverse drug reactions and hospital-acquired infections. The study conducted a cost benefit analysis using a decision analysis model. The model assessed the costs associated with ordering a blood culture in the ED, including microbiology, pharmacy, and indirect hospital expenditure | The study assumed that all bacterial growth identified from a BC was subject to a full microbiological identification and susceptibility testing, however this is not generalisable to a range of settings, as not all institutions are likely to subject every organism identification as a potential skin contaminant to full antimicrobial susceptibility testing. The model did not account for any wastage of the ISDD, or additional time needed to use or dispose of the device | The study was supported by a research grant from Magnolia Medical Technologies, Inc., Seattle, WA |

| Study | What are the main differences in resource use and clinical outcomes between the technologies? | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the decision model? | Which cost analysis was done in the study? Explain the results. | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|---|---|
| Dempsey, C et al. 2019[30] | Increased LOS and antibiotic use | The systematic literature review demonstrated that interventions to reduce the risk of blood culture contamination would avoid downstream economic costs | It supports the claim that increased hospital LOS and unnecessary treatment with antibiotics is a result of blood culture contamination | No | The cost analysis was performed considering only the costs that a single hospital would incur (hospital perspective) | There is a potential that there was an incomplete retrieval of relevant articles | The study was funded in part by Magnolia Medical |
| Alahmadi, M et al. 2011[12] | The increased LOS and additional hospital costs are the main differences between blood culture collection techniques | This study details the costs of contaminated blood cultures within an NHS hospital. These costs can be applied to the impact of reducing blood culture contamination and the impact Kurin has on this effect | This evidence supports the claim that contaminated blood cultures cost on average £5,001 and an extra 5.4 bed days within an NHS Hospital. Therefore, demonstrating that false-positive blood cultures have an incremental impact on increased hospital LOS, laboratory, and pharmacy costs | Yes, specifically:<br>• The cost of antibiotic, microbiology, biochemistry, and haematology test<br>• The LOS in hospital from admission to discharge for false-positive and true negative results will be included for patients in the general hospital subgroup setting | The cost analysis was performed considering only the costs that a single hospital would incur (hospital perspective).<br>The objective of the present investigation was to determine the impact of the false-positive blood culture results on the following outcomes: length of stay, hotel costs, antimicrobial costs, and costs of laboratory and | The data from this study is now over 12 years old, so the costs will have altered in that time<br>The estimated charges associated with contaminants in the study site hospital may not be directly generalisable to other hospitals since this study was conducted in a single medium-sized teaching hospital, and other hospitals may vary in their healthcare | No funding sources were reported |

| Study | What are the main differences in resource use and clinical outcomes between the technologies? | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the decision model? | Which cost analysis was done in the study? Explain the results. | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|---|---|
| | | | | | radiological investigation<br>General characteristics of the study population are listed in Table I of the study. Median hotel costs for cases were £5,060 compared with £1,890 for controls. Median antibiotic use and median microbiology test charges for cases and controls were £157 vs £14 and £120 vs £32, respectively. Details of the charges for cases and controls are shown in Table II of the study | practices and charges | |

| Study | What are the main differences in resource use and clinical outcomes between the technologies? | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the decision model? | Which cost analysis was done in the study? Explain the results. | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|---|---|
| Waltzman, M., & Harper, M. 2001[11] | | The findings demonstrate the additional costs associated with follow-up tests | No | No | The cost analyses were performed considering only the costs that a single (large urban) hospital would incur (hospital perspective). | The study is over 20 years old, so the costs will not be reflective of current practice. Furthermore, the study does not outline the additional LOS or antibiotic treatment associated with false positives versus true negatives | Funding is not reported |
| Zwang, O & Albert, R. 2006[31] | There was no comparison between technologies, rather the results demonstrated the cost impact that false-positive blood culture results have on the health service. The results demonstrate that false-positive blood culture result have a significant impact on annualised costs and hospital days/year | The findings demonstrate that the LOS for patients with a false-positive (8 days) is 3 days longer than those with a true negative (5 days) | The results support the impact that blood culture contamination has on hospital resource use and costs | No | A cost analysis was performed considering only the costs that a single hospital would incur (hospital perspective)<br>Costs associated with a true-negative blood culture was determined by summing the changes for phlebotomy and microbiological testing and applying the cost- | The study is not able to demonstrate a cause-effect relationship between false-positive cultures and the charges associated resulting from them. However, recent studies suggested that the excess LOS from such patients is attributable to the false-positive culture itself | Funding is not reported |

| Study | What are the main differences in resource use and clinical outcomes between the technologies? | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the decision model? | Which cost analysis was done in the study? Explain the results. | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|---|---|
| | | | | | to-charge ratio reported on the Medicare Cost report for inpatient services.<br>The cost of a false-positive was determined by adjusting the data reported by Bates et al. (1991) for changes in the Consumer Price index and comparing the hospital charges for the patients in their sample who had a false-positive culture against those who did not | | |
| Geisler, B et al. 2019[32] | The hospital LOS and increased antimicrobial therapy are the main differences between the technologies | The results highlight that blood culture contamination increases LOS and unnecessary antimicrobial therapy<br>The results specifically show | The results support that false-positive blood cultures generate incremental diagnostic and treatment costs (£6,000), because of prolonged | No | A cost analysis compared standard of care with interventions for reducing blood culture contamination from the hospital perspective | The LOS data originated from an annual dataset from a single institution. However, following comparison across studies, the projections are conservative. Furthermore, the | The study was funded by Magnolia Medical Technologies, Inc |

| Study | What are the main differences in resource use and clinical outcomes between the technologies? | How are the findings relevant to the decision problem? | Does this evidence support any of the claimed benefits for the technology? If so, which? | Will any information from this study be used in the decision model? | Which cost analysis was done in the study? Explain the results. | What are the limitations of this evidence? | How was the study funded? |
|---|---|---|---|---|---|---|---|
| | | that ISDD is the single most effective intervention to reduce costs related to false-positive blood cultures | periods of hospitalisation | | | calculations did not include the cost of implementing the respective intervention strategies. However, it is assumed that ISDD costs will account for no more than 20% of the per culture cost saving | |
| Sheppard, C. et al. 2008[33] | Quality of care improves when samples are taken by a phlebotomist | The results highlight that care is improved when standards of practice are in place | This study does not analyse the impact of technology on blood culture contamination rates, rather the person trained (phlebotomist versus non phlebotomist). However, it does support that quality of care is improved | No | The cost analysis included in the study was from the hospital perspective | Patient selection bias could not be excluded | No funding is reported |

Abbreviations: ED, emergency department; ICU, intensive care unit; ISDD, initial specimen diversion device; ISDT, initial-specimen diversion techniques; LOS, length of stay; NHS, National Health Service.

## 3.4 Results from the economic evidence base

*Describe the results from each of the relevant economic studies. Use a table if appropriate.*

The results of the economic evidence base and how these data are utilised in the economic model are reported in Table 11.

**Table 11: Results from the economic evidence base**

| Study | Input used in the economic model | Source |
|---|---|---|
| Hodson et al. (2022)[18] | • Number of patients requiring a blood culture collection (1,279) | Hodson, J., Stebbing, J., Nneoma, O. Reducing blood culture contamination rates in accident and emergency (A&E) using an initial specimen diversionary device. Guy's and St Thomas' NHS Foundation Trust. 2022. |
| Alahmadi et al. (2011)[12] | Follow-up tests:<br>• Microbiology test<br>• Biochemistry test<br>• Haematology test | Alahmadi, Y. et al., Clinical and economic impact of contaminated blood cultures within the hospital setting. 2011 |
| Skoglund et al. (2019)[9] | • Use of vancomycin<br>LOS in the **A&E**:<br>• True negative: 5.0<br>• False-positive: 7.0<br>• True positive: 9.0 | Skoglung, E. et al., Estimated clinical and economic impact through use of a novel blood collection device to reduce blood culture contaminatino in the emergency department: a cost-benefit analysis. 2019 |
| Rupp et al. (2017)[34] | Baseline bacteraemia risk: 7.4%<br>Probability of empirical antibiotics at culture collection | Rupp et al., Reduction in Blood Culture Contamination Through Use of Initial Specimen Diversion Device. Clinical Infection Diseases. 2017 |
| Atta et al. (2022)[13] | Rate of BC contamination (SoC): 9% | Atta, M., Mcguire, R. Reducing false positive blood cultures in an adult NHS emergency department using a Kurin Lock blood culture collection device. King's College Hospital poster |
| Atta et al. (2022)[13] | Reduction of BC contamination from using Kurin Lock: 65.5% | Atta, M., Mcguire, R. Reducing false positive blood cultures in an adult NHS emergency department using a Kurin Lock blood culture collection device. King's College Hospital poster |
| Skoglund et al. (2019)[13] | Duration of empirical antibiotics:<br>• Stopped by culture finalisation: 1.5 days<br>• Identification of false positive: 3.0 days<br>• Confirmed bacteraemia: 9.0 days | Skoglung, E. et al., Estimated clinical and economic impact through use of a novel blood collection device to reduce blood culture contamination in the emergency department: a cost-benefit analysis. 2019 |

Abbreviations: A&E, accident and emergency; BC, blood culture; LOS, length of stay; SoC, standard of care.

# 4 Decision model description

*Company decision model*

*This section refers to the decision model that you have submitted.*

## 4.1 Patients

*Describe which patient groups are included in the decision model.*

Kurin Lock is used for the collection of blood samples for blood culture analysis. The technology diverts and isolates the first flash (0.15 mL) of blood, which may contain contaminants that can lead to a false-positive blood culture result.[35] Kurin Lock is used for patients who require a blood culture test within a secondary care NHS setting, including general hospitals wards, the ICU, A&E, acute medical and surgical wards, renal dialysis, and cancer treatment departments. Although blood culture contamination can happen in any hospital setting, the literature identified by the SLR (Section 3) has found increased blood culture contamination rates in the A&E, ICU and general hospital wards settings.[9] The analysis therefore considers these three settings. The A&E was chosen as the base case setting due to the literature identified from the SLR frequently modelling and reporting outcomes within the A&E setting,[9, 13, 25]. Furthermore, the literature identified by the SLR postulated that contamination rates are higher in the A&E than other hospital settings.[36] As empiric antibiotic treatment is often initiated based on clinical suspicion of bacteraemia, patients were therefore also split by age group (adults and paediatrics) to align with antibiotic treatment posology,[9, 11, 12, 29, 30] where different doses for patients aged >12 and <12 years are recommended.

The patient groups modelled in the analysis were patients:

- Requiring a blood culture within the A&E setting
- Aged >12 years
- Aged <12 years

## 4.2 Technology and comparator(s)

*State the technology and comparators used in the decision model. Provide a justification if the comparator(s) used in the decision model is different to that in the scope.*

The technology used in the model was Kurin Lock, a CE-marked class IIa medical device, intended for blood culture sample collection in the hospital setting. Kurin Lock is self-contained and consists of a blood collection tube and needle, a flash chamber that collects, isolates, and shows the first flash (0.15 mL) of blood, and a blood collection tube that collects the remaining sample to be sent for culturing and analysis. The first flash is that most likely to contain a contaminant such as skin microbes. In blood samples collected with Kurin Lock, these contaminants are isolated in the first flash which has been shown to result in a lower rate of false-positive results compared with a standard blood culture collection set. A picture of Kurin Lock is presented below (Figure 5).

**Figure 5. Kurin Lock**[37]

The comparator used in the cost analysis was the standard blood culture collection set, as defined in the scope and used as standard of care (SoC) in the NHS. Standard of care is defined as the collection of blood through a safety needle and adaptor cap for connecting to the blood culture bottle. The standard approach for collecting a sample for blood culture analysis involves a tight band around the arm and cleaning the injection site with antiseptic (2% w/v chlorhexidine gluconate in 70% isopropyl alcohol, such as ChloraPrep). The needle is then inserted, blood is drawn directly into the blood culture bottles, and pressure is applied to the skin using a cotton wool pad. Finally, the blood sample tubes are prepared for transportation. An example product is pictured in

**Figure 6**.

**Figure 6: Example standard of care product**[38]

## 4.3 Decision model structure

*Provide a diagram of the decision model structure you have chosen in Appendix F*: Model structure.

*Justify the chosen structure of the decision model by referring to the clinical care pathway outlined in section 1.3. Decision model structures should normally incorporate clinical parameters based on appropriate estimates of clinical effectiveness. This allows for sensitivity analyses to be done on the impact of varying the clinical parameters to explore any uncertainty in the estimates. For this reason, decision model structures should not just be based on simple cost calculations.*

Since no economic evaluations for Kurin Lock have been published (as identified by the SLR), a de novo economic evaluation was performed. Blood culture analysis is considered the "gold standard" method for the detection of micro-organisms in the blood.[39] A decision tree was therefore used to explore the clinical pathway of patients who require blood culture sample collection (Figure 9). The model was built in Excel and was informed by literature identified by the SLR which assessed the cost impact of blood culture contamination in the secondary care setting.[9, 40]

It was assumed that all patients have two blood culture sets drawn (both aerobic and anaerobic), as recommended by NICE and PHE, as a single set misses 10–40% of bacteraemia.[41] All patients in both arms of the model therefore had two blood culture collections taken, in line with current clinical practice. A positive blood culture finding from either one or both culture sets is considered as a positive blood culture sample. A positive blood culture indicates bacteraemia or a blood stream infection, also known as sepsis (a true positive) or a contamination (a false positive[42]). Bacteraemia is defined as bacteria in the blood.[42] Literature identified from the SLR defined contamination to be blood culture growth due to skin-residing organisms including coagulase-negative staphylococci, *Propionibacterium* spp, *Micrococcus* spp, viridians group streptococci, *Corynebacterium* spp, or *Bacillus* spp.[9] To align with the literature identified by the SLR,[9] immediately following a blood culture collection, empirical antibiotic treatment was initiated in a proportion of the population based on clinical suspicion of bacteraemia pending definitive

diagnosis, with the remaining awaiting initiation until a definitive diagnosis was made. Those with an initial positive blood culture sample underwent confirmatory follow-up testing (microbiology, biochemistry, and haematology testing) to determine whether the positive result was a contaminant or true bacteraemia. In patients for whom empirical treatment had been initiated, a negative blood culture confirmation would result in cessation of antibiotics and would include those who were deemed to have a false-positive (contaminant). A positive blood culture confirmation would trigger an initiation of antibiotic treatment in those who had not started empirical treatment or continuation of the empiric treatment.

Empiric antibiotic therapy aims to provide early treatment to patients who present with signs and symptoms suggestive of infection, such as fever, inflammation, or other clinical indicators. The choice of antibiotics for empiric therapy is based on several factors, including the most common pathogens associated with the suspected infection, local antimicrobial resistance patterns, patient factors (such as age, underlying health conditions, and allergies), and the site of infection.

Healthcare providers select broad-spectrum antibiotics that are effective against a wide range of potential pathogens commonly associated with the suspected infection. The goal is to cover the most likely causative organisms until more specific information, such as culture and sensitivity results, is available to guide targeted therapy. For the purposes of the current analysis, it is assumed that vancomycin is used as the empiric therapy. Literature identified by the SLR initiated vancomycin as the empiric antibiotic therapy.[9] Due to the low cost, and for simplicity, only vancomycin is considered for treatment. While other therapies are available for treatment, the choice of therapy is not likely to be influenced by the method of blood sample collection.

In clinical practice, once the specific pathogen is identified, the initial empiric antibiotic therapy may be modified or narrowed based on the susceptibility profile of the identified organism. This allows for more effective and tailored treatment, considering the susceptibility pattern and potential adverse effects of the chosen antibiotics. As the blood sample collection with Kurin Lock would not impact the pathogen present, the model therefore assumes that vancomycin treatment would continue. While the true cost of treating the infection may vary, because the analysis assumes that the rate of true-positive infections is the same in each arm, the subsequent cost of treating said infections will be nullified.

Vancomycin administration often necessitates pharmacokinetic monitoring to ensure that a patient does not overdose which result in serious adverse events. The primary aim for monitoring and adjusting serum vancomycin concentration is to achieve a serum concentration above the

minimum inhibitory concentration and to avoid potential adverse events including nephrotoxicity or ototoxicity. The cost of vancomycin serum concentration testing is conservatively excluded in the base case but considered in a subsequent scenario analysis.

As the population being considered are already present in a hospital setting, there is an assumed hospital LOS. For true negative patients, i.e. those without an infection, the LOS will be reflective of the patients in the respective care setting and will therefore be the same in both arms of the model (and as such be nullified). For true positive patients with bacteraemia, there will be an extended LOS while the bacteraemia is treated and resolved. As with the true negative patients, this will be the same in both arms of the analysis (and as such will effectively cancel out). For false positive patients with a contaminated blood culture, there will be an unnecessary increased LOS which will be greater than that of true negative patients and less than that of false positive patients.

Kurin Lock is intended for use in departments within the secondary care setting that routinely perform blood culture sample collection. The rate of blood culture contamination will vary substantially between different settings due to several factors including the patients presenting, local protocols, and implementation. The literature identified by the SLR provided blood culture contamination rates for several settings including the A&E, ICU, and general hospital ward. The decision tree was therefore used to inform the cost consequence model comparing Kurin Lock with SoC for the routine use of blood culture collection in the identified secondary care settings with subsequent scenario analyses exploring varying rates of blood culture contamination in different hospital settings.

The base case cost-consequence analysis modelled the total cost for both Kurin Lock and SoC associated with ordering a blood culture in the A&E setting, the processing cost associated with a blood culture collection, the cost of confirmation, empiric antibiotic therapy, subsequent antibiotic therapy, and LOS costs. Scenario analyses presented individual treatment costs in the ICU and general hospital ward; adult and paediatric cohorts were considered separately. The primary outcomes were per-patient costs associated with intervention and false-positive (blood culture contaminations) avoided.

## 4.4 Assumptions in the decision model

*In this table, list the main assumptions in the decision model and justify why each has been used.*

**Table 12: Assumptions in the decision model**

| Assumption | Justification | Source |
|---|---|---|
| The model assumes that the baseline risk of bacteraemia is 7.4%, which is applied to both arms of the model.[34] | The model assumes that the underlying risk of bacteraemia is the same in each arm of the model, i.e. all true positives will be identified and treated appropriately. As such, the choice of base line risk in the model will not influence the final results as the number of patients identified and associated treatment costs will be equal in each arm and thus cancel out. This figure is included for completeness. | Rupp et al., Reduction in Blood Culture Contamination Through Use of Initial Specimen Diversion Device. Clinical Infection Diseases. 2017 |
| The model assumed a base line contamination rate for SoC of 9% in the A&E .[13] | Kurin Lock was trialled in the A&E at King's Princess Royal Hospital to determine if the introduction of an ISDD would reduce the number of false-positive blood cultures. The baseline contamination rate at the trial hospital A&E was 9%.[13] The SoC at the trial hospital was the widely adopted practice of collecting blood culture samples from newly inserted peripheral intravenous cannula and injecting into the blood culture bottles with a needle. | Atta M, Mcguire R. Reducing False Positive Blood Cultures in an Adult NHS Emergency Department using a Kurin Lock Blood Culture Collection Device. King's College Hospital. 2022 |
| The model assumed that the reduction in blood culture contamination rate for Kurin Lock is at 65.5%.[13] | A trial of Kurin Lock at King's College Hospital, London, demonstrated that the introduction of an initial specimen diversionary device reduces the number of false-positive blood cultures by 65.5%.[13] This parameter is explored in sensitivity analysis. | Atta M, Mcguire R. Reducing False Positive Blood Cultures in an Adult NHS Emergency Department using a Kurin Lock Blood Culture Collection Device. King's College Hospital. 2022 |
| It was assumed that all patients with a positive, or the suspicion of, bacteraemia would receive (empiric) vancomycin. | Literature identified by the SLR-initiated vancomycin as the empiric antibiotic therapy.[9] While other antibiotics therapies are available, the choice of treatment is unlikely to be influenced by the method of blood sample collection. Due to the relative low cost, and for simplicity, only vancomycin is considered for | Skoglung, E. et al., Estimated clinical and economic impact through use of a novel blood collection device to reduce blood culture contamination in the emergency department: a cost-benefit analysis. 2019 |

| Assumption | Justification | Source |
|---|---|---|
| | treatment of bacteraemia. In addition, while specific antibiotics may be used following confirmatory blood tests, in the model these costs would be equal in each treatment arm considered and so for simplicity it is assumed that vancomycin is used throughout. | |
| In scenario analysis the model assumed that a patient receiving ≤3 days of vancomycin underwent one serum concentration assay, while patients receiving >3 days of treatment underwent two serum concentration assays. | The administration of vancomycin often necessitates pharmacokinetic monitoring, therefore additional pharmacy labour costs were considered for therapeutic drug monitoring of vancomycin, to ensure that patients do not overdose and cause serious adverse events.[43] In the base case this is conservatively excluded. | Liu C, Bayer A, Cosgrove S et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011; 52(3):e18-e55 |
| The model assumed no adverse events of vancomycin. | Common side effects of vancomycin include nephrotoxicity, ototoxicity, “red man” or “red person syndrome, when patients receive too much vancomycin, or an infusion is administered too rapidly.[44] As, the cost of a serum concentration is included in the model to account for monitoring of vancomycin administration, adverse events associated with the rapid infusion of vancomycin were not included. | Patel S, Preuss CV, Bernice F. Vancomycin. StatPearls [Internet]. Last update Feb 2020. |
| The model assumed that two blood cultures were drawn per collection and that the contamination rates were the same irrespective of the number of bottles drawn. | It was assumed that one Kurin Lock or SoC set can be used to draw two bottles for blood culture testing. The gold standard is two samples from two sites (aerobic and anaerobic), so utilising two sets and four bottles.[39] A patient with a positive culture from either bottle is considered as having a single positive culture. It is therefore assumed that the patient samples are contaminated, rather than the specific bottle. PHE standards for the investigation of blood cultures recommend that a blood culture set for diagnosing blood stream infection is defined as 1 aerobic and 1 anaerobic bottle. For patients, it is recommended that 20–30 mL of blood is | Public Health England. UK Standards for Microbiology Investigations. 2021. |

| Assumption | Justification | Source |
|---|---|---|
| | cultured per set, and that 2 consecutive blood culture sets from 2 separate venepuncture sites should be collected during any 24-hour period.[39] | |
| The model assumed that a proportion of patients will start empirical antibiotics at culture collection and whilst it will only be initiated a positive blood culture in the remaining cohort. | The duration of antibiotic therapy was estimated on the basis of the probability of three separate events: (i) receiving empirical therapy at the time of blood culture collection, (ii) initiation of therapy following a positive initial blood sample, and (iii) stopping therapy at the time of culture finalisation.[9] | Skoglung, E. et al., Estimated clinical and economic impact through use of a novel blood collection device to reduce blood culture contamination in the emergency department: a cost-benefit analysis. 2019. |
| The model assumed that the cost for staff training would not be incurred by the NHS and was therefore not included. | Aligning with the company scope, the company will provide training for free. [35]Training is expected to be simple and to only take a few minutes.[35] | National Institute for Health and Care Excellence. Kurin Lock for blood culture collection. MID297. Available from: https://www.nice.org.uk/advice/mib297/chapter/The-technology |
| The model assumed the patient age was split by adults (>12 years) and paediatrics (<12 years). The model assumed costs sourced from the NHS national costing tariff for adults and paediatrics were not impacted by the age category. | This was to align with the recommended dose of vancomycin.[45] Aligning with the SmPC for the posology and method of administration of vancomycin, the model split adults and paediatrics. | Electronic medicines compendium. Vancomycin 500mg powder for concentrate for solution for infusion vials. Available from: https://www.medicines.org.uk/emc/product/8759/smpc#gref |
| The model does not consider false negative patients | There is no evidence to suggest that the method of blood culture collection would result in different levels of false negative patients (i.e. patients with bacteraemia being mis-diagnosed). While this could technically occur in clinical practice, because the rate would not vary due to the method of blood culture collection the occurrence of false negative patients is excluded from the analysis | Assumption |
| No impact hospital acquired infection and/or on associated mortality | There is a small increased risk of hospital acquired infections linked to length of stay.[9] Inappropriately increasing a patients hospital length of stay could result in a small increase in hospital acquired infections, and small incremental risk of mortality. This has been conservatively excluded from the analysis. | Assumption |

Abbreviations: A&E, accident and emergency; ISDD, initial specimen diversionary device; NHS, National Health Service; PHE, Public Health England; SLR, systematic literature review; SmPC, summary of product characteristic; SoC, standard of care.

## 4.5 Clinical parameters and variables

***Table 13 Clinical parameters, patient and carer outcomes and system outcomes used in the decision model***
*In this table, describe the clinical parameters, patient and carer outcomes and system outcomes used in the decision model. Please include sufficient detail to allow the reader to clearly identify the input from the source data.*

Clinical parameters used in the model were derived from Rupp et al. (2017), Skoglung et al (2019) and Atta et al. (2022), as reported in Table 13. As described in Table 12, no differences in baseline bacteraemia risk (true positive rate) were assumed between Kurin Lock and SoC, as this would not be impacted by the choice of blood sample collection.

The base case considered the difference in the blood culture contamination rate between the two technologies in the A&E. The A&E was the most frequently reported setting in literature identified by the SLR, notably due to the higher rates of contamination in the A&E.[9] The calculated risk of blood culture contamination rate was lower with Kurin Lock compared with SoC (Kurin Lock 3.1% versus SoC 9.0%). Patients with a false-positive contamination had a longer hospital LOS compared with those with a true negative result (7 days versus 5 days, respectively) (Table 13).

**Table 13: Clinical parameters**

| Parameter/outcomes | Source | Relevant results | Range or distribution | How are these values used in the decision model? |
|---|---|---|---|---|
| Baseline bacteraemia risk (in the A&E) | Rupp et al. 2017[34] | 7.4% | 7.2–7.6% | This estimate is the underlying risk of bacteraemia (the true risk of contamination). Bacterial growth and true bacteraemia are impacted by the baseline risk of bacteraemia. |
| Standard of care rate of blood culture contamination (false positives), in the A&E | Atta et al. 2022[13] | 9% | 8.1–9.9% | This is used to estimate the bacterial growth in the SoC arm (baseline bacteraemia risk + SoC rate of blood culture contamination). |
| Reduction of BC contamination by using Kurin Lock | Atta et al. 2022[13] | 65.5% | 59–72% | This is used to calculate the Kurin Lock rate of BCC, in the A&E. Specifically, the reduction of BCC is multiplied by the SoC rate of BCC to estimate the Kurin Locks rate of blood contamination (3.1%). The estimated BCC rate for Kurin Lock (3.1%) is added to baseline bacteraemia risk to estimate the bacterial growth in the Kurin Lock arm of the decision tree. |

| Parameter/outcomes | Source | Relevant results | Range or distribution | How are these values used in the decision model? |
|---|---|---|---|---|
| Probability of starting empiric antibiotics prior to initial BC results | Skoglung et al. 2019[9] | 71% | 64–78% | The probability of starting empirical antibiotics prior to BC collection was used to estimate the number of patients who would initiate empiric antibiotics as a precaution prior to BC results, versus taking no action. |
| Probability of starting antibiotics following a positive BC | Assumption | 100% | NA | Patients were assumed to receive antibiotics at the initial report of a bacterial growth from blood culture, if they were not started empirically. This was applied to the number of patients with a true bacteraemia growth, in whom empiric antibiotics had not been initiated, following a positive BC confirmation test result. |
| Stopping empirical antibiotics by culture finalisation (true negative, no BC growth), in the A&E (days) | Skoglung et al. 2019[9] | 3.0 | 1.0–4.0 | This is applied to the no growth arm of the 'initiation of empiric antibiotics as a precaution prior to BC results'. It is used to estimate the number of days patients are on empiric antibiotics, the cost of empiric antibiotics and the cost of empiric antibiotics concentration assay in both the SoC and Kurin Lock arm. |
| Stopping empirical antibiotics by the identification of false positive result (following initial positive BC), in the A&E (days) | Skoglung et al. 2019[9] | 4.0 | 3.0–7.0 | This is used to estimate the duration of antibiotics by stopping antibiotics by culture finalisation following a contaminant (false-positive) result, in both arms of the decision tree (no action versus initiation of empiric antibiotics as a precaution prior to BC results. As above, it is used to estimate the number of days patients are on empiric antibiotics, the cost of empiric antibiotics and the cost of empiric antibiotics concentration assay in both the SoC and Kurin Lock arm. |
| Stopping empirical antibiotics following confirmed bacteraemia (true positive, following initial positive BC), in the A&E (days) | Skoglung et al. 2019[9] | 10.0 | 7.0–13.0 | This is applied to the decision tree to estimate the duration of empiric antibiotics in patients who continue antibiotics following a true bacteraemia result, in both the no action and initiate empiric antibiotics as a precaution arm. As above, it is used to estimate the number of days patients are on empiric antibiotics, the cost of empiric antibiotics and the cost of empiric antibiotics concentration assay in both the SoC and Kurin Lock arm. |
| Length of stay duration for a patient with a true negative BC, in the A&E (days) | Skoglung et al. 2019[9] | 5.0 | 3.0–9.0 | The LOS is applied to both arms of the model (no action and initiation of empiric antibiotics) to estimate the hospital LOS for patients with a no growth. It is used to estimate the cost of LOS, the days of stay, and cost of adverse event (duration). |

| Parameter/outcomes | Source | Relevant results | Range or distribution | How are these values used in the decision model? |
|---|---|---|---|---|
| Length of stay duration for a patient with a false positive (contaminated) BC, in the A&E (days) | Skoglung et al. 2019[9] | 7.0 | 4.0–11.0 | The LOS is applied to both arms of the model (no action and initiation of empiric antibiotics) to estimate the hospital LOS for patients with a contaminant (false-positive) bacterial growth. It is used to estimate the cost of LOS, the days of stay, and cost of adverse event (duration). |
| Length of stay duration for a patient with a true positive (bacteraemia) BC, in the A&E (days) | Skoglung et al. 2019[9] | 9.0 | 7.0–13.0 | The LOS is applied to both arms of the model (no action and initiation of empiric antibiotics) to estimate the hospital LOS for patients with a true bacteraemia, who must continue antibiotics. It is used to estimate the cost of LOS, the days of stay, and cost of adverse event (duration). |

Abbreviations: A&E, accident and emergency; BC, blood culture; BCC, blood culture contamination; LOS, length of stay; SoC, standard of care.

*If expert elicitation methods were used to identify any model parameters and/or a plausible distribution, fully justify this and the methods outlined*.

N/A.

*If any outcomes listed in table 10 are extrapolated beyond the study follow-up periods, explain the assumptions that underpin this extrapolation*.

N/A.

### 4.5.1 Other parameters in the decision model

*Describe any other parameters in the decision model. Examples are provided in the table. You can adapt the parameters as needed. Please include sufficient detail to allow the reader to clearly identify the input from the source data.*

**Table 14: Additional parameters in the model**

| Parameter | Description | Justification | Source |
|---|---|---|---|
| Time horizon | One year | To align with literature identified by the SLR, the model was built to estimate the cost savings per year.[9] However, the model estimates both the population and patient outcomes. Consequentially, the population estimates are estimated over a year, whereas patient estimates are estimated over a patient's blood culture collection cycle and the maximum length of stay of the patient. | Skoglung, E. et al., Estimated clinical and economic impact through use of a novel blood collection device to reduce blood culture contamination in the emergency department: a cost-benefit analysis. 2019. |
| Discount rate | N/A | Time horizon of the model was one year. | N/A |
| Perspective (NHS/personal social services) | NHS | Only NHS costs were modelled | N/A |
| Cycle length | N/A | A decision tree model was used | N/A |
| Transition probabilities | N/A | A decision tree model was used | N/A |
| Health states | N/A | As this was a cost consequence model, no health states were explicitly modelled (i.e. the interventions considered don't influence the true health states of patients). The analysis implicitly considers patients with and without bacteraemia. Consequentially, the model also considers the number of (false-positive) blood culture contaminations avoided. | N/A |
| Sources of unit costs | Unit costs for consumables, tests, and hospital overhead costs | Unit cots were sourced from the most robust UK sources available[46-49] | • Kurin Lock equipment: Manufacturer[46]<br>• SoC equipment: Manufacturer[46]<br>• Blood culture collection and follow-up costs: NHS NCC Direct Access[48]<br>• Hospital costs: NHS NCC PLICS data[49]<br>• Antibiotic costs: British National Formulary (BNF). Medical forms for vancomycin. Ennogen Healthcare Ltd. 2023. Available at: https://bnf.nice.org.uk/drugs/vancomycin/medicinal-forms/. [Accessed 18th April 2023][47] |

Abbreviations: BNF, British National Formulary; Ltd, limited; N/A, not applicable; NCC, National cost collection; NHS, National Health Service; PLICS, patient level information and costing system; SLR, systematic literature review; UK, United Kingdom.

*Explain the transition matrix used in the decision model and the transformation of clinical outcomes, health states or other details.*

N/A.

## 4.6 Resource identification, measurement and valuation

*NB: the sections below should be completed with a view to ensuring the EAG can understand clearly and quickly where all figures have been obtained e.g. all source detail should be sufficiently detailed. It is also important to describe how any figures have been calculated (including all assumptions, sources, calculations etc.).*

### 4.6.1 Intervention and comparator technology costs

*Provide the price for the intervention technology, which should reflect as closely as possible the price(s) paid in the NHS (excluding VAT). Describe any uncertainty over the appropriate price to use in the submission.*

The cost of Kurin Lock is estimated at £19.50 per unit cost of collection. The total cost for collection of two cultures with Kurin Lock is £39.00.[46]

The current standard of care for blood culture collection (tubes and container) is estimated at £1.50. The total cost for collection of two cultures is £3.00.[35]

### 4.6.2 NHS and unit costs

*Describe how the clinical management of the condition is currently costed in the NHS, for example using the latest Health Resource Group (HRG) codes via the National Cost Collection (NCC; previously called 'reference costs'), the unit costs (from the Personal Social Services Research Unit. Provide relevant codes and values (for example, OPCS codes and ICD codes) for the operations, procedures and interventions included in the decision model. Present the value using inflation indices appropriate to the cost perspective (see User Guide for suggested sources), and ensure all costs are presented in GBP.*

The cost of blood culture collection methods is presented in Table 15.

**Table 15: NHS and unit costs**

| Input | Currency description | Unit cost | Reference |
|---|---|---|---|
| Collection and process of blood culture collection (organism identification and antimicrobial susceptibility testing)[48] | Estimated as a composite of a microbiology, biochemistry and haematology test | £15.66 | 2020-21 NCC Direct Access DAPS https://www.england.nhs.uk/publication/2020-21-national-cost-collection-data-publication/ |
| Microbiology test[48] | N/A | £10.18 | 2020-21 NCC Direct Access DAPS https://www.england.nhs.uk/publication/2020-21-national-cost-collection-data-publication/ |
| Biochemistry test[48] | N/A | £1.85 | 2020-21 NCC Direct Access DAPS https://www.england.nhs.uk/publication/2020-21-national-cost-collection-data-publication/ |
| Haematology test[48] | N/A | £3.63 | 2020-21 NCC Direct Access DAPS https://www.england.nhs.uk/publication/2020-21-national-cost-collection-data-publication/ |
| Vancomycin (cost per vial)[47] | N/A | £11.25 | British National Formulary (BNF). Medical forms for vancomycin. Ennogen Healthcare Ltd. 2023. Available at: https://bnf.nice.org.uk/drugs/vancomycin/medicinal-forms/. [Accessed 18th April 2023] |
| Vancomycin serum concentration assay†[48] | PHCD00026 | £72.93 | NHS England. National Cost Collection for the NHS. National schedule of NHS costs 2021/22 Code: PHCD00026.Available from: https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/ |

Abbreviations: BNF, British National Formulary; DAPS, data alliance partnership board; N/A, not applicable; NCC, national costing code; PHC, primary care services.
†Scenario analysis only.

The cost of a blood culture test was estimated assuming routine identification and that testing was performed for all initial blood samples. The cost of a follow-up test occurs when there is an initial positive blood culture test (bacterial growth detected), and is conducted to confirm if the initial blood culture result is a true or false positive.

The cost of antimicrobial treatment and duration was estimated utilising data from the British National Formulary (BNF) for the intravenous administration of vancomycin.[47] Weight-based dosing is required for vancomycin, with an estimated dose of 20 mg/kg per administration for patients aged >12 years (administered twice daily), and 15 mg/kg for patients aged <12 years (administered 4 times a day).[45]

The cost of vancomycin serum concentration assay was estimated at £72.93 per test.[50] Patients receiving ≤3 days of vancomycin have one serum concentration assay, while patients receiving

>3 days undergo two serum concentration assays.[43] As previously noted, this cost is conservatively excluded in the base case and considered in a scenario analysis.

### 4.6.3 Resource use

*Describe any relevant resource data for the NHS from published and unpublished studies. Provide sources and rationale if relevant. If a literature search was done to identify evidence for resource use, provide details in appendix D.*

In addition to the blood culture collection and antibiotic costs, the model also considers hospital LOS (Table 16).

**Table 16: Hospital costs for adults and paediatrics**

| Input | Currency description | Unit cost | Reference |
|---|---|---|---|
| Occupation of a single-patient non-elective emergency room (general ward) - adults[49] | Primary Diagnosis ICD10 T808 and T809 | £844.13 | 2020-21 NCC PLICS data Non elective short episode, Treatment Function code excl Padiatrics, Primary Diagnosis ICD10:<br>• T808<br>• T809 |
| Occupation of a single-patient non-elective emergency room (general ward) - paediatrics[48] | TFC 211 -290 | £1,091.62 | 2021-22 NCC TFC 420 (Paediatrics) and all Paediatric sub-specialties (TFC 211 -290) Non elective short episodes https://www.england.nhs.uk/publication/2021-22-national-cost-collection-data-publication/ |

Abbreviations: ICD10, international classification of disease 10th revision; NCC, national cost collection; PLICS, patient level information and costing system; TFC, treatment function code.

*Describe the resources needed to implement the technology in the NHS. Provide sources and rationale.*

No additional resources will be required to implement the technology. Blood cultures are obtained by trained, registered nurses. As previously described, training on the use of the Kurin Lock will be provided free of charge, with no change in clinical practice required.

*Describe the resources needed to manage the change in patient outcomes after implementing the technology. Provide sources and rationale.*

Regular training on the use of the device will be required, although no change in clinical practice is required. Training will be provided to demonstrate how blood cultures should be taken with the device, and will be provided free of charge.[35]

*Describe the resources needed to manage the change in system outcomes after implementing the technology. Provide sources and rationale.*

N/A.

### 4.6.4 Resource use costs

*In this table, summarise how the decision model calculates the results of these changes in resource use. Adapt the table as necessary.*

**Table 17: Resource use costs**

| Cost | Kurin Lock costs | SoC costs | Difference in resource use costs (Kurin Lock versus SoC) |
|---|---|---|---|
| Blood culture collection | £39.00 | £3.00 | £36.00 |
| Initial blood culture processing | £15.66 | £15.66 | £0.00 |
| Cost of confirmation | £1.65 | £2.57 | -£0.92 |
| Antibiotics | £99.72 | £103.69 | -£3.97 |
| Length of stay | £4,716.40 | £4,820.18 | -£103.78 |
| **Total costs** | **£4,872.42** | **£4,945.10** | **-£72.67** |

Abbreviations: SoC, standard of care.

### 4.6.5 Adverse event costs

*If costs of adverse events were included in the analysis, explain how and why the risk of each adverse event was calculated.*

Adverse events were not modelled within the cost consequence analysis. No needlestick injuries or potential bloodborne pathogen exposures have been reported with blood culture collection.[34]

While adverse events are known to be associated with the IV administration and monitoring on vancomycin, costs to treat adverse events have been conservatively excluded in the model.

*Table 11 Adverse events and costs in the decision model*

*In this table, summarise the costs associated with each adverse event included in the decision model. Include all adverse events and complication costs, both during and after long-term use of the technology. Explain whether costs are provided per patient or per event.*

N/A.

### 4.6.6 Miscellaneous costs

*Describe any additional costs or resource considerations that have not been included elsewhere (for example, Personal Social Services costs, and patient and carer costs). If none, state.*

N/A.

*Are there any other opportunities for resource savings or redirection of resources that have not been possible to quantify?*

The incidence of multidrug resistance in Gram-positive organisms has increased in recent years. Consequentially, the number of patients for whom initial empirical antibiotic therapy is ineffective is also increasing. Demonstrating the need for accurate and timely blood culture results is therefore required to ensure antibiotic stewardship through correct antibiotic administration and decreasing the unnecessary administration of broad-spectrum antibiotics. The reduced risk of blood culture contamination (false-positive) results with Kurin Lock may reduce unnecessary antibiotic administration and therefore help towards improving antibiotic stewardship, in addition to resulting in cost savings to the NHS.

### 4.6.7 Total costs

*In the following tables, summarise the total costs:*

- *Summarise total costs for the technology in Table 18.*
- *Summarise total costs for the comparator in Table 19. This can only be completed if the comparator is another technology.*

**Table 18: Total costs for Kurin Lock in the decision model**

| Description | Cost | Source |
|---|---|---|
| Cost per treatment/patient over lifetime of device | £39.00 per blood culture collection | Manufacturer, total cost of collection[46] |
| Training cost over lifetime of device | £0.00 | National Institute for Health and Care Excellence. Kurin Lock for blood culture collection. 2022[35] |
| **Total cost per treatment/patient over lifetime of device** | **£39.00** | Manufacturer, total cost of collection[46] |

**Table 19: Total costs for SoC in the decision model**

| Description | Cost | Source |
|---|---|---|
| Cost per treatment/patient over lifetime of device | £3.00 | Manufacturer, total cost of collection[46] |
| Training cost over lifetime of device | £0 | N/A |
| **Total cost per treatment/patient over lifetime of device** | **£3.00** | Manufacturer, total cost of collection[46] |

Abbreviations: N/A, not applicable; SoC, standard of care.

Administration time and therefore costs are assumed to be equal between the two interventions.

*Summary of all resource use and unit costs used in decision model. Please ensure you identify all component costs and include sufficient detail to allow the reader to clearly identify the input from the source data.*

**Table 20: Summary of all resource use and unit costs used in decision model**

| Description | Unit costs | Resource use | Included cost | Source |
|---|---|---|---|---|
| Kurin Lock[46] | £19.50 per collection | 2 cultures drawn | £39.00 | Manufacturer |
| SoC[35] | £1.50 per collection | 2 cultures drawn | £3.00 | National Institute for Health and Care Excellence. Kurin Lock for blood culture collection |
| Blood culture collection and processing[35] | • £10.18 (microbiology test)<br>• £1.85 (cost of a biochemistry test)<br>• £3.63 (cost of a haematology test) | 1 blood culture collection (1 use of each test) | £15.66 | 2020-21 NCC Direct Access DAPS https://www.england.nhs.uk/publication/2020-21-national-cost-collection-data-publication/ |
| Follow-up costs (following a positive blood culture)[50] | • £10.18 (microbiology test)<br>• £1.85 (cost of a biochemistry test)<br>• £3.63 (cost of a haematology test) | 1 use of each test | £15.66 | 2020-21 NCC Direct Access DAPS https://www.england.nhs.uk/publication/2020-21-national-cost-collection-data-publication/ |
| Vancomycin[47] | £11.25 (pack cost) | 1 vial per pack, 1000 mg per vial | • £0.01 cost per mg<br>• £37.53 (cost per day for a patient aged >12 years at a weight of 83.40 kg)<br>• £27.00 (cost per day for a patient aged >12 years at a weight of 40 kg) | British National Formulary (BNF). Medical forms for vancomycin. Ennogen Healthcare Ltd. 2023. Available at: https://bnf.nice.org.uk/drugs/vancomycin/medicinal-forms/. [Accessed 18th April 2023] |

| Description | Unit costs | Resource use | Included cost | Source |
|---|---|---|---|---|
| Serum concentration assay (vancomycin)*[48] | £72.93 per unit | 1 unit cost | £72.93 | NHS England. National Schedule of NHS Costs Year 21/22 . Code: PHCD00026. 2023. |
| Daily cost of stay in a ward (adult)[49] | £844.13 per day | Unit cost per day | £844.13 | 2020-21 NCC PLICS data Non elective short episode, Treatment Function code excl Paediatrics, Primary Diagnosis ICD10 T808 and T809 |
| Daily cost of stay in a ward (paediatric)[48] | £1,091.62 per day | Unit cost per day | £1,091.62 | 2021-22 NCC TFC 420 (Paediatrics) and all Paediatric sub specialties (TFC 211 -290) Non elective short episodes https://www.england.nhs.uk/publication/2021-22-national-cost-collection-data-publication/ |
| Daily cost of stay in an ICU ward (adult)[48] | £2,389.06 per day | Unit cost per day | £2,389.06 | 2021-22 NCC Unit CCU01 (Adult Critical Care) organ support for 2 organs. https://www.england.nhs.uk/publication/2021-22-national-cost-collection-data-publication/ |
| Daily cost of stay in an ICU ward (paediatric)[48] | £3,024.60 per day | Unit cost per day | £3,024.60 | 2021-22 NCC Unit CCU04 (Paediatric critical care) Level 1 Critical Care . https://www.england.nhs.uk/publication/2021-22-national-cost-collection-data-publication/ |

Abbreviations: ICU, intensive care unit; NCC, national cost collection; NHS, National Health Service; PHC, primary care service; PLICS, patient level information and costing system; SoC, standard of care; TFC; treatment function code. * Scenario analysis only

It should be noted that the cost of the initial blood culture processing will be equal in both arms considered within the analysis and therefore would result in net zero cost difference.

# 5 Results

### 5.1.1 Base-case results

*In this table, report the results of the base-case analysis. Specify whether costs are provided per treatment or per year. Adapt the table as necessary to suit the decision model. If appropriate, describe costs by health state. In line with section 4.7.12 of the manual, results should be presented as probabilistic cost savings where possible unless a deterministic approach can be justified.*

The base case results of the analysis show that, although use of Kurin Lock is associated with an incremental cost of £36 per patient, this is offset completely by the reduction in antibiotic use (£3.97 saved per patient) and reduced LOS (£103.78 saved per patient) resulting in a potential cost-saving of £72.67 per patient (Table 21 and Table 22).

**Table 21: Total base case results per patient – By category of cost**

| Cost | Mean cost per patient using Kurin Lock (£) | Mean cost per patient using the SoC (£) | Difference in mean cost per patient (£): Kurin Lock versus SoC (negative values indicate a cost saving) |
|---|---|---|---|
| Device cost | £39.00 | £3.00 | £36.00 |
| Initial blood culture processing costs | £15.66 | £15.66 | £0.00 |
| Confirmation testing costs | £1.65 | £2.57 | -£0.92 |
| Cost of antibiotics | £99.72 | £103.69 | -£3.97 |
| Cost of length of stay | £4,716.40 | £4,820.18 | -£103.78 |
| **Total** | **£4,872.42** | **£4,945.10** | **-£72.67** |

Abbreviations: SoC, standard of care.

**Table 22: Total base case results per patient – By blood culture response**

| Technology | True positive (negative values indicate a cost saving for Kurin Lock) | False-positive (negative values indicate a cost saving for Kurin Lock) | True negative (negative values indicate a cost saving for Kurin Lock) | Total cost (negative values indicate a cost saving for Kurin Lock) |
|---|---|---|---|---|
| Kurin Lock | £618.08 | £197.97 | £4,057.37 | £4,872.42 |
| SoC | £615.41 | £570.60 | £3,759.09 | £4,945.10 |
| **Difference** | **£2.66** | **-£372.62** | **£297.29** | **-£72.67** |

Abbreviations: SoC, standard of care.

While the primary analysis considered the cost impact of Kurin Lock, the patient benefits are the number of reduced false positive results, which result in opportunity cost savings via reduced use of antibiotics, and bed days saved (Table 23). Avoiding false positives reduces undue stress on the patient and avoids a small risk of hospital acquired infections (conservatively excluded from the analysis) through a reduction in unnecessary hospital LOS. These avoided false positive results also help to ensure antibiotic stewardship through correct antibiotic administration and decreasing the unnecessary administration of broad-spectrum antibiotics which could also result in adverse events (also conservatively excluded from the analysis).

**Table 23: Total base case results per patient for relevant clinical outcomes**

| Technology | Contaminated blood samples (negative values indicate a saving) | Days of antibiotics (negative values indicate a saving) | Bed days (negative values indicate a saving) |
|---|---|---|---|
| Kurin Lock | 0.03 | 2.77 | 5.36 |
| SoC | 0.09 | 2.88 | 5.48 |
| **Difference** | **-0.06** | **-0.11** | **-0.12** |

Abbreviations: SoC, standard of care.

### 5.1.2 Scenario analysis

*If relevant, explain how scenario analyses were identified and done. Cross-refer your response to the decision problem in section 1.1. Justify if scenario analyses are not probabilistic. See the user guide for full details of the information required.*

#### 5.1.2.1 Alternative settings

Two scenario analyses were explored in addition to the A&E base case setting. As described in Section 4.1, this submission also presents evidence for Kurin Lock in the ICU and general hospital setting.

The downstream effects of false-positive blood cultures on hospitals has been well published including increases in LOS, hospital-acquired infections, unnecessary antimicrobial administration, and overuse of laboratory resources [11, 12, 24, 25, 31] The A&E was utilised as the model base case setting as research has indicated a higher contamination rate of 9.0% in the A&E versus 2.5% in other areas of the hospital (including those in general wards and the ICU).[13, 30, 36] The higher contamination rate observed in the A&E is a result of a fast-paced environment, frequent changes in staff, lack of adequate training, pressure for rapid culture collection ahead of antimicrobial administration, and lack of adherence to the correct procedure to draw a blood sample.

However, underlying contamination rate can vary significantly depending on several factors as demonstrated in the literature identified by the SLR (See Section 3). Data for two alternative settings were identified and were therefore explored in scenario analyses:

- Scenario 1: Where the model considered the ICU as the model setting.
- Scenario 2: Where the model considered the general hospital as the model setting.

*Describe the differences between the base case and each scenario analysis*.

As previously described, the main differences between the populations in the model included the contamination rate, hospital LOS, associated hospital LOS costs, and the duration of empiric antibiotics prescribed. Contamination rates are higher in an A&E due to the nature of it being a fast-paced environment, with frequent staff changes and a lack of adequate training compared with the general hospital and ICU.[30]

The key differences between each scenario are presented in Table 24.



**Table 24: Key differences between each scenario**

| Parameter | Base case: A&E setting | Scenario 1: ICU setting | Scenario 2: Hospital setting |
|---|---|---|---|
| Contamination rate | 9.0% | 2.5% | 4.7% |
| LOS for patients with a true negative BC | 5.0 days | 5.73 days | 8 days |
| LOS for patients with a false-positive BC | 7.0 days | 8.08 days | 13 days |
| LOS for patients with a true positive BC | 9.0 days | 11.06 days | 13 days |
| Duration of empirical antibiotics – stopped by culture finalisation | 3.0 days | 1.5 days | 3.0 days |
| Duration of empirical antibiotics – identification of false positive | 4.0 days | 5.0 days | 4.0 days |
| Duration of empirical antibiotics – confirmed bacteraemia | 10.0 days | 6.5 days | 10.0 days |
| Daily cost of stay in a ward (adult) | £844.13 | £2,389.06 | £844.13 |
| Daily cost of stay in a ward (paediatric) | £1,091.62 | £3,024.60 | £1,091.62 |

Abbreviations: A&E, accident and emergency; BC, blood culture; LOS, length of stay; ICU, intensive care unit.

*Describe how the scenario analyses were included in the cost comparison analysis.*

The scenario analyses were included in the cost consequence model in addition to the base case calculation. Each scenario was run and reported separately, with all parameters used in the scenario analyses the same as those used in the base case, except for those listed in Table 24.

*Describe the evidence that justifies including any scenario analyses.*

Evidence suggests that the contamination rate, LOS, and antibiotic use differ across hospital settings. As previously described, most notably, the contamination rate is higher in the A&E (9.0% versus 2.5% in other areas of the hospital).[13, 24] As discussed in literature identified by the SLR, the ICU and medical wards incur high rates of false-positive cases, highlighting the importance of more effective methods for blood culture sample collection in these settings.[24, 29]

***Table 18 Scenario analyses results***
*In this table, describe the results of any scenario analyses that were done. Adapt the table as necessary.*

Scenario analyses results for Kurin Lock in the ICU, general hospital, and in both settings are presented in Table 25, Table 26, and Table 27, respectively.

**Table 25: Kurin Lock in the ICU setting**

| Technology | True positive cost | False-positive cost | True negative cost | Total cost (negative values indicate a cost saving for Kurin Lock) |
|---|---|---|---|---|
| Kurin Lock | £2,053.71 | £175.11 | £13,130.94 | **£15,359.76** |
| SoC | £2,051.04 | £506.68 | £12,864.12 | **£15,421.84** |
| **Difference** | **£2.66** | **-£331.56** | **£266.82** | **-£62.08** |

Abbreviations: ICU, intensive care unit; SoC, standard of care.

**Table 26: Kurin Lock in a general hospital setting**

| Technology | True positive cost | False-positive cost | True negative cost | Total cost (negative values indicate a cost saving for Kurin Lock) |
|---|---|---|---|---|
| Kurin Lock | £878.63 | £189.02 | £6,526.09 | **£7,593.75** |
| SoC | £875.96 | £546.20 | £6,273.62 | **£7,695.79** |
| **Difference** | **£2.66** | **-£357.18** | **£252.47** | **-£102.04** |

Abbreviations: SoC, standard of care.

**Table 27: Total cost of Kurin in both scenarios**

| Care setting | Mean cost per patient using Kurin Lock (£) | Mean cost per patient using SoC (£) | Difference in cost per patient (£; negative values indicate a cost saving) |
|---|---|---|---|
| ICU (total costs) | £15,359.76 | £15,421.84 | **-£62.08** |
| Hospital (total costs) | £7,593.75 | £7,695.79 | **-£102.04** |

Abbreviations: ICU, intensive care unit; SoC, standard of care.

Despite varying baseline contamination rates and different costs associated with hospital stay, Kurin Lock remains cost saving in each of the settings considered. Subsequent consideration of base line contamination rates and cost of hospital stay is considered in Section 5.2.

### 5.1.2.2 Adults versus paediatric

Kurin lock can be used for blood sample collection in all patients; the base case model considers a combined adult and paediatric cohort. Antibiotic dosing varies between adult and paediatric patients, and the associated hospital costs also differ (reflecting the additional time and resource often associated with paediatric patients). The following analysis considers adult and paediatric patient groups individually (Table 28 and Table 29 , respectively).

**Table 28: Total costs per adult patient – Category of cost**

| Cost | Mean cost per patient using Kurin Lock (£) | Mean cost per patient using the SoC (£) | Difference in mean cost per patient (£): Kurin Lock versus SoC (negative values indicate a cost saving) |
|---|---|---|---|
| Device cost | £39.00 | £3.00 | £36.00 |
| Initial blood culture processing costs | £15.66 | £15.66 | £0.00 |
| Confirmation testing costs | £1.65 | £2.57 | -£0.92 |
| Cost of antibiotics | £103.98 | £98.12 | -£4.14 |
| Cost of length of stay | £4,522.54 | £4,622.06 | -£99.51 |
| **Total** | **£4,682.83** | **£4,751.41** | **-£68.58** |

Abbreviations: SoC, standard of care.

**Table 29: Total costs per paediatric patient – Category of cost**

| Cost | Mean cost per patient using Kurin Lock (£) | Mean cost per patient using the SoC (£) | Difference in mean cost per patient (£): Kurin Lock versus SoC (negative values indicate a cost saving) |
|---|---|---|---|
| Device cost | £39.00 | £3.00 | £36.00 |
| Initial blood culture processing costs | £15.66 | £15.66 | £0.00 |
| Confirmation testing costs | £1.65 | £2.57 | -£0.92 |
| Cost of antibiotics | £74.80 | £77.78 | -£2.98 |
| Cost of length of stay | £5,849.01 | £5,977.71 | -£128.70 |
| **Total** | **£5,980.12** | **£6,076.72** | **-£96.60** |

Abbreviations: SoC, standard of care.

With weight-based dosing the cost of antibiotics is higher in the adult cohort than in the paediatric cohort resulting in larger antibiotic cost savings in adult patients. However, this is offset by the higher LOS costs in the paediatric population. In both cohorts Kurin Lock remains cost saving with total costs savings of £68.58 per adult patient and £96.60 per paediatric patient.

#### 5.1.2.3 Inclusion of antibiotic monitoring

As presented in section 4.3, antibiotic treatment can often be associated with other costs. Within the context of this analysis vancomycin administration often necessitates pharmacokinetic monitoring to ensure that a patient does not overdose which may result in serious adverse events. The cost of vancomycin serum concentration testing was conservatively excluded in the base case but considered in the following scenario analysis.

The cost of vancomycin serum concentration assay was estimated at £72.93 per test.[48] Patients receiving ≤3 days of vancomycin have one serum concentration assay, while patients receiving >3 days undergo two serum concentration assays.[43] Patients receiving empiric treatment, who are

true negative or identified as false positive, will therefore only receive a single assay while patients that are true positive will receive two assays. The inclusion of antibiotic monitoring increases the costs saving of Kurin Lock by £5.55 per patient to £78.22 (Table 30).

**Table 30: Costs including antibiotic monitoring - Category of cost**

| Cost | Mean cost per patient using Kurin Lock (£) | Mean cost per patient using the SoC (£) | Difference in mean cost per patient (£): Kurin Lock versus SoC (negative values indicate a cost saving) |
|---|---|---|---|
| Device cost | £39.00 | £3.00 | £36.00 |
| Initial blood culture processing costs | £15.66 | £15.66 | £0.00 |
| Confirmation testing costs | £1.65 | £2.57 | -£0.92 |
| Cost of antibiotics | £99.72 | £103.69 | -£3.97 |
| Antibiotic concentration assay | £61.66 | £67.21 | £5.55 |
| Cost of length of stay | £4,716.40 | £4,820.18 | -£103.78 |
| **Total** | **£4,872.42** | **£4,945.10** | **-£78.22** |

Abbreviations: SoC, standard of care

## 5.2 Sensitivity analysis

### 5.2.1 Probabilistic sensitivity analysis

*Describe the methods of the probabilistic sensitivity analysis. See the user guide for full details of the information required. If no probabilistic sensitivity analyses have been done, explain why.*

The probability of Kurin Lock being cost saving was assessed by probabilistic sensitivity analysis (PSA) by estimating the level of confidence in the model outputs and accounting for uncertainty in the model inputs. The PSA was run for 10,000 simulations and the parameters were represented as distributions around the point estimate. The parameters varied in the PSA were unit costs of treatment (SoC, cost of blood culture collection), number of blood culture samples drawn, antibiotic use, LOS, blood culture contamination rates, and duration of empirical antibiotic therapy.

A normal distribution was used for patient baseline weight. Gamma distributions were used for all cost parameters. The risk of bacteraemia, probability of blood culture contamination, and probability of empirical antibiotics were assumed to have a beta distribution.

*Present the results of the probabilistic sensitivity analysis.*

A PSA was run for 10,000 simulations. Kurin Lock was cost saving across all, 99.94%, 10,000 simulations performed. The mean cost saving was £72.67 (95% CI: £72.64 to £73.61) versus SoC.

### 5.2.2 Deterministic sensitivity analyses

*Describe the methods of the deterministic sensitivity analyses. See the user guide for full details of the information required.*

A series of analyses were performed to evaluate the sensitivity of the model results to individual inputs when all other inputs remained constant. As drug acquisition costs are endogenous, they were not varied. To determine the most sensitive parameter outcome, all other parameters (including LOS, costs, and antimicrobial administration) items were varied ±10%, if their respective confidence intervals were not sourced from the literature identified by the SLR.

The variables used in the sensitivity analyses, complete with their respective ranges, are presented in Table 31.

**Table 31: Variables used in the DSA**

| Variable | Base case value | Range of values in DSA |
|---|---|---|
| Blood culture collection and processing | £15.66 | £14.09–£17.23 |
| Cost of a microbiology test | £10.18 | £9.16–£11.50 |
| Cost of a biochemistry test | £1.85 | £1.67–£2.04 |
| Cost of a haematology test | £3.63 | £3.27–£3.99 |
| Vancomycin pack cost | £11.25 | £10.13–£12.38 |
| Vancomycin serum concentration assay cost | £72.93 | £65.64–£80.22 |
| Patients aged >12 years (weight, kg) | 83.40 | 75–92 |
| Patients aged <12 years (weight, kg) | 40.00 | 36–44 |
| Daily cost of a stay in an A&E ward – adult | £844.13 | £760–£929 |
| Daily cost of a stay in an A&E ward - paediatric | £1,091.62 | £982–£1,201 |
| LOS duration – true negative blood culture (days) | 5.0 | 3.0–9.0 |
| LOS duration – false-positive blood culture (days) | 7.0 | 7.0–11.0 |
| LOS – true positive (days) | 9.0 | 7.0–13.0 |
| Baseline bacteraemia risk | 7.40% | 7.20–7.60% |
| Rate of blood culture contamination (false-positive) – SOC | 9.00% | 8.10–9.90% |
| Reduction in BC contamination – from using Kurin Lock | 65.50% | 59.00–72.10% |
| Probability of empiric antibiotics at culture collection – prior to blood culture results | 71.00% | 64.00–78.00% |

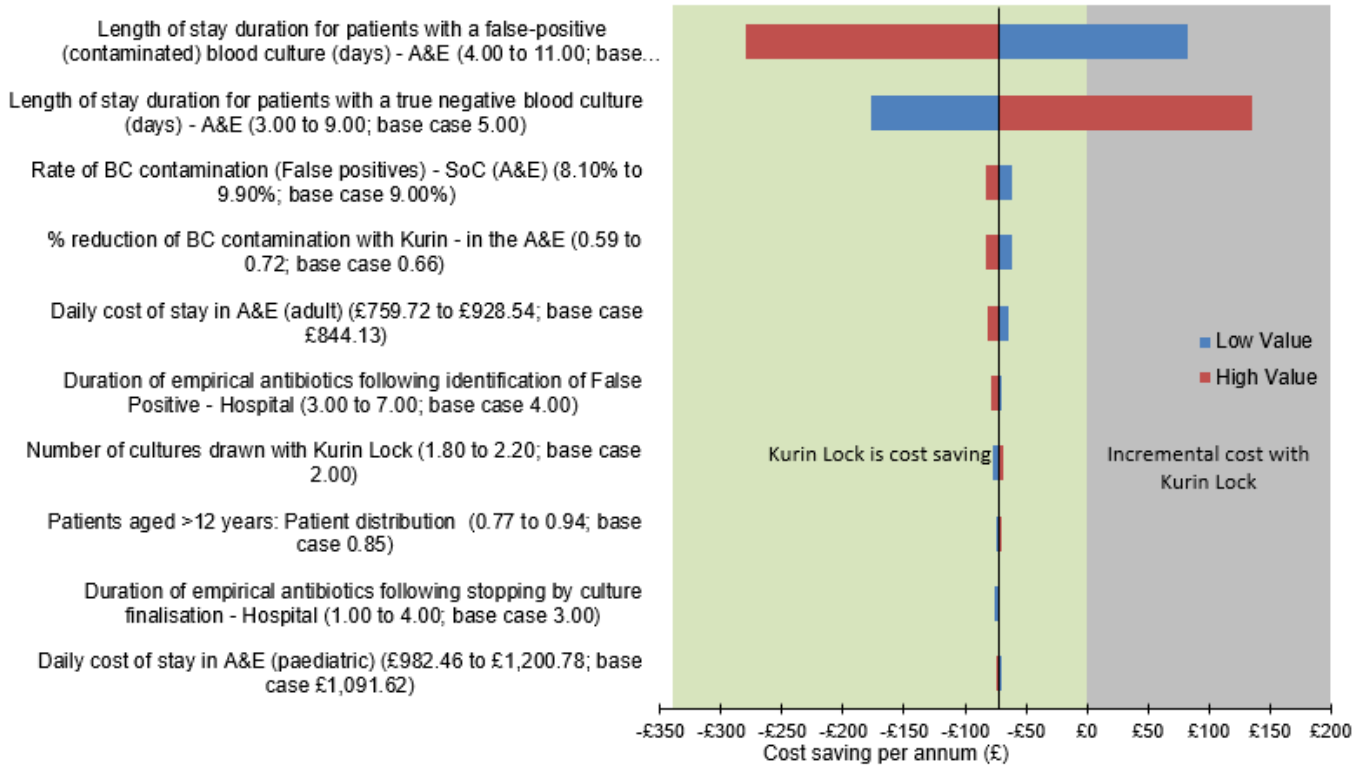
| Variable | Base case value | Range of values in DSA |
|---|---|---|
| Probability of empiric antibiotics at culture collection – following positive blood culture | 100.00% | 90.00%–100.00% |
| Duration of empiric antibiotics – identification of true negative (days) | 3.0 | 1.0–4.0 |
| Duration of empiric antibiotics – identification of false positive (days) | 4.0 | 3.0–7.0 |
| Duration of empiric antibiotics – confirmed bacteraemia (days) | 10.0 | 7.0–13.0 |

Abbreviations: A&E, accident and emergency; BC, blood culture; DSA, deterministic sensitivity analysis; LOS, length of stay; SoC, standard of care.

*Present the results of the deterministic sensitivity analyses, focusing on the key drivers of the decision model. Consider the use of tornado diagrams.*

Results of the DSA are presented in a tornado diagram (Figure 7) and Table 32. The key drivers of the DSA are the LOS duration for patients with a false-positive (contaminated) and true negative blood culture sample. In both instances, extreme values can result in Kurin Lock no longer being cost saving. However, it is clinically implausible for patients with a false-positive blood culture result to be in hospital for less time than those with a true negative result as such, while feasible in the model, these extremes are illogical and should be excluded from consideration. Kurin Lock remained cost saving across all other variables and ranges tested within the DSA.

**Figure 7. Tornado diagram of DSA results**




Abbreviations: A&E, accident and emergency; BC, blood culture; DSA, deterministic sensitivity analysis; SoC, standard of care.

**Table 32: DSA results**

| Variable (lower bound to upper bound; base case value) | Cost-difference per annum with lower bound | Cost difference per annum with upper bound |
|---|---|---|
| Length of stay duration for patients with a false-positive (contaminated) blood culture (days) - A&E (4.00 to 11.00; base case 7.00) | £83* | -£280 |
| Length of stay duration for patients with a true negative blood culture (days) - A&E (3.00 to 9.00; base case 5.00) | -£176 | £135* |
| Rate of BC contamination (False positives) - SoC (A&E) (8.10% to 9.90%; base case 9.00%) | -£62 | -£84 |
| % reduction of BC contamination with Kurin - in the A&E (0.59 to 0.72; base case 0.66) | -£62 | -£84 |
| Daily cost of stay in A&E (adult) (£759.72 to £928.54; base case £844.13) | -£64 | -£81 |
| Duration of empirical antibiotics following identification of False Positive - Hospital (3.00 to 7.00; base case 4.00) | -£71 | -£79 |
| Number of cultures drawn with Kurin Lock (1.80 to 2.20; base case 2.00) | -£77 | -£69 |
| Patients aged >12 years: Patient distribution (0.77 to 0.94; base case 0.85) | -£75 | -£70 |
| Duration of empirical antibiotics following stopping by culture finalisation - Hospital (1.00 to 4.00; base case 3.00) | -£76 | -£71 |
| Daily cost of stay in A&E (paediatric) (£982.46 to £1,200.78; base case £1,091.62) | -£71 | -£75 |

Abbreviations: A&E, accident and emergency; BC, blood culture; DSA, deterministic sensitivity analysis; LOS, length of stay; SoC, standard of care. * In these scenarios LOS is longer for true negative patients which in the context of the model is illogical.

### 5.2.3 Threshold analysis

*Identify and present relevant parameter boundaries via threshold analyses. Explain whether these boundaries will fall within the expected uncertainty boundaries.*

A threshold analysis was performed on the top 10 model parameters (as identified in the univariate sensitivity analysis above) to determine at which values Kurin Lock would no longer result in a cost-saving (Table 33). In this analysis, all other parameters were kept at their original value.

**Table 33: Results of threshold analysis**

| Variable | Base case (Lower bound to Upper bound) | Value to achieve cost parity |
|---|---|---|
| Length of stay duration for patients with a false-positive (contaminated) blood culture (days) - A&E | 7.00 (4.00–11.00) | 5.60 |
| Length of stay duration for patients with a true negative blood culture (days) - A&E | 5.00 (3.00–9.00) | 6.40 |
| Rate of BC contamination (False positives) - SoC (A&E) | 9.00% (8.10%–9.90%) | 2.98% |
| % reduction of BC contamination with Kurin - in the A&E | 665 (59%–72%) | 22% |
| Daily cost of stay in A&E (adult) | £844.13 (£759.72–£928.54) | £122.46 |
| Duration of empirical antibiotics following identification of False Positive - Hospital | 4.00 (3.00–7.00) | -30.25 |
| Number of cultures drawn with Kurin Lock | 2.00 (1.80–2.20) | 5.73 |
| Patients aged >12 years: Patient distribution | 85% (77%–94%) | 345% |
| Duration of empirical antibiotics following stopping by culture finalisation - Hospital | 3.00 (1.00–4.00) | 51.24 |
| Daily cost of stay in A&E (paediatric) | £1,091.62 (£982.46–£1,200.78) | -£3,133.19 |

Abbreviations: A&E, accident and emergency; BC, blood culture; DSA, deterministic sensitivity analysis; SoC, standard of care.

In the threshold analysis when parameters are considered individually, in order for Kurin Lock to be cost neutral compared with SoC:

- The LOS for patients with a false-positive (contaminated) blood culture needs to drop to 5.6 days.
- The LOS for patients with a true-negative blood culture needs to drop to increase to 6.4 days
    - Note in both instances this equates to a differential between true and false positives as an incremental 0.6 day LOS of stay associated with a contaminated blood culture (See Section 5.2.5)
- The rate of blood culture contamination (false positives) for SoC decreases to 2.98%

- Relative reduction of blood culture contamination with Kurin Lock reduces to 22%
- The daily cost of a stay in the A&E reduces to £122.46
- The duration of antibiotics following a false-positive (contaminated) blood culture needs to be -30.25 days, which is not possible
- The number of cultures drawn with Kurin Lock increases to 5.73
- The proportion of patients aged over 12 would need to increase to 345%, which is not possible
- The duration of empirical antibiotics stopped in false positive patients following a confirmatory test would need to be given for 51.24 days
- The daily cost of a stay in the emergency department reduces to -£3,133.19, which is not possible.

### 5.2.4 Two-way sensitivity analysis

The DSA and associated threshold analysis demonstrate that the rate of blood culture contamination (false positives) for SoC and the relative reduction of blood culture contamination with Kurin Lock are two of the key drivers of cost-saving. As many factors can influence the rate of blood culture contamination with SoC, and to demonstrate the robustness of the reduction in contamination required with Kurin Lock, a two-way sensitivity analysis was conducted to illustrate the relationship between these parameters (Table 34). The gold standard (baseline rate) for blood culture contamination is <3%.[51] At a baseline rate of 3%, Kurin Lock would remain cost-saving with the baseline 65.5% reduction in blood culture contamination.[13] The analysis shows that as baseline rate with SoC increases the required reduction with Kurin Lock decreases. If the baseline rate of contamination is below 2% the Kurin Lock would need to prevent nearly 100% of blood contaminations to be cost-neutral, i.e. If other means of intervention have already lowered the rate of contamination, then Kurin Lock is unlikely to be cost saving. However, the reality is that current rates are much higher than this and as such Kurin Lock is highly likely to be cost saving.

**Table 34: Two-way sensitivity analysis comparing baseline risk of BC contamination with SoC and the reduction in BC contamination with Kurin Lock**

| | | Baseline rate of BC contamination with SoC (A&E) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | £73 | 1% | 2% | 3% | 4% | 5% | 6% | 7% | 8% | 9% | 10% |
| % reduction of BC contamination with Kurin | 10.0% | -£34 | -£32 | -£30 | -£29 | -£27 | -£25 | -£23 | -£21 | -£19 | -£18 |
| | 20.0% | -£32 | -£29 | -£25 | -£21 | -£18 | -£14 | -£10 | -£7 | -£3 | £1 |
| | 30.0% | -£30 | -£25 | -£19 | -£14 | -£8 | -£3 | £3 | £8 | £14 | £19 |
| | 40.0% | -£29 | -£21 | -£14 | -£7 | £1 | £8 | £16 | £23 | £30 | £38 |
| | 50.0% | -£27 | -£18 | -£8 | £1 | £10 | £19 | £29 | £38 | £47 | £56 |
| | 60.0% | -£25 | -£14 | -£3 | £8 | £19 | £30 | £41 | £52 | £64 | £75 |
| | 65.5% | -£24 | -£12 | £0 | £12 | £24 | £36 | £49 | £61 | **£73** | £85 |
| | 70.0% | -£23 | -£10 | £3 | £16 | £29 | £41 | £54 | £67 | £80 | £93 |
| | 80.0% | -£21 | -£7 | £8 | £23 | £38 | £52 | £67 | £82 | £97 | £111 |
| | 90.0% | -£19 | -£3 | £14 | £30 | £47 | £64 | £80 | £97 | £113 | £130 |
| | 100.0% | -£18 | £1 | £19 | £38 | £56 | £75 | £93 | £111 | £130 | £148 |

Abbreviations: A&E, accident and emergency; BC, blood culture.
Key: Red cells – Kurin Lock is more costly; Green cells – Kurin Lock is cost saving; Yellow cell – base case result.

### 5.2.5 Length of stay

In the DSA, LOS is determined to be a key driver although the analysis only shows Kurin Lock to not be cost saving when clinically illogical data is considered (i.e. when the LOS is shorter for those with a blood culture contamination than those without). The model considers three patient groups: those without infections (True negatives), those with infections (True positives) and those with blood culture contaminations (False positives). The model implicitly assumes that true negatives and true positives will be treated appropriately in both arms, essentially nullifying the associated LOS costs. The main driver of cost is therefore associated with those who have a blood culture contamination (false positives). The following one-way analysis considers the incremental LOS for these patients (i.e. it does not consider the LOS for true positive and true negative patients as the resulting costs will be net zero across both arms).

| Incremental LOS associated with a blood culture contamination (False positive) | Total cost (negative values indicate a cost saving for Kurin Lock) |
|---|---|
| 0.50 | £5 |
| 1.00 | -£21 |
| 1.50 | -£47 |
| 2.00 | -£73 |
| 2.50 | -£99 |
| 3.00 | -£125 |
| 3.50 | -£151 |
| 4.00 | -£176 |
| 4.50 | -£202 |
| 5.00 | -£228 |

Assuming all other parameters remain constant this analysis demonstrates that if the incremental LOS associated with a contaminated blood culture is greater than 0.6 days, Kurin Lock will remain cost saving.

### 5.2.6 Summary of sensitivity analysis results

*Summarise the main findings of the sensitivity analyses. What are the main sources of uncertainty about the decision model's conclusions?*

The main sources of uncertainty from the model stem from parameter uncertainty, for the underlying rate of contamination, reduction of blood culture contamination with Kurin Lock and the duration of LOS. However, both univariate analysis and PSA show that Kurin Lock remains cost saving when compared with both SoC. Within univariate analysis only implausible LOS inputs resulted in incremental costs for Kurin Lock and extensive sensitivity analysis around the inputs demonstrated the robustness of the cost savings. The PSA showed the results to be extremely stable with more than 99.94% of simulations resulting in cost savings versus SoC.

### 5.2.7 Miscellaneous results

*Include any other relevant results here.*

N/A.

# 6 Validation

*Describe the methods used to validate, cross-validate (for example, with external evidence sources) and quality assure the decision model, and complete the checklist in Appendix E. Provide sources, and cross-refer to evidence when appropriate.*

The model structure was adapted from a decision tree taken from the published literature identified by the SLR.[9, 40] Technical validation and quality assurance of the model was undertaken by a Senior Health Economist who was not involved in the development of the model itself.

*Give details of any clinical experts who were involved in validating the decision model, including names and contact details. Highlight any personal information as confidential*.

N/A.

# 7 Summary and interpretation of economic evidence

*Describe the main findings from the economic evidence and decision model. Explain any potential cost savings and the reasons for them.*

The model base case demonstrated that Kurin Lock results in an average cost saving of £72.67 per patient. This is due to an average of 0.06 fewer contaminated blood samples per patient, 0.11 fewer days of empiric antibiotics, and reduction of hospital LOS by 0.12 bed days. While there is uncertainty around the base line rate of blood culture contamination, the model and associated analysis demonstrate the robustness of the analysis with Kurin Lock only resulting in incremental costs in a small number of extreme scenarios (Base line rate of blood culture contamination is below 2%, relative reduction in contamination with Kurin Lock is less than 22%, cost of stay is below £122.46 per day or the LOS associated with blood culture contamination is less than 0.6 days). While the base case evidence is associated with the A&E setting, scenario analysis considering other secondary care hospital settings also demonstrate Kurin Lock to be cost saving compared with SoC and the wider sensitivity analysis, which can be considered agnostic of setting, also support Kurin Lock being cost saving. The PSA results were highly congruent to the deterministic results, with 99.94% of simulations resulting in cost-savings further demonstrating the robustness of the findings.

This analysis can be considered conservative as there are several other theoretical benefits that have not been quantified within the analysis. There is a small increased risk of hospital-acquired infections linked to LOS. Inappropriately increasing a patient's hospital LOS could therefore result in a small increase in hospital-acquired infections, and an associated incremental risk of mortality, this has been conservatively excluded from the analysis. In certain settings such as gastroenterology, cancer and renal specialisations, false positive blood cultures may result in unplanned removal of central venous access devices; however, these have been conservatively excluded. Finally, combatting antimicrobial resistance is a priority in global health. Overuse and misuse of antibiotics and other antimicrobial drugs have accelerated the development of resistant bacteria and so antimicrobial stewardship programs aim to improve patient care by ensuring that antimicrobial therapy is appropriate, effective, and safe. By reducing the inappropriate initiation of empiric antibiotic treatment Kurin Lock could help improve antimicrobial stewardship programs within the NHS.

*Briefly discuss the relevance of the evidence base to the scope.*

The model included patients expected to require a blood culture within the A&E and compared Kurin Lock with SoC, which is reflective of the population, intervention, and comparator defined in the scope. As previously described, evidence for patients in the ICU and general hospital setting was also presented, as identified in the scope.

The scope defined a range of outcomes; however, it was not possible to model treatment delays, patient-reported outcomes (such as health-related quality of life), and adverse events due to the paucity of these data and conservative estimates within the model. The scope outcomes considered in the model (either implicitly or explicitly) were blood culture contamination rate, positive and negative predictive values, rates of antimicrobial prescriptions, use of unnecessary antibiotic treatment, unnecessary further interventions (such as laboratory tests), LOS, and hospital-acquired infection.

The time horizon of the model was the duration of one blood culture (contamination/bacteraemia) result, which was deemed adequate to accurately consider the direct impact of Kurin Lock on costs and outcomes. The number of patients included in the model was based on the number of blood cultures drawn over a one-year time horizon within the model. This approach allowed results to be presented at the patient level (time horizon for one blood culture) or as costs over a year.

Costs considered in the model were relevant to the NHS and a variety of subgroup settings were considered in the sensitivity analysis.

*Briefly discuss if the results are consistent with the published literature. If they are not, explain why and justify why the results in the submission be favoured over those in the published literature.*

The results are consistent with those in the literature identified by the SLR, demonstrating that a blood culture device which diverts the first 0.15 mL of blood reduces the risk of blood culture contamination. Skoglund et al. (2019) demonstrated that implementing an ISDD in a US-hospital resulted in overall hospital cost savings of $272 per blood culture, and $28 in direct-only costs.[9] This mirrors the estimated £72.67 cost savings reported in our model and analysis within the A&E.

Similarly, Skoglund et al. (2019) reported that the main cost drivers were baseline contamination rates and duration of antibiotics provided to patients with a negative blood culture, thereby demonstrating that unnecessary hospital resources are often used to treat patients.[9]

While no published studies have directly evaluated the economic impact of routine implementation of Kurin Lock, the cost-effectiveness of other interventions designed to decrease the rate of blood culture contamination have been assessed, including the implementation of an ISDD to reduce blood culture contamination rates.[9, 34] A decision-tree cost analysis, which demonstrated the use of sterile kits for blood culture collection, showed a net hospital saving compared with usual practices.[40] Compared with Skoglung et al. (2019) and Self et al. (2014), the results of this analysis demonstrated a similar cost-benefit associated with the introduction of Kurin Lock into clinical practice.[9, 40]

*Describe if the cost comparison analysis is relevant to all patient groups and NHS settings in England that could potentially use the technology as identified in the scope.*

This cost consequence analysis is relevant to all patient groups identified in the scope (Section 1.1), as well as the population for whom the use of Kurin Lock is indicated (patients who require a blood culture collection). While the model considers several specific secondary care hospital settings, the agnostic sensitivity analysis demonstrates that the cost savings and clinical benefits of Kurin Lock will persist if the underlying rate of blood culture contamination is high (>3%) irrespective of the clinical setting. While there will be different levels of savings in different settings.

*Briefly summarise the strengths and limitations of the cost analysis, and how these might affect the results.*

**Strengths**

To our knowledge, this is the first analysis that has evaluated the potential cost impact of Kurin Lock versus the SoC for blood culture collection in the UK. The analysis used clinical data from published studies with a study population directly applicable to the indication for the technology and the scope.[9, 12, 29]

The model structure was derived from a published economic study, with data inputs and model outcomes based on published evidence on ISDDs. [9, 12, 13, 29, 34, 40] The model is therefore considered the best possible reflection of the data and outcomes that are available for Kurin Lock versus SoC.

The model considered additional subpopulations costs and outcomes to estimate the impact of Kurin Lock within other NHS hospital settings.

Extensive sensitivity analyses were conducted to determine the key drivers of the incremental cost between Kurin Lock and SoC, and to assess the magnitude of uncertainty in the base case results. The results generated were shown to be robust with the cost saving output being realised even at extreme parameter limits.

**Limitations**

The majority of the data has been derived from prospective real-world studies, including those from non-UK settings.[9] In addition, there is a lot of heterogeneity in the datasets which result in challenges with the robustness of combining the studies. However, the model structure utilises the best available data and, combined with extensive sensitivity analysis, to account for the study uncertainty, demonstrate that Kurin Lock is highly likely to result in substantial cost savings to the NHS.

*Detail any further analyses that could be done to improve the reliability of the results.*

Further analyses would be dependent on the generation of new data, such as data from a real-world study in the UK that assessed hospital LOS and the use of antimicrobial therapy associated directly with the use of Kurin Lock versus SoC. Additional real-world data may be able to help quantify any association with unnecessary empirical antimicrobial use and adverse events, reduced hospital LOS and risk of hospital-acquired infections. Exploration of the use of Kurin in other clinical settings may be able to demonstrate further clinical benefits such as reducing unplanned removal of central venous access devices due to false positive blood cultures.

# 8 Resource impact analysis

*The resource impact team at NICE estimates the costs or savings (budget impact) associated with technologies so the NHS can plan for and implement guidance. In order to produce a resource impact report and template the team requests the following information:*

## 8.1 Population and uptake estimates

In Table 35, provide estimates of the number of people who would be eligible to use your technology in Years 1 to 5 and the expected uptake in each of the 5 years.

**Table 35: Population and uptake estimates**

| Year | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Number of people eligible to use technology | 1,500,000 | 1,500,000 | 1,500,000 | 1,500,000 | 1,500,000 |
| Uptake of technology (Market Adoption) | c. 1.5% | c. 5% | c. 10% | c. 15% | +20% |

It is estimated that around 3,000,000 (+/-10%) blood culture bottles are processed in the UK every year but there is a paucity of validated data to support this assumption other than internal market assessments.

## 8.2 Sales

In Table 36, provide estimates of the number of items of this technology you expect to sell in Years 1 to 5 in the UK.

**Table 36: Sales estimates (Estimations from Year 2024 onwards)**

| Year | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Sales of technology (Units) | 30,000 | 75,000 | 150,000 | 300,000 | 500,000 |

## 8.3 Acquisition costs

*The price of the technology should reflect as closely as possible the price(s) paid in the NHS, and analyses should be based on price reductions, if the price reduction is available across the NHS. In Table 37, provide an estimate of the aggregate purchase costs of the technology and associated set-up and implementation costs across the NHS in each of the 5 years, excluding VAT.*

**Table 37: Aggregate total costs**

| Year | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Purchase cost of technology excluding VAT | £19.50 | £19.50 | £19.50 | £19.50 | £19.50 |
| Other set-up and implementation costs | £0.00 | £0.00 | £0.00 | £0.00 | £0.00 |
| **Total costs excluding VAT** | **£19.50** | **£19.50** | **£19.50** | **£19.50** | **£19.50** |

Abbreviations: NHS, National Health Service; VAT, value added tax.

The cost of all types of Kurin Lock is currently £19.50 per device at current prices and based on predicted exchange rates, import duty rates, freight charges and delivery costs.

The company reserves the right to adjust prices up or down in accordance with market demand and forces.
As a supplier to the NHS we are open discussing discounts on this price for wider adoption of the device throughout the NHS.

*If the purchase cost reported in Table 37 does not represent the technology price and other charges used in the base case of the decision model, record which unit prices are used and explain the differences.*

# 9 References

Include all references below using NICE's standard referencing style.


1. Bentley J, Thakore S, Muir L, Baird A, Lee J. A change of culture: reducing blood culture contamination rates in an Emergency Department. BMJ Open Quality. 2016;5(1):u206760. w2754.
2. Nannan Panday R, Wang S, Van De Ven P, Hekker T, Alam N, Nanayakkara P. Evaluation of blood culture epidemiology and efficiency in a large European teaching hospital. PLoS One. 2019;14(3):e0214052.
3. Doern GV, Carroll KC, Diekema DJ, Garey KW, Rupp ME, Weinstein MP, et al. A comprehensive update on the problem of blood culture contamination and a discussion of methods for addressing the problem. Clin Microbiol Rev. 2019;33(1):e00009-19.
4. Dargère S, Cormier H, Verdon R. Contaminants in blood cultures: importance, implications, interpretation and prevention. Clinical Microbiology and Infection. 2018;24(9):964-9.
5. Bates DW, Goldman L, Lee TH. Contaminant blood cultures and resource utilization: the true consequences of false-positive results. Jama. 1991;265(3):365-9.
6. Klucher JM, Davis K, Lakkad M, Painter JT, Dare RK. Risk factors and clinical outcomes associated with blood culture contamination. Infection Control & Hospital Epidemiology. 2022;43(3):291-7.
7. Nielsen LE, Nguyen K, Wahl CK, Huss JL, Chang D, Ager EP, et al. Initial Specimen Diversion Device® reduces blood culture contamination and vancomycin use in academic medical centre. Journal of Hospital Infection. 2022;120:127-33.
8. Hughes J, Cabilan C, Williams J, Ray M, Coyer F. The effectiveness of interventions to reduce peripheral blood culture contamination in acute care: a systematic review protocol. Systematic Reviews. 2018;7(1):1-6.
9. Skoglund E, Dempsey CJ, Chen H, Garey KW. Estimated clinical and economic impact through use of a novel blood collection device to reduce blood culture contamination in the emergency department: a cost-benefit analysis. Journal of Clinical Microbiology. 2019;57(1):e01015-18.
10. Michaelidis CI, Zimmerman RK, Nowalk MP, Fine MJ, KJ S. Cost -effectiveness of 372 procalcitonin -guided antibiotic therapy for outpatient management of acute respiratory tract 373 infections in adults. . J Gen Intern Med 2014;29(579).
11. Waltzman ML, Harper M. Financial and clinical impact of false-positive blood culture results. Clinical infectious diseases. 2001;33(3):296-9.
12. Alahmadi Y, Aldeyab M, McElnay J, Scott M, Elhajji FD, Magee F, et al. Clinical and economic impact of contaminated blood cultures within the hospital setting. Journal of Hospital Infection. 2011;77(3):233-6.
13. Atta M, Mcguire R. Reducing False Positive Blood Cultures in an Adult NHS Emergency Department using an Kurin. 2022.
14. Burnie J, Vining S. Clinical Nurse Specialist Practice: Impact on Emergency Department Blood Culture Contamination. Clinical Nurse Specialist. 2021;35(6):314-7.
15. Arnaout S, Ellison RT, Greenough TC, Wedig A, Mitchell MJ, St John L, et al., editors. 114. Prospective Trial of Passive Diversion Device to Reduce Blood Culture Contamination. Open Forum Infectious Diseases; 2021: Oxford University Press.
16. Baxter M, Cook C, James A. Passive Engineering Controls Result in Sustained 66% Reduction in Blood Culture Contamination. Infection Control & Hospital Epidemiology. 2020;41(S1):s342-s3.
17. Allain M. Top Scoring Abstracts From the 2018 National Association of Clinical Nurse Specialists Annual Conference: Not Your ''Average'' ED: A CNS-Led Project That Reduced Blood Culture Contaminations in One Emergency Department to Below Expected Levels. Clinical Nurse Specialist. 2018:E1-E2.
18. Hodson J, Stebbing J, Nneoma O. Reducing blood culture contamination rates in accident and emergency (A&E) using an initial specimen diversionary device. Guy's and St Thomas' NHS Foundation Trust. 2022.
19. Arenas M, Boseman GM, Coppin JD, Lukey J, Jinadatha C, Navarathna DH. Asynchronous testing of 2 specimen-diversion devices to reduce blood culture contamination: a single-site product supply quality improvement project. Journal of Emergency Nursing. 2021;47(2):256-64. e6.
20. O'Sullivan DM, Steere L. Reducing False-Positive Blood Cultures: Using a Blood Diversion Device. Connecticut Medicine. 2019;83(2).

21. Ostwald CM. Reduction of False-positive Blood Culture Rates Using a Passive Blood Diversion Device in an Urban Academic Pediatric Emergency Department. American Journal of Infection Control. 2021;49(6):S3.
22. Sutton J, Fritsch P, Moody M, Dinaro K, Holder C. Preventing Blood Culture Contamination using a Novel Engineered Passive Blood Diversion Device. Association for Professionals in Infection Control. 2018.
23. England N. Improving the blood culture pathway – executive summary. 2022. Available from: https://www.england.nhs.uk/publication/improving-the-blood-culture-pathway-executive-summary/. Accessed
24. Souvenir D, Anderson Jr DE, Palpant S, Mroch H, Askin S, Anderson J, et al. Blood cultures positive for coagulase-negative staphylococci: antisepsis, pseudobacteremia, and therapy of patients. Journal of clinical microbiology. 1998;36(7):1923-6.
25. Gander RM, Byrd L, DeCrescenzo M, Hirany S, Bowen M, Baughman J. Impact of blood cultures drawn by phlebotomy on contamination rates and health care costs in a hospital emergency department. Journal of clinical microbiology. 2009;47(4):1021-4.
26. Kilgore ML, Ghosh K, Beavers CM, Wong DY, Hymel Jr PA, Brossette SE. The costs of nosocomial infections. Medical care. 2008;46(1):101-4.
27. Parson K, Webb D. Reducing Contaminated Blood Cultures in Adult ED using Kurin Lock Blood Culture Collection Set. Telford NHS Hospital Emergency Department, UK. 2023.
28. Rhew D, Childress C. Decreasing blood culture contamination rates when using an initial peripheral IV: implementing the 5 P's and using a closed system device. Nur Primary Care. 2021;5(3):1-6.
29. Lalezari A, Cohen M, Svinik O, Tel-Zur O, Sinvani S, Al-Dayem YA, et al. A simplified blood culture sampling protocol for reducing contamination and costs: a randomized controlled trial. Clinical Microbiology and Infection. 2020;26(4):470-4.
30. Dempsey C, Skoglund E, Muldrew KL, Garey KW. Economic health care costs of blood culture contamination: a systematic review. American Journal of Infection Control. 2019;47(8):963-7.
31. Zwang O, Albert RK. Analysis of strategies to improve cost effectiveness of blood cultures. Journal of Hospital Medicine: An Official Publication of the Society of Hospital Medicine. 2006;1(5):272-6.
32. Geisler BP, Jilg N, Patton RG, Pietzsch JB. Model to evaluate the impact of hospital-based interventions targeting false-positive blood cultures on economic and clinical outcomes. Journal of Hospital Infection. 2019;102(4):438-44.
33. Sheppard C, Franks N, Nolte F, Fantz C. Improving quality of patient care in an emergency department: a laboratory perspective. American journal of clinical pathology. 2008;130(4):573-7.
34. Rupp ME, Cavalieri RJ, Marolf C, Lyden E. Reduction in blood culture contamination through use of initial specimen diversion device. Clinical Infectious Diseases. 2017;65(2):201-5.
35. National Institute for Health and Care Excellence. Kurin Lock for blood culture collection [MIB297]. 2022. Available from: https://www.nice.org.uk/advice/mib297/chapter/The-technology. Accessed on: May.
36. Robertson P, Russell A, Inverarity DJ. The effect of a quality improvement programme reducing blood culture contamination on the detection of bloodstream infection in an emergency department. Journal of Infection Prevention. 2015;16(2):82-7.
37. Iskus Health. Internal stock image. 2023.
38. National Health Service Supply Chain. Blood Collection Set Safety with Blood Culture Holder 21G 19cm tubing (KFK850). 2023. Available from: https://my.supplychain.nhs.uk/catalogue/product/kfk850. Accessed
39. England PH. UK Standards for Microbiology Investigations. 2021. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1020471/ID_1i3.pdf. Accessed on: May.
40. Self WH, Talbot TR, Paul BR, Collins SP, Ward MJ. Cost analysis of strategies to reduce blood culture contamination in the emergency department: sterile collection kits and phlebotomy teams. Infection Control & Hospital Epidemiology. 2014;35(8):1021-8.
41. Fabre V, Carroll KC, Cosgrove SE. Blood culture utilization in the hospital setting: a call for diagnostic stewardship. Journal of clinical microbiology. 2022;60(3):e01005-21.
42. Smith DA, Nehring SM. Bacteremia. StatPearls [Internet]: StatPearls Publishing; 2022.
43. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant



Staphylococcus aureus infections in adults and children. Clinical infectious diseases. 2011;52(3):e18-e55.
44. Patel S, Preuss CV, Bernice F. Vancomycin. StatPearls [internet]: StatPearls Publishing; 2022.
45. Electronic Medicines Compendium. Vancomycin 500mg powder for concentrate for solution for infusion vials. 2023. Available from: https://www.medicines.org.uk/emc/product/8759/smpc#gref Accessed
46. Iskus Health. Internal assumption. 2023.
47. British National Formulary, BNF. Medical forms for vancomycin, Ennogen Healthcare Ltd. 2023. Available from: https://bnf.nice.org.uk/drugs/vancomycin/medicinal-forms/. Accessed on: May.
48. National Health Service England. 2020/21 National Cost Collection Data Publication. 2022. Available from: https://www.england.nhs.uk/publication/2020-21-national-cost-collection-data-publication/. Accessed on: May.
49. NHS Digital. Patient Level Activity and Costing, 2020-21. 2022. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/patient-level-activity-and-costing/2020-21/relationship-to-national-cost-collection. Accessed on: May.
50. England NHS. 2020/21 National Cost Collection Data Publication. NHS 75 England; 2022. Available from: https://www.england.nhs.uk/publication/2020-21-national-cost-collection-data-publication/. Accessed on: May.
51. Clinical and laboratory Standards Institute (CLSI). Principles and procedures for blood cultures: approved guideline. CLSI document M47-A. Wayne (PA): Clinical and Laboratory Standards Institute. 2007.

**Attachments**

1_GMED_EC Certificate, II.3_35591-1_exp052624

2_Declaration of Conformity, TF-01, Rev 2_030620

3_IFU 920 KUR-4000_F_EU-IFU_DFT3.1

4_GSTT_Blood Culture Procedure_Oct22

5_GSTT_Infection_Prevention__Control_Chapter_14_Guideline_for_Taking_Blood_for_Culture_v8.0).

# 10 Appendices

## Appendix A: Identification and selection of relevant studies

### Search methods for clinical evidence

Describe the process and methods used to identify and select the studies relevant to the technology; a pragmatic literature search is acceptable if justified. Include searches for published studies, abstracts and ongoing studies in separate tables as appropriate. See section 1.2 of the user guide for full details of how to complete this section.

<table>
<tr><th>Topic</th><th>Method details</th></tr>
<tr><td>Eligibility criteria</td><td>Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.<br><br><u>Inclusion criteria</u>:<br><br><u>Population</u>:<br>Blood cultures collection studies which used Kurin or ISDD within a secondary care setting.<br><br><u>Intervention and comparators</u>:<br>Kurin blood culture collection, including Kurin Lock, ISDD devices<br>Standard of care: Standard blood culture collection (tubes and container)</td></tr>
<tr><td>Information sources</td><td>Use the table below to specify all databases (e.g. MEDLINE), registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted and the number of results.<br><br>PubMed was searched (January 2017 to April 2023).<br><br>
<table>
<tr><th>Database/other source</th><th>Database provider</th><th>Database segment/version</th><th>Date search conducted</th><th>No of results</th></tr>
<tr><td>Medline</td><td>PubMed</td><td>1.0</td><td>April 20th 2023</td><td>8</td></tr>
<tr><td><u>https://www.kurin.com/studies/</u></td><td></td><td></td><td>April 20th 2023</td><td>10</td></tr>
</table>
<br>Provide details of the reference management system used (for example, EndNote, Zotero, RefWorks etc):<br><br>EndNote was used to manage references<br><br>Language: English language publications</td></tr>
</table>

| Topic | Method details |
|---|---|
| Search strategy | Present the full search strategies for all databases, registers and websites i.e. all the search terms: textwords (free text), subject index headings (for example, MeSH; medical subject headings) and the relationship between the search terms (for example, Boolean).<br><br>Search terms for PubMed: “Kurin” or “Kurin Lock Blood culture collection” and “initial specimen diversion device”<br>Abstracts were reviewed for eligible articles that reported the impact of Kurin / ISDD on blood culture contamination rates.<br><br>Also https://www.kurin.com/studies/ has been a good source of data both journal articles and poster presentations.<br><br>PubMed identified 14 relevant articles by title search with 8 included after abstract review<br><br>Record brief details of any additional searches, such as searches of company or professional organisation databases (include a description of each database):<br><br>Provide details of any limits applied to the search strategy (e.g.<br><br>English language and published between 2017 (Kurin launch date) and April 2023:<br><br>Record brief details of any additional searches, such as searches of company or professional organisation databases (include a description of each database):<br><br>NA |
| Selection process | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.<br><br>Assessment that the study was done using Kurin Lock Blood culture collection device vs standard collection methods.<br>As a company we are aware of all Kurin related studies as documented in this submission with links on https://www.kurin.com/studies/<br>Independently done. |
| Data collection process | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.<br><br>As a company we are aware of all Kurin related studies as documented in this submission with links on https://www.kurin.com/studies/<br>Independently done. |
| Any other notes helpful for reviewer | Enter text. |

### Excluded clinical effectiveness studies

List any excluded studies below. These are studies that were initially considered for inclusion at the level of full text review, but were later excluded for specific reasons, hyperlink text to the available abstract online e.g. PubMed. Highlight any studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.

| Excluded study | Design and intervention(s) | Rationale for exclusion | Company comments |
|---|---|---|---|
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |

Record the numbers of published studies included and excluded at each stage in an appropriate format (for example, the PRISMA flow diagram).

Enter text.

### Structured abstracts for unpublished studies

| |
|---|
| **Study title and authors** |
| **Introduction** |
| **Objectives** |
| **Methods** |
| **Results** |
| **Conclusion** |
| **Article status and expected publication:** Provide details of journal and anticipated publication date |

# Appendix B: Critical appraisal of relevant clinical effectiveness studies

### Table 38: Quality assessment results for parallel group RCTs

| Trial number (acronym) | Trial 1 | Trial 2 | [Add more columns as needed] |
|---|---|---|---|
| Was randomisation carried out appropriately? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Was the concealment of treatment allocation adequate? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Were the groups similar at the outset of the study in terms of prognostic factors? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Were the care providers, participants and outcome assessors blind to treatment allocation? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Were there any unexpected imbalances in dropouts between groups? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Is there any evidence to suggest that the authors measured more outcomes than they reported? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Did the analysis include an intention-to-treat analysis? If so, was this appropriate and were appropriate methods used to account for missing data? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |

Abbreviations: CRD, Centre for Reviews and Dissemination; RCT, randomised controlled trial.
Adapted from Systematic reviews: CRD's guidance for undertaking reviews in health care (University of York Centre for Reviews and Dissemination).

### Table 39: Quality assessment results for non-randomised and non-controlled studies

| Study name | Study 2 | [Add more columns as needed] | Study name |
|---|---|---|---|
| Was the cohort recruited in an acceptable way? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Was the exposure accurately measured to minimise bias? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Was the outcome accurately measured to minimise bias? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Have the authors identified all important confounding factors? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Have the authors taken account of the confounding factors in the design and/or analysis? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |
| Was the follow up of patients complete? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |

| Study name | Study 2 | [Add more columns as needed] | Study name |
|---|---|---|---|
| How precise (for example, in terms of confidence interval and p values) are the results? | Yes / no / not clear / N/A | Yes / no / not clear / N/A | |

Adapted from Critical Appraisal Skills Programme (CASP): Making sense of evidence 12 questions to help you make sense of a cohort study.

# Appendix C: Identification and selection of adverse events

**Table 40: Reporting search for adverse events –**
No Adverse events have been reported, therefore this section is not applicable.

<table>
<tr><th>Topic</th><th>Method details</th></tr>
<tr><td>Eligibility criteria</td><td>Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.<br><br>Enter text.</td></tr>
<tr><td>Information sources</td><td>Use the table below to specify all databases (e.g. MEDLINE), registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted and the number of results.<br><br>Enter text.<br><br>
<table>
<tr><th>Database/other source</th><th>Database provider</th><th>Database segment/version</th><th>Date search conducted</th><th>No of results</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
</table>
<br>Provide details of the reference management system used (for example, EndNote, Zotero, RefWorks etc):<br><br>Enter text.</td></tr>
<tr><td>Search strategy</td><td>Present the full search strategies for all databases, registers and websites i.e. all the search terms: textwords (free text), subject index headings (for example, MeSH; medical subject headings) and the relationship between the search terms (for example, Boolean).<br><br>Database name 1 search strategy:<br><br>Database name 2search strategy:<br><br>Database name 3 search strategy:<br><br>Record brief details of any additional searches, such as searches of company or professional organisation databases (include a description of each database):<br><br>Enter text.</td></tr>
</table>

| Topic | Method details |
|---|---|
| | Provide details of any limits applied to the search strategy (e.g. English language, date limits):<br><br>Enter text.<br>Provide details of any search filters applied to the search strategy (provide citations where relevant):<br>Enter text. |
| Selection process | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.<br><br>Enter text. |
| Data collection process | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.<br><br>Enter text. |
| Any other notes helpful for reviewer | Enter text. |

### Adverse events evidence

List any relevant studies below. If appropriate, further details on relevant evidence can be added to the adverse events section.

| Study | Design and intervention(s) | Details of adverse events | Company comments |
|---|---|---|---|
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |
| Enter text. | Enter text. | Enter text. | Enter text. |

Record the numbers of published studies included and excluded at each stage in an appropriate format (for example, the PRISMA flow diagram).

Enter text.

## Appendix D: Identification and selection of relevant economic evidence

Describe the process and methods used to identify and select the studies relevant to the technology being evaluated. See section 2 of the user guide for full details of how to complete this section.

The process and methods used to identify and select the studies relevant to the technology being evaluated are presented in Table 41.

**Table 41: Process and methods used to identify and select the studies**

| Topic | Method details |
|---|---|
| Eligibility criteria | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.<br><br>**Inclusion criteria**:<br><br>Population:<br>People who need a blood culture test within a secondary care setting.<br><br>Subgroups of interest include:<br>- Patients within the ICU setting.<br>- Patients within the general hospital setting.<br><br>Intervention and comparators:<br>Kurin blood culture collection, including Kurin Lock, ISDD devices<br>Standard of care: Standard blood culture collection (tubes and container)<br><br>Outcomes:<br>- Economic evaluation:<br>  - Summary of cost and hospital outcomes (e.g. bed stay)<br>  - Model structure and summary<br>  - Assumptions underpinning resource use<br>  - Cost drivers<br>  - Cost-effectiveness estimates<br>- Cost/ resource use<br>  - Direct costs<br>  - Medical costs (e.g. medications, staff, hospitalisation)<br>  - Indirect costs<br>  - Healthcare resource use<br><br>Study design:<br>- Economic evaluation:<br>  - Cost-utility analyses<br>  - Cost-effectiveness analyses<br>  - Cost-minimisation analyses<br>  - Cost-benefit analyses<br>- Cost/ resource use<br>  - Clinical studies |

<table>
<tr><th>Topic</th><th>Method details</th></tr>
<tr><td></td><td>
<ul><li>Economic evaluation reporting original cost data</li></ul>
-<br><br>
Geography:<br>
No restriction<br><br>
Publication date:<br>
Studies published in 1998 and later<br><br>
Language:<br>
English language publications
</td></tr>
<tr><td>Information sources</td><td>
Use the table below to specify all databases (e.g. MEDLINE), registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted and the number of results.<br><br>
PubMed was searched (January 1983 to March 16, 2023).<br><br>
<table>
<tr><th>Database/other source</th><th>Database provider</th><th>Database segment/version</th><th>Date search conducted</th><th>No of results</th></tr>
<tr><td>Medline</td><td>PubMed</td><td>1.0</td><td>March 16th 2023</td><td>91</td></tr>
</table>
<br>
Provide details of the reference management system used (for example, EndNote, Zotero, RefWorks etc):<br><br>
EndNote was used to manage references
</td></tr>
<tr><td>Search strategy</td><td>
Present the full search strategies for all databases, registers and websites i.e. all the search terms: textwords (free text), subject index headings (for example, MeSH; medical subject headings) and the relationship between the search terms (for example, Boolean).<br><br>
Search terms for PubMed: “False-positive blood culture contamination emergency department” or “Blood culture contamination” or “False-positive blood cultures” or “Reduced false-positive blood cultures” or “Best practice collection of blood culture” or “blood specimen diversion device” and “economic” and “cost”. Abstracts were reviewed for eligible articles that reported immediate or downstream economic costs of blood culture contamination.<br>
PubMed identified 91 relevant articles by title search with 8 included after abstract review<br><br>
Record brief details of any additional searches, such as searches of company or professional organisation databases (include a description of each database):<br><br>
Additional searches online for initial specimen diversion device and SteriPath were conducted.<br><br>
Provide details of any limits applied to the search strategy (e.g. English language, date limits):<br><br>
Limitations to the search strategy:<br><br>
Language:<br>
English language,
</td></tr>
</table>

| Topic | Method details |
|---|---|
| | Date:<br>1983 to 2023.<br><br>Provide details of any search filters applied to the search strategy (provide citations where relevant):<br>N/A |
| Selection process | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.<br><br>The inclusion/ exclusion of citations (both at the title/ abstract phase and full publication review) was conducted by one analyst, and a second analyst confirmed the decisions. Any disagreements were referred to the project manager and resolved by consensus. |
| Data collection process | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.<br><br>Relevant data were extracted into the pre-approved summary tables and checked by a second independent analyst against the original publications. Any disputes were resolved by consensus. |
| Any other notes helpful for reviewer | N/A |

Abbreviations: N/A, not applicable.

### Excluded economic studies

List any excluded studies below. These are studies that were initially considered for inclusion at the level of full text review, but were later excluded for specific reasons. Provide hyperlinks to the paper or abstract where possible. If not possible, please explain why.

A list of excluded studies is presented in Table 42.

**Table 42: List of excluded studies**

| Excluded study | Design and intervention(s) | Rationale for exclusion | Company comments |
|---|---|---|---|
| Self WH, Speroff T, Grijalva CG, McNaughton CD, Ashburn J, Liu D, Arbogast PG, Russ S, Storrow AB, Talbot TR. Reducing blood culture contamination in the emergency department: an interrupted time series quality improvement study. Academic Emergency Medicine. 2013 Jan;20(1):89-97. | N/A | Excluded – no economic/ financial data | N/A |
| Murofushi Y, Furuichi M, Shoji K, Kubota M, Ishiguro A, Uematsu S, Gai R, Miyairi I. Adverse economic impact associated with blood culture contamination in a pediatric emergency department. The Pediatric Infectious Disease Journal. 2018 Aug 1;37(8):755-8. | N/A | Excluded – no economic/ financial data | N/A |
| Hall RT, Domenico HJ, Self WH, Hain PD. Reducing the blood culture contamination rate in a pediatric emergency department and subsequent cost savings. Pediatrics. 2013 Jan;131(1):e292-7. | N/A | Excluded – no economic/ financial data | N/A |
| Thuler LC, Jenicek M, Turgeon JP, Rivard M, Lebel P, Lebel MH. Impact of a false positive blood culture result on the management of febrile children. The Pediatric infectious disease journal. 1997 Sep 1;16(9):846-51. | N/A | Excluded – no economic/ financial data | N/A |
| Hopkins K, Huynh S, McNary C, Walker A, Nixon R, Craighead JE. Reducing blood culture contamination rates: a systematic approach to improving quality of care. American journal of infection control. 2013 Dec 1;41(12):1272-4. | N/A | Excluded – no economic/ financial data | N/A |

| Excluded study | Design and intervention(s) | Rationale for exclusion | Company comments |
|---|---|---|---|
| Shafazand S, Weinacker AB. Blood cultures in the critical care unit: improving utilization and yield. Chest. 2002 Nov 1;122(5):1727-36. | N/A | Excluded – no economic/ financial data | N/A |
| Weinbaum FI, Lavie S, Danek M, Sixsmith D, Heinrich GF, Mills SS. Doing it right the first time: quality improvement and the contaminant blood culture. Journal of Clinical Microbiology. 1997 Mar;35(3):563-5. | N/A | Excluded – no economic/ financial data | N/A |
| Tepus D, Fleming E, Cox S, Hazelett S, Kropp D. Effectiveness of Chloraprep™ in reduction of blood culture contamination rates in emergency department. Journal of Nursing Care Quality. 2008 Jul 1;23(3):272-6. | N/A | Excluded – no economic/ financial data | N/A |
| Elmer J, Yamane D, Hou PC, Wilcox SR, Bajwa EK, Hess DR, Camargo CA, Greenberg SM, Rosand J, Pallin DJ, Goldstein JN. Cost and utility of microbiological cultures early after intensive care unit admission for intracerebral hemorrhage. Neurocritical care. 2017 Feb;26:58-63. | N/A | Excluded – underlying condition is difficult to assess blood culture contamination | N/A |
| Parikh K, Davis AB, Pavuluri P. Do we need this blood culture?. Hospital pediatrics. 2014 Mar 1;4(2):78-84. | N/A | Excluded – underlying condition is difficult to assess blood culture contamination | N/A |
| Segal GS, Chamberlain JM. Resource utilization and contaminated blood cultures in children at risk for occult bacteremia. Archives of pediatrics & adolescent medicine. 2000 May 1;154(5):469-73. | N/A | Excluded – underlying condition is difficult to assess blood culture contamination | N/A |
| Sadow KB, Chamberlain JM. Blood cultures in the evaluation of children with cellulitis. Pediatrics. 1998 Mar 1;101(3):e4 | N/A | Excluded – underlying condition is difficult to assess blood culture contamination | N/A |
| Ramanujam P, Rathlev NK. Blood cultures do not change management in hospitalized patients with community-acquired pneumonia. Academic emergency medicine. 2006 Jul;13(7):740-5. | N/A | Excluded – underlying condition is difficult to assess blood culture contamination | N/A |
| Perl B, Gottehrer NP, Raveh D, Schlesinger Y, Rudensky B, Yinnon AM. Cost-effectiveness of blood cultures for adult patients with | N/A | Excluded – underlying condition is difficult to assess blood culture contamination | N/A |

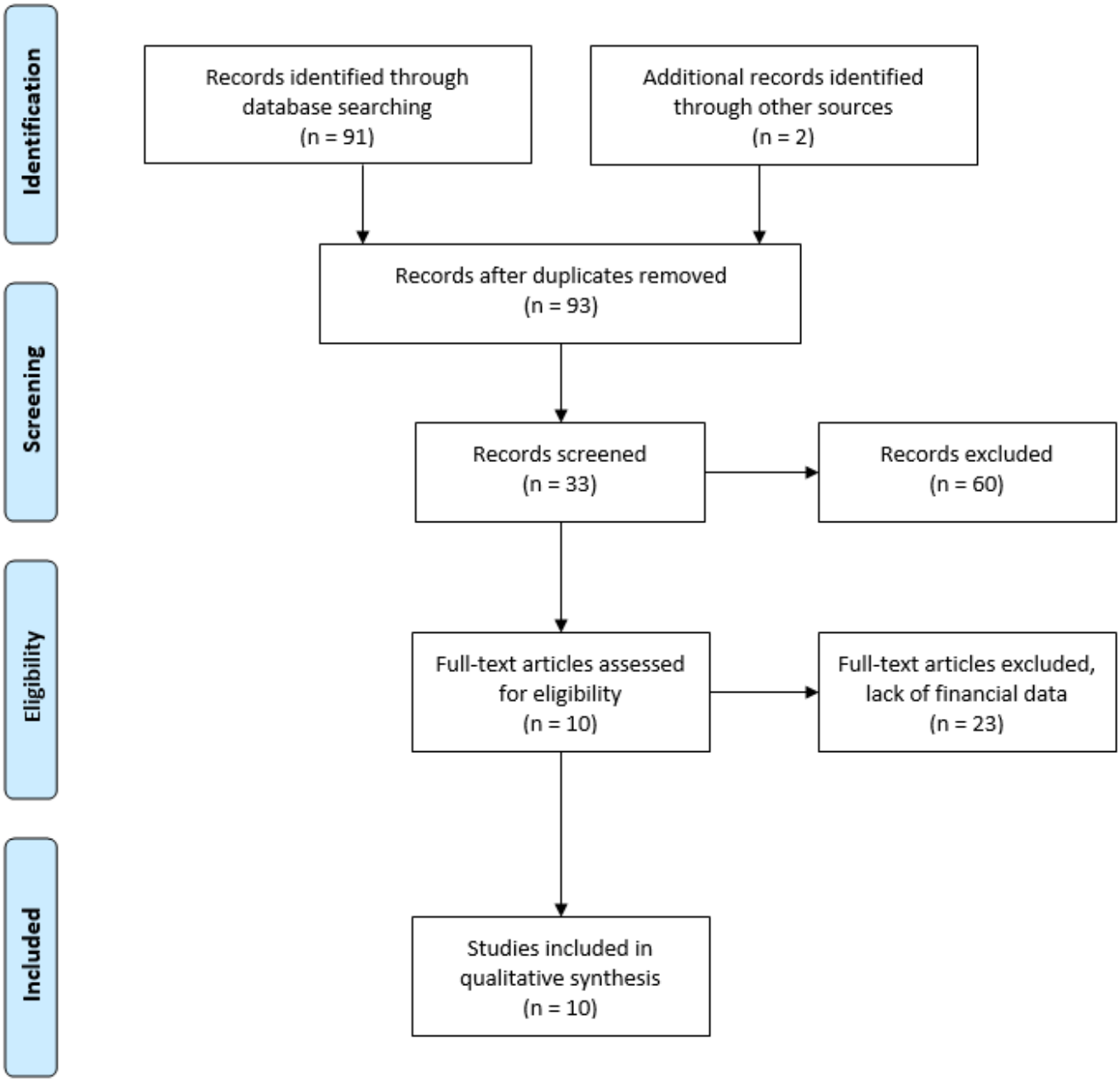
| Excluded study | Design and intervention(s) | Rationale for exclusion | Company comments |
|---|---|---|---|
| cellulitis. Clinical infectious diseases. 1999 Dec 1;29(6):1483-8. | | | |
| Henke PK, Polk Jr HC. Efficacy of blood cultures in the critically ill surgical patient. Surgery. 1996 Oct 1;120(4):752-9. | N/A | Excluded – underlying condition is difficult to assess blood culture contamination | N/A |
| Surdulescu S, Utamsingh D, Shekar R. Phlebotomy teams reduce blood-culture contamination rate and save money. Clinical performance and quality health care. 1998 Apr 1;6(2):60-2. | N/A | Exclude – no relevant comparator | N/A |
| Gander RM, Byrd L, DeCrescenzo M, Hirany S, Bowen M, Baughman J. Impact of blood cultures drawn by phlebotomy on contamination rates and health care costs in a hospital emergency department. Journal of clinical microbiology. 2009 Apr;47(4):1021-4. | N/A | Exclude – no relevant comparator | N/A |
| Boyce JM, Nadeau J, Dumigan D, Miller D, Dubowsky C, Reilly L, Hannon CV. Obtaining Blood Cultures by Venipuncture versus from Central Lines Impact on Blood Culture Contamination Rates and Potential Effect on Central Line–Associated Bloodstream Infection Reporting. Infection Control & Hospital Epidemiology. 2013 Oct;34(10):1042-7. | N/A | Exclude – no relevant comparator | N/A |
| Siegman-Igra Y, Anglim AM, Shapiro DE, Adal KA, Strain BA, Farr BM. Diagnosis of vascular catheter-related bloodstream infection: a meta-analysis. Journal of Clinical Microbiology. 1997 Apr;35(4):928-36. | N/A | Excluded – evidence >20 years | N/A |
| The significance of changing needles when inoculating blood cultures: a meta-analysis | N/A | Excluded – evidence >20 years | N/A |

Abbreviations: N/A, not applicable.

*Record the numbers of published studies included and excluded at each stage in an appropriate format (for example, the PRISMA flow diagram).*

The numbers of published studies included and excluded at each stage are presented in Figure 8.

**Figure 8: PRISMA diagram**



# Appendix E: Critical appraisal of relevant economic evidence

### Figure 43: Quality assessment results for economic studies

| Study | Response | Comments |
|---|---|---|
| **Section 1: Applicability (relevance to specific review questions and the NICE reference case)** | – | – |
| 1.1 Is the study population appropriate for the review question? | Yes / partly / no / not clear / N/A | Enter text. |
| 1.2 Are the interventions appropriate for the review question? | Yes / partly / no / not clear / N/A | Enter text. |
| 1.3 Is the system in which the study was done sufficiently similar to the current UK context? | Yes / partly / no / not clear / N/A | Enter text. |
| 1.4 Are the perspectives clearly stated and are they appropriate for the review question? | Yes / partly / no / not clear / N/A | Enter text. |
| 1.5 Are all direct effects on individuals included, and are all other effects included where they are material? | Yes / partly / no / not clear / N/A | Enter text. |
| 1.6 Are all future costs and outcomes discounted appropriately? | Yes / partly / no / not clear / N/A | Enter text. |
| 1.7 Is quality-adjusted life year (QALY) used as an outcome, and was it derived using NICE's preferred methods? If not, describe the rationale and outcomes used in line with the analytical perspectives taken (row 1.4, above). | Yes / partly / no / not clear / N/A | Enter text. |
| 1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued? | Yes / partly / no / not clear / N/A | Enter text. |
| 1.9 Overall judgement: directly applicable | Yes / partly / no / not clear / N/A | Enter text. |
| **Section 2: Study limitations (the level of methodological quality)** | – | – |
| 2.1 Does the model structure adequately reflect the nature of the topic under evaluation? | Yes / partly / no / not clear / N/A | Enter text. |
| 2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? | Yes / partly / no / not clear / N/A | Enter text. |
| 2.3 Are all important and relevant outcomes included? | Yes / partly / no / not clear / N/A | Enter text. |
| 2.4 Are the estimates of baseline outcomes from the best available source? | Yes / partly / no / not clear / N/A | Enter text. |
| 2.5 Are the estimates of relative intervention effects from the best available source? | Yes / partly / no / not clear / N/A | Enter text. |

| Study | Response | Comments |
|---|---|---|
| 2.6 Are all important and relevant costs included? | Yes / partly / no / not clear / N/A | Enter text. |
| 2.7 Are the estimates of resource use from the best available source? | Yes / partly / no / not clear / N/A | Enter text. |
| 2.8 Are the unit costs of resources from the best available source? | Yes / partly / no / not clear / N/A | Enter text. |
| 2.9 Is an appropriate incremental analysis presented or can it be calculated from the data? | Yes / partly / no / not clear / N/A | Enter text. |
| 2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? | Yes / partly / no / not clear / N/A | Enter text. |
| 2.11 Is there any potential conflict of interest? | Yes / partly / no / not clear / N/A | Enter text. |
| 2.12 Overall assessment: | Minor limitations/Potentially serious limitations/Very serious limitations | Enter text. |

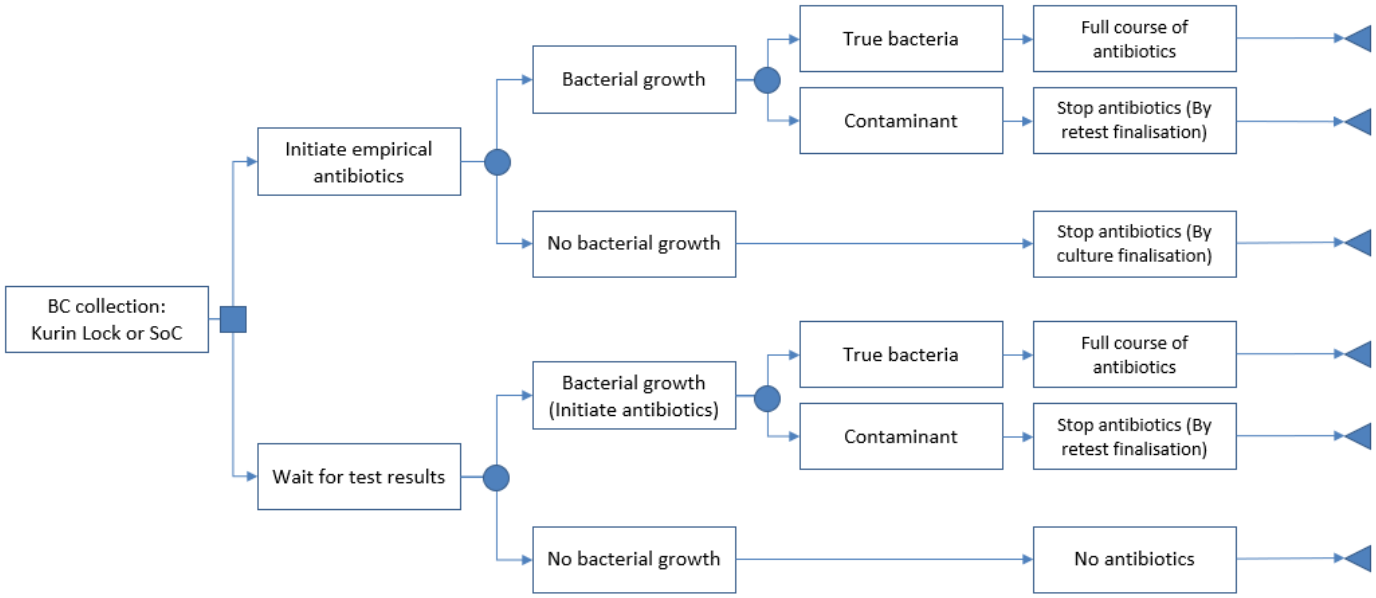
*See Appendix H of the Developing NICE guidelines: the manual (updated 2022), pages 10 and 11 have additional questions if the study is a cost benefit or cost consequences analysis, respectively. Pages 12 to 23 contain notes for how to carry out the critical assessment for each question.*

## Appendix F: Model structure

*Provide a diagram of the structure of your decision model.*

A diagram of the structure of the decision tree model is presented in Figure 9.

**Figure 9. Decision tree**




Abbreviations: BC, blood collection; SoC, standard of care.

## Appendix G: Checklist of confidential information

See section 1 of the user guide for instructions on how to complete this section.

Does your submission of evidence contain any confidential information? Check the appropriate box:

## No X

If no, proceed to declaration (below).

If yes, complete the table below, and insert or delete rows as necessary. Ensure that all relevant sections of your submission of evidence are clearly highlighted and underlined in your submission document (see User Guide for more details on how to do this) and match the information in the table. Add the referenced confidential content (text, graphs, figures, illustrations and so on) to which this applies.

| Page number | Nature of confidential information | Rationale for confidential status | Timeframe of confidentiality restriction |
|---|---|---|---|
| Enter text. | ☐ Commercial in confidence<br>☐ Academic in confidence<br>☐ Depersonalised data | Enter text. | Enter text. |
| Details | Enter text. | – | – |
| Enter text. | ☐ Commercial in confidence<br>☐ Academic in confidence<br>☐ Depersonalised data | Enter text. | Enter text. |

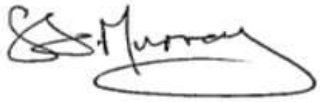
**Confidential information declaration**

I confirm that:

- All relevant data pertinent to the development of medical technology guidance (MTG) has been disclosed to NICE.
- All confidential sections in the submission have been marked correctly.
- If I have attached any publication or other information in support of this notification, I have obtained the appropriate permission or paid the appropriate copyright fee to enable my organisation to share this publication or information with NICE.

**Note that NICE does not accept any responsibility for the disclosure of confidential information through publication of documentation on our website that has not been correctly marked. If a completed checklist is not included, then NICE will consider all information contained in your submission of evidence as not confidential.**

**Signed*:**
** Must be medical director or equivalent*



**Date: 06-06-23**

**Print:** STUART MURRAY

**Role / organisation:**
**COMMERCIAL DIRECTOR – ISKUS HEALTH**

**Contact email:** stuart.murray@iskushealth.com

# National Institute for Health and Care Excellence

## Collated comments table

**MTG Medtech Guidance:**

**Expert contact details and declarations of interest:**

<table>
<tr><td>Expert #1</td><td>Bruno Coelho, Senior Staff Nurse / Clinical Research Nurse, Emergency Department, Guy’s and St. Thomas’ Hospital</td></tr>
<tr><td></td><td>Nominated by: company</td></tr>
<tr><td></td><td>DOI: NONE</td></tr>
<tr><td>Expert #2</td><td>Jane Hodson, Lead IV Practitioner, GSTT</td></tr>
<tr><td></td><td>Nominated by: company</td></tr>
<tr><td></td><td>DOI: NONE</td></tr>
<tr><td>Expert #3</td><td>Andrew Barton, Chairman and Nurse Consultant, NIVAS</td></tr>
<tr><td></td><td>Nominated by: NICE</td></tr>
<tr><td></td><td>DOI: NONE</td></tr>
<tr><td>Expert #4</td><td>David Partridge, Consultant Microbiologist, Sheffield Teaching Hospitals</td></tr>
<tr><td></td><td>Nominated by: NICE</td></tr>
<tr><td></td><td>DOI:
<table>
<tr><th rowspan="2">Type of interest *</th><th rowspan="2">Description of interest</th><th colspan="2">Relevant dates</th></tr>
<tr><th>Interest arose</th><th>Interest ceased</th></tr>
<tr><td>Non-financial professional</td><td>Vice President of the British Infection Association</td><td>May 2021</td><td>Ongoing</td></tr>
</table></td></tr>
</table>

| | | |
|---|---|---|
| 1 | Please describe your level of experience with the procedure/technology, for example:<br>Are you familiar with the procedure/technology?<br><br>Have you used it or are you currently using it?<br>Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake?<br>Is this procedure/technology performed/used by clinicians in specialities other than your own?<br>− If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it. | Expert #1<br>I have been facilitating the introduction of Kurin Lock in the department (arranging storage, teaching sessions with the company, training the multidisciplinary team, …)<br>I have used Kurin Lock several times in my clinical practice and I was also present when a study about this device was being done in the department.<br>This device is currently being introduced in the NHS. I am aware that some NHS Truts are starting to use Kurin Lock. GSTT has introduced the device in ED and ICU and it is expected to be used in the whole trust within the next months. |
| | | Expert #2<br>I am very familiar with the product. I oversaw a 5 month trial of the product in our very busy A & E department in central London. To the best of my knowledge at the time, we were the first Trust in the UK to undertake a study on the product which aims to reduce the contamination rates of blood cultures. False positive blood cultures have serious implications for the patient such as unnecessary hospitalisation, treatments and medications among other things. hese are associated with a significant financial burden on the hospital system. Tour pre- trial contamination rates were approximately 6%. Many interventions had been implemented to attempt to reduce these but there had been so significant change in these rates. Post-trial saw our contamination rates drop by approximately 66% to under 2%. This has been shown to be statistically significant. Due to the impressive results we are now in the process of implementing the product across the Trust. Currently it is being used routinely in A & E and ITU with roll out across all the other divisions in process. |
| | | Expert #3<br>I am an expert in the taking of blood cultures, I am familiar with the technology and the process for taking blood cultures. I have not used this specific device but have used a device similar in training. I take blood cultures the traditional way daily<br>Blood cultures are taken daily through the NHS by all specialties, contamination of blood cultures is a universal complication and can be as much as 20% in some centres. |

| | | |
|---|---|---|
| | | This device could be used in all departments to reduce this complication |
| | | Expert #4<br>No experience of the technology itself and don't believe it is widely used in the NHS but my specialty handles blood culture results and has to consider the potential that growth represents contamination and balance the risks of assuming this with possible downsides of inappropriately treated infection vs patient, operational and antimicrobial stewardship impact of treating false positive cultures. |
| 2 | − Please indicate your research experience relating to this procedure (please choose one or more if relevant): | Expert #1<br>I have done bibliographic research on this procedure.<br>I have done clinical research on this procedure involving patients or healthy volunteers.<br>Other (please comment): A study was done in St. Thomas' Hospital Emergency Department. I am currently facilitating the introduction of this device in the department. |
| | | Expert #2<br>I have done clinical research on this procedure involving patients or healthy volunteers.<br>I will publish this research. |
| | | Expert #3<br>I have done bibliographic research on this procedure.<br>Other (please comment) – I have used the device in simulation |
| | | Expert #4<br>I have had no involvement in research on this procedure.<br>Other (please comment) |

**Current management**

| | | |
|---|---|---|
| 3 | How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design?<br><br>Which of the following best describes the procedure (please choose one): | Expert #1<br><br>Definitely novel and of uncertain safety and efficacy. |
| | | Expert #2<br>The first in a new class of procedure. |
| | | Expert #3<br>Definitely novel and of uncertain safety and efficacy. |
| | | Expert #4<br>The first in a new class of procedure. |
| 4 | Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care? | Expert #1<br>It could be used as a standard of care if it's efficiency is proved. At the moment its used as an addiction to the current practice. I believe that if it's benefit it's proved, it could be used as a standard of practice. |
| | | Expert #2<br>It does not replace current standards of care. The device is solely used when taking a blood culture. If a blood culture is not required then standard phlebotomy equipment is used. If a blood culture is required all subsequent bloods are taken using the same device. |
| | | Expert #3<br>Yes if it can reduce blood culture contaminations. Such contaminations are very costly to the NHS and to patents as they can incur additional treatment and cost. |
| | | Expert #4<br>In addition to current standard care |

**Potential patient benefits**

| | | |
|---|---|---|
| 5 | Please describe the current standard of care that is used in the NHS. | Expert #1<br>• Clean trolley with large 2% chlorhexidine in 70% alcohol wipe.<br>• Explain the procedure to the patient and obtain consent.<br>• Set up equipment.<br>• Wash hands with bactericidal soap and water, or decontaminate physically clean hands with alcohol-based handrub.<br>• Apply disposable tourniquet and palpate vein. Release tourniquet.<br>• Clean skin with 2% chlorhexidine in 70% alcohol swab for 30 seconds. Do NOT re-palpate site.<br>• Remove flip-off cap from culture bottles and clean with second 2% chlorhexidine in 70% alcohol swab for 30 seconds<br>and allow to dry for 30 seconds.<br>• Was or decontaminate hands with 2% chlorhexidine in 70% alcohol. Put on sterile gloves.<br>• Reapply tourniquet.<br>• Remove sheath covering wings and perform venepuncture.<br>• Discard the first 8 – 10 ml i.e. one yellow top vacutainer tube, to reduce the risk of sample contamination.<br>• Blood cultures require 8 – 10 ml/bottle for adults. Hold upright and use bottle gradations to accurately gauge sample<br>volume. Inoculate the aerobic bottle first.<br>• Activate safety device.<br>• Remove gloves and wash/decontaminate hands.<br>• Apply appropriate dressing. |
| | | Expert #2<br>There is variation in the current standard for taking a blood culture. Some places will use a standard needle and syringe to obtain the sample from a patients vein. The needle is then changed and the blood culture bottle is inoculated with blood sample. There is significant risk of |

| | | |
|---|---|---|
| | | needle stick injury, contamination of the specimen and is more painful for the patient. Other places will use a butterfly needle and vacutainer system to collect the blood culture. This method has the potential to decrease the risks stated above. A final method is to take the blood culture when inserting a peripheral intravenous cannula. This method has the highest associated risk of contamination of the blood culture. |
| | | Expert #3<br>ANTT procedure suing a needle and vacutainer, the is currently no way of avoiding the first few mls of blood which can be contaminated with skin flora if the skin isn't cleaned properly |
| | | Expert #4<br>Blood cultures sampled directly from phlebotomy device or from newly inserted cannula (latter discouraged but happens in practice) |
| 6 | Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this?<br>If so, how do these differ from the procedure/technology described in the briefing? | Expert #1<br>According to the documentation sent by the NICE team, there is another similar device in the market (Steriporth). The technique itself (discarding the initial flush of blood) is known and used, but manually by the health care professional. Also, the use of aseptic technique and materials (including serial gloves, for example) is a common practice around the world. |
| | | Expert #2<br>None available in the UK to the best of my knowledge. |
| | | Expert #3<br>Not aware |
| | | Expert #4<br>No |
| 7 | What do you consider to be the potential benefits to patients from using this procedure/technology? | Expert #1<br>Reduce the use of antibiotics; decrease the risk of antibiotic multi resistance; reduce hospital stay and admissions; decrease emotional stress for patient; increase patient safety; increase quality of care; |

| | | |
|---|---|---|
| | | Expert #2<br>False positive blood cultures have significant impact on patients. These include delays in diagnosis, the administration of unnecessary administration of intravenous antibiotics, increased risks of complications related to unnecessary intravenous cannulation, unplanned removal of central venous access device, additional laboratory testing, delayed discharge by 2 days which increases the overall cost of hospitalisation. There are also associated time and cost pressures associated with the manpower required to investigate each false positive. |
| | | Expert #3<br>Recuing blood culture contaminates will save huge amounts of money for the NHS and ensure patients do receive unnecessary treatment based on the false positive results |
| | | Expert #4<br>Reduction in number of false positive blood cultures with resulting improvements in antimicrobial stewardship, reduced staff time managing results, reduced length of stay and potentially reduced risk of failing to treat genuine infection if positive cultures are more likely to be genuine |

**Potential system impact**

| | | |
|---|---|---|
| 8 | Are there any groups of patients who would particularly benefit from using this procedure/technology? | Expert #1<br>The device can be used in any patient requiring blood cultures. |
| | | Expert #2<br>Patients in A & E and those that are significantly vulnerable: Children, elderly, immunosuppressed, cancer, renal disease, on parenteral nutrition. |
| | | Expert #3<br>All patients will benefit |

| | | |
|---|---|---|
| | | Expert #4<br>Emergency department patients, paediatric patients, intravenous drug users. |
| 9 | Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system?<br>Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment? | Expert #1<br>Yes, if its efficiency and cost-benefits are proved. |
| | | Expert #2<br>Yes, as outlined above its implantation can shorten hospital stays, prevent unnecessary treatment modalities and invasive treatments |
| | | Expert #3<br>Yes and it can lead the reduction in antibiotic use for false positive results and costs involved in keeping a patent in hospital with a suspect bacteraemia when they don't have one. |
| | | Expert #4<br>See above |
| 10 | Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the procedure/technology likely to cost more or less than current standard care, or about the same? (in terms of staff, equipment, care setting etc) | Expert #1<br>The procedure will cost more to the NHS. Although, it's important to study how much the costs will decrease in the long term (less false positive BC will conduct to less hospital admissions, less use of antibiotics… - it's important to study this values and assess cost-benefit).<br>Apart from the equipment itself, it is required to have a storage room available and to involve the costs of disposing. The staff can be trained but no extra staff will be required. |
| | | Expert #2<br>It has the potential of reducing costs overall. The estimated cost of a false positive blood culture is £2000– 4200 during the trial period (May – Sept 2021) the Trust had a potential savings of £28 -72K. This was in a single area. Once fully implemented across the Trust the savings are likely to be significant. |
| | | Expert #3<br>Less in the long term |

| | | |
|---|---|---|
| | | Expert #4<br>Depends upon the cost of the device but I would expect it to be cost incurring |
| 11 | What do you consider to be the resource impact from adopting this procedure/technology (is it likely to cost more or less than standard care, or about same-in terms of staff, equipment, and care setting)? | Expert #1<br>It will cost more to the NHS because of the cost of the device. Storage needs to be arranged and appropriate disposal. This cost will also need to be included. No extra staff is necessary. |
| | | Expert #2<br>The resource impact has the potential to be less costly than standard care. The reduction in the time and cost of manpower required to investigate false positive blood culture results will free staff up to focus on other things. |
| | | Expert #3<br>May cost more than a basic needle but long term the cost will be less as false positive cultures are reduced |
| | | Expert #4<br>I would expect it to be cost incurring unless its use was restricted to specific groups at high risk of blood culture contamination |
| 12 | What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely? | Expert #1<br>Storage room to keep the devices. |
| | | Expert #2<br>None. It is extremely easy to use and comes in a number of styles to suit all ages and two methods of taking a blood culture (vacutainer and from a cannula). |
| | | Expert #3<br>This is low impact change in current practice |
| | | Expert #4 |

| | | |
|---|---|---|
| | | Nil |

**General advice**

| | | |
|---|---|---|
| 13 | Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety? | Expert #1<br>Training sessions are being provided by the company. Also, according to the company, education by trained colleagues is safe for a correct practice. |
| | | Expert #2<br>Training is readily available but requires no adjustment in current processes. It is a safety engineered device therefore meets all current standards. |
| | | Expert #3<br>Very basic training which would take minuets |
| | | Expert #4<br>Minimal |

**Other considerations**

| | | |
|---|---|---|
| 14 | What are the potential harms of the procedure/technology?<br>Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: | Expert #1<br>Cannot identify any potential harms. |
| | | Expert #2<br>None other than the standard risks associated with taking a blood culture (hematoma formation, bleeding, bruising, pain, damage to the vein, discomfort, lightheaded, fainting |

| | | |
|---|---|---|
| | Adverse events reported in the literature (if possible, please cite literature)<br>Anecdotal adverse events (known from experience)<br>Theoretical adverse events | Expert #3<br>No harms that I can think of |
| | | Expert #4<br>None |
| 15 | Please list the key efficacy outcomes for this procedure/technology? | Expert #1<br>Less false positive BC will conduct to less hospital admissions, less use of antibiotics… - it's important to study this values and assess cost-benefit.<br>Decrease the use of antibiotics; decrease the risk of antibiotic multi resistance; decrease hospital stay and admissions; decrease emotional stress for patient; increase patient safety; increase quality of care; |
| | | Expert #2<br>Reduction in the contamination of blood cultures which may lead to false positives results |
| | | Expert #3<br>Reliable blood culture results which will reduce cost of false positive results and ensure patient safety |
| | | Expert #4<br>Reduction in blood culture contamination rate. Reduction in antibiotic use due to contaminated blood cultures. Reduced length of stay |
| 16 | Please list any uncertainties or concerns about the efficacy and safety of this procedure/? | Expert #1<br>Cost-benefit<br>Can/should this product be used when taking blood cultures from central lines? |
| | | Expert #2<br>None |
| | | Expert #3 |

| | | |
|---|---|---|
| | | None |
| | | Expert #4<br>Lack of current evidence of reduced contamination rate in clinical practice |
| 17 | Is there controversy, or important uncertainty, about any aspect of the procedure/technology? | Expert #1<br>Cost-benefit in the UK should be studied. According to the bibliography presented by the NICE team, the studies are done in the USA and might not represent the reality in the UK. |
| | | Expert #2<br>No |
| | | Expert #3<br>No |
| | | Expert #4<br>Lack of evidence of real world effectiveness |
| 18 | If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one): | Expert #1<br>Most or all district general hospitals. |
| | | Expert #2<br>Most or all district general hospitals. |
| | | Expert #3<br>Most or all district general hospitals. |
| | | Expert #4<br>Most or all district general hospitals. |
| 19 | Please list any abstracts or conference proceedings that you are aware of that have | Expert #1 |

| | | |
|---|---|---|
| | been recently presented / published on this procedure/technology (this can include your own work).<br><br>Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important. | The Emergency Department at St. Thomas' Hospital has done a study and a poster about the impact of Kurin Lock. |
| | | Expert #2<br><br>I produced a poster on the results of the trial we undertook in our A & E department. It is our intent to write up the results of this trial for publication. |
| | | Expert #3<br><br>Blank |
| | | Expert #4<br><br>Nil |
| 20 | Are there any major trials or registries of this procedure/technology currently in progress? If so, please list. | Expert #1<br><br>Blank |
| | | Expert #2<br><br>Unsure |
| | | Expert #3<br><br>Blank |
| | | Expert #4<br><br>Not that I am aware of |
| 21 | Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)? | Expert #1<br><br>I believe this device can be used in anyone needing Blood Cultures. |
| | | Expert #2<br><br>Blank |

| | | |
|---|---|---|
| | | Expert #3<br>Everyone who needs a blood culture, hundreds of thousands of patients. |
| | | Expert #4<br>Hundreds of thousands |

| | | |
|---|---|---|
| 22 | Are there any issues with the usability or practical aspects of the procedure/technology? | Expert#1<br>Using Kurin Lock is very easy and intuitive once people are aware of it. |
| | | Expert#2<br>No |
| | | Expert#3<br>No |
| | | Expert #4<br>Not that I am aware of but no experience |
| 23 | Are you aware of any issues which would prevent (or have prevented) this procedure/technology being adopted in your organisation or across the wider NHS? | Expert#1<br>Alert/education of staff about taking blood cultures, aseptic technique and infection control. |
| | | Expert#2<br>The cost of the product can be off putting in the first instance. This needs to be looked at in the wider context of the economic model of reducing contamination rates, the benefits to the patient and the resultant improvement of the experience and satisfaction. |
| | | Expert#3<br>No |
| | | Expert #4<br>Not if cost-effective |
| 24 | Is there any research that you feel would be needed to address uncertainties in the evidence base? | Expert#1<br>Blank |
| | | Expert#2<br>No - our results have supported the results demonstrated in multiple studies taken across many areas of the USA. |

| | | |
|---|---|---|
| | | Expert#3<br>Nil |
| | | Expert #4<br>UK based evidence of effectiveness |
| 25 | Please suggest potential audit criteria for this procedure/technology. If known, please describe:<br>− Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured.<br>− Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured | Expert#1<br>Beneficial outcome measures:<br>Decrease the use of antibiotics; decrease the risk of antibiotic multi resistance; decrease hospital stay and admissions; decrease emotional stress for patient; increase patient safety; increase quality of care; possible reduce in costs.<br>Adverse outcome measures:<br>Low adherence from staff to the use of the device<br>No equality of care in the NHS<br>No standard of practice / care |
| | | Expert#2<br>Beneficial outcome measures:<br>Reduction in contamination rates – must know what the contamination rates are pre - trial to measure against those on completion.<br>During and after implementation continue to measure the contamination rates of blood cultures<br>Adverse outcome measures:<br>Monitor blood culture rates monthly to observe for a subsequent rise in contamination rates. Investigate to see what is causing this rise – reduction or unavailability in access to Kurin, staff training needs not met, poor practice issues. |
| | | Expert#3<br>Beneficial outcome measures:<br>Blank |

| | | |
|---|---|---|
| | | Adverse outcome measures:<br>Blank |
| | | Expert #4<br>Beneficial outcome measures:<br>Reduced rate of blood culture contaminants<br>Reduced antibiotic use for blood culture contaminants<br>Reduced length of stay due to blood culture contamination<br><br>Adverse outcome measures:<br>Cost<br>Failed venepuncture as a result of using device<br>Increased time to perform venepuncture as a result of device |
| 26 | Please add any further comments on your particular experiences or knowledge of the procedure/technology | Expert#1<br>Blank |
| | | Expert# 2<br>This is an excellent product and has the potential to significantly improve patient experience. I am a vascular access nurse and it saddens me when a patient dependant on central venous access loses their line due to a contaminated blood culture result. Many of these patient end up with significant damage to their vasculature which ultimately can be life limiting. Doing all that we can to reduce the impact of false positive blood cultures is far reaching for patients. |
| | | Expert#3<br>Blank |
| | | Expert #4 |

| | | |
|---|---|---|
| | | Nil |

NICE National Institute for Health and Care Excellence

## External Assessment Group correspondence log

## MT582 Kurin Lock for Blood Collection

The purpose of this log is to show where the External Assessment Group relied in their assessment of the topic on information or evidence not included in the company's original submission. This is normally where the External Assessment Group:

a) become aware of additional relevant evidence not submitted by the company;
b) needs to check "real world" assumptions with NICE's expert advisers, or;
c) needs to ask the company for additional information or data not included in the original submission, or;
d) needs to correspond with an organisation or individual outside of NICE

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is captured. The table is shared with the NICE medical technologies advisory committee (MTAC) as part of the committee documentation, and is published on the NICE website at public consultation.

| # | Date | Who / Purpose | Question/request | Response received |
|---|---|---|---|---|
| ***1.*** | 13/06/2023 | Company start-up meeting to discuss clinical submission. | The EAG sent a list of questions in advance of the meeting. These were then discussed at the meeting. | Notes from this meeting, and written responses to the questions sent in advance are noted in Appendix 1 (Table 1). |
| ***2.*** | 19/06/2023 | Clinical expert engagement meeting. | The EAG sent a list of questions in advance of the meeting (Table 2). These were then discussed at the meeting. The list of questions were also sent to a second group of clinical experts not in attendance at the meeting. | Notes from this meeting are in Appendix 2 (note: not verified by all clinical experts in attendance). Written responses from the second group of clinical experts are in Appendix 3 (Tables 3-4). |

| | | | | |
|---|---|---|---|---|
| ***3.*** | 20/06/2023 | Email sent to company. | EAG clarified some data sources and population age cut-offs with the company. | The company confirmed: "The "English population estimates" tab provides the data to estimate the proportion that are adults (currently assumed to be >12) which in turn is used to calculate the antibiotic costs." |
| ***4.*** | 22/06/2023 | Email sent to company. | EAG sought clarification on numbers and publication types of evidence identified in company submission. | The company confirmed there are in total to date 12 pieces of specific evidence supporting the effectiveness of Kurin in the hospital setting. |
| ***5.*** | 30/06/2023 | Email sent to company. | Follow-up questions for the company regarding the economic model and choice of inputs. | Written responses from the company are in Appendix 4 (Table 5) |
| ***6.*** | 07/07/2023 | Email sent to clinical experts. | EAG sent a list of additional questions to four clinical experts. | Written responses received from clinical experts are in Appendix 5 (Tables 6-8). |
| ***7.*** | 25/07/2023 | Email sent to company. | EAG sought response on adverse event reports identified on MAUDE database during assessment process. | The company stated they were not aware of the reports but would raise it with Kurin in the US for a response. Company stated they are unaware of any product failures in the UK. |
| ***8.*** | 25/07/2023 | Email to clinical expert, Dr Mustafa Atta. | EAG sought clarification on results reported in publication included in evidence base (Atta 2023), regarding data presented in table, number of patients included in study and methods of calculating estimated bed days saved. | No response received at time of report submission (01/08/2023).<br><br>Response received via email on 09/08/2023, details are in Appendix 6. The EAG note that MA also sent over PDF files of economic model |

| | | | | |
|---|---|---|---|---|
| | | | | outputs relating to Kurin Lock. The EAG considered the information provided by MA to be relevant, but would not have any major impact on the assessment report submitted. |

## Appendix 1. Notes from meeting with Iskus Health LTD Post-Submission

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

Medical Technologies Evaluation Programme

**Company Start-up Meeting**

**MTG582 Kurin Lock for Blood Collection**

This document summarises the discussions that took place at the company post clinical submission meeting for MTG582, which took place on Tuesday 13th June,12:00 to 13:00pm.

**Attendees:**

**NICE**

- Bernice Dillon
- Amy Barr
- Aamer Jawed

**EAG**

- Ayesha Rahim
- Megan Dale

**Company**

- Stuart Murray (Iskus Health LTD Commercial Director)
- Anthony Bentley (Mtech Health Economist)

**Introduction**

The EAG and NICE had provided the list of queries to the company in advance of the meeting, these are reported in **Error! Reference source not found.**. The written responses from the company were provided to the EAG after the meeting took place. The questions provided to the company centred around some key themes including:

- The technology
- Use of the technology
- Evidence and benefits

Additional questions that were not provided in advance to the company were also discussed in this meeting, and are reflected in these notes.

NICE confirmed that the EAG would be able to contact the company directly with any queries relating to the assessment after this meeting.

## The Technology (Table 1, questions 1-6)

**Question 1) There are 14 versions of the same device listed in Table 2 of the company submission. Do these versions of the device differ in any way that would mean evidence would not be generalisable between the different versions?**

**Company:** Stated that the different versions of the device exist to facilitate the different ways of taking blood cultures in practice. 90% are taken using a closed system. There are different versions to accommodate different bottle tops. St Thomas's data used 2 different types of devices, one for standard blood taking and one for taking blood from peripheral intravenous cannulas (PIVs). In A&E, 60% are taken from PIVs even though this is not considered best practice. The evidence is generalisable between the different versions of the device.

**EAG**: Sought clarification around the procedure of taking blood from PIV cannulas, and whether this was only done from freshly inserted PIVs.

**Company:** Confirmed that blood is only taken from freshly inserted PIVs, as per local protocols and guidance.

**Question 2) Are you aware of any instances/reports of device failure or malfunction?**

**Company**: Stated they are not aware of any reports of failure or malfunction.

**Question 3) Are there cost differences between the different versions of the device, and if so, which one is represented by the cost of £19.50? & Question 4) Does the cost of £19.50 per unit vary depending on the configuration of bottles/methods shown in Fig.1 of the submission?**

**Company**: Stated that the pricing is very simple, every single code is the same. Whether it has a needle or not or whether it has a collection set or not has no impact on the cost.

**NICE**: Sought clarification on whether the cost includes VAT.

**Company**: Confirmed it does not include VAT.

**Question 5) In section 1.2 of the submission: "The technology", it is stated that an alternative name for the Kurin Lock device is 'blood culture collection division device'. Can we check, is this supposed to say 'diversion device'?**

**Company**: Confirmed this was a typographical error and the wording is supposed to read: 'diversion device'.

**Question 6) Please could you explain how the pressure-rated extension set is used, and if it is relevant to the submission?**

**Company**: Stated that when clinicians take blood from a peripheral line, sometimes those PIVs are not closed systems and there's no extension. With the Kurin Lock PIV set, the customer is getting a pressure tested extension set free of charge. The Kurin device can be removed and then the patient has an extension set in place for other purposes such as delivering fluids.

**EAG**: Queried whether there was any difference in the device itself, or any cost difference.

**Company**: Confirmed there is no difference, cost or otherwise. The extension is just an additional practical benefit for the user.

## Use of the technology (Table 1, questions 7-9)

**Question 7) Are you aware of any issues or barriers relating to staff adherence to using the Kurin Lock device?**

**Company:** Described that in their experience, it is not a matter of issues with using the device itself but rather there are some practical barriers. The company conducts a lot of training and how clinicians use Kurin is very simple. The training consists of a 1 or 2 minute conversation with clinicians on how to use it effectively. The issue that has been observed the most is related to where the stock of the device is located, where it is kept, and whether it is convenient to access. As using Kurin Lock constitutes a change in practice, it can be tricky for staff to remember to pick up the Kurin Lock set instead of the standard set they are used to. Rates of staff compliance vary. In the data from Kings, there was a correlation between compliance and contamination with higher compliance being associated with lower rates of blood culture contamination (BCC).

**Question 8) When using Kurin Lock, is preparation of the skin (cleaning) intended to be the same as standard of care? Is this carried out in practice?**

**Company**: Stated that it is hard to tell if clinicians are bypassing the cleaning step in practice. However, the training and education provided by the company is explicit in that the skin must be cleaned as per local protocols. For example, creating an aseptic field, using chlorohexidine, wearing gloves etc. This is all encouraged with Kurin Lock training, as per best practice guidelines. It is known that not all microbes can be removed from the skin but cleaning is advised whether Kurin Lock is used or not.

**Question 9) Is Kurin Lock compatible with any type of collection bottle or only specific bottles provided as part of the Kurin Lock system?**

**Company:** Kurin Lock is compatible with the 2 types of bottles used in the NHS (BD and bioMerieux). Those are the only 2 commercially available systems.

## Evidence and benefits (Table 1, questions 10-15)

**Question 10) How widespread is the use of Kurin Lock in the NHS? Which settings is it most commonly used in?**

**Company:** Stated that Guys and St Thomas' have fully introduced Kurin into their policy, and have been big supporters of introducing it as part of quality improvement initiatives, reducing their BCC rate from 6% to 2%.
[redacted]The privately owned HCA group is also using Kurin Lock. Kurin Lock is not 'widespread', it is not cheap but there are downstream benefits which need to be acknowledged. Many other trusts are due to start using Kurin Lock, with approximately 50 trusts engaging in active discussions regarding this. The NHS Supply Chain are due to list Kurin Lock on the national contract on a value based procurement initiative.

**NICE:** Queried whether it is in the accident and emergency (A&E) departments that Kurin Lock is mainly used.

**Company**: Confirmed that no, not just in A&E. For example, Guys and St Thomas' use it for every peripheral blood culture taken which includes A&E but also renal units, oncology units and elderly care pathways. A lot of the evidence for evaluating Kurin Lock comes from A&E settings as this is where BCC rates are highest, partially due to the environment and patient groups present. 30-40% of blood cultures in hospitals occur in A&E. The effect of false positives is not realised until later on in the patient pathway, after the patient is on the ward.

**Question 11) In section 4.3 of the submission 'Decision model structure', it states: "For false positive patients with a contaminated blood culture, there will be an unnecessary increased length of stay (LOS) which will be greater than that of true negative patients and less than that of false positive patients."**

**Please can you clarify this statement?**

**Company:** Confirmed this was a typographical error. The statement should read: "For false positive patients with a contaminated blood culture, there will be an unnecessary increased length of stay which will be greater than that of true negative patients and less than that of *true positive* patients."

**Additional question: The EAG queried what form of Excel the economic model was created in, as there appears to be some issues in accessing the full model in Excel 2019 that the EAG uses.**

**Company:** Clarified that the model was created in Excel 365 on Sharepoint. Stated that if the EAG do not manage to get it working as needed properly by end of the day then the company will look and see if they can amend the code.

**EAG**: Queried whether the macros were password protected as these were inaccessible to the EAG.

**Company**: Stated that they would check this and also that the company were happy to walk the EAG through the model to help answer any questions if needed.

**Question 12) Please could you explain how the costs for daily stay on an adult or paediatric ward were obtained and where the data can be accessed?**

**Company:** Stated that these costs were accessed via the local Patient Level Information and Costing System (PLICS), this is a restricted dataset for the NHS Trust who supply the data. Data will be specific to that trust, but it is the latest data available. Stated the company is happy to provide the contact they used to access this data.

**EAG:** Queried with NICE on how to proceed.

**NICE**: Agreed to investigate if they can have access to the PLICS data and assist the EAG in verifying the source of this cost data.

**Question 13) Does the model assume that all blood collection is via venepuncture and does that reflect standard practice?**

**Company:** Stated this has not been explicitly specified, but it is assumed that standard practice would be via venepuncture. There is no expectation of any impact on costs in relation to this and the company would not change anything in the model.

**Question 14) The economic model uses length of stay data from Skoglund, which is based in the USA. Is there any evidence that compares this to normal practice within the NHS?**

**Company:** Stated that they are aware that the length of stay (LOS) is a bit longer in the US than in the UK. They were mindful of sourcing the most consistent parameters possible. The model includes the LOS for the true negatives and true positives, it is that incremental bit that is the key driver of the costs. The LOS figure varied from 1.3 to 5 days in the literature. The model contains sensitivity analysis to explore the variation. In the literature the LOS is variable as it depends on the conditions being treated. It was challenging to identify appropriate sources of data. The data from Skoglund reflects current practice, even though it is US data. There is a lack of health economic (HE) evidence from UK hospitals on the impact of blood culture contaminants. The Ahmadi paper was carried out in Northern Ireland and that is the primary source of the HE impact of contaminated blood cultures. It is just 1 hospital, and reported a LOS of 5.1 days. That is the frame of reference for the UK market.

**Question 15) Vancomycin serum concentration assay cost is based on the High Drugs list from NHS Cost collection. Can you explain more about this please?**

**Company:** Stated that this needs to be checked with a colleague. This has not been included in the base case analysis, only in the scenario analysis. Whatever that cost is, it will add to the cost saving of Kurin Lock; it has been conservatively excluded from the base case. The main benefit is not putting patients on antibiotics unnecessarily.

**Additional question: The EAG queried the number of clinical studies that were included as the submission states 12 studies were included, consisting of 4 full-text published studies, 7 conference abstracts and 9 unpublished posters.**

**Company**: Confirmed there are 12 unique studies, with the conference abstracts and posters being related to these.

**Additional question: NICE queried the choice of vancomycin as the antibiotic included in the economic model, whether this was for sepsis or something else.**

**Company**: Stated that they picked one antibiotic to be consistent across the arms in the model, but they are conscious there could have been other antibiotics to be considered. The company noted that one of the scenarios that has not been modelled because it is difficult, is if the contaminant in the blood culture is MRSA, for which the downstream costs to the system are very high with patient isolation etc.

**Additional question: NICE sought clarification on the statement in the company submission located at the bottom of page 54: "As Kurin is a device that prevents the consequences of contaminated blood cultures it is often an assumption that the consequences have actually been prevented."**

**Company:** Agreed that this is worded in a slightly confusing way, but clarified that the benefits of Kurin Lock are reliant on minimising downstream events that occur as a result of blood culture contamination but in reality, these events may not materialise. The company wanted to be clear on this.

**Additional question: NICE sought confirmation that there was no confidential information or data included in the company submission.**

**Company**: Confirmed there is no confidential information or data in their submission.

**Concluding comments:**

- NICE explained that the second company engagement meeting which is provisionally scheduled for Monday 10th July at 13:00-14:00pm may not be required, and this will be confirmed with the company closer to the time. This is dependent on whether the EAG have outstanding queries at this time, particularly in relation to the economics.

- Regarding the earlier discussion relating to the economic model, the company confirmed that the macros of the model were password protected, and they will upload an unprotected version to NICE Docs for the EAG to access.

*Table 1: Questions provided by the EAG to the company in advance of the meeting, and company responses.*

| No. | EAG Question | Company response |
|---|---|---|
| **The technology** | | |
| 1. | There are 14 versions of the same device listed in Table 2 of the company submission. Do these versions of the device differ in any way that would mean evidence would not be generalisable between the different versions? | No. |
| 2. | Are you aware of any instances/reports of device failure or malfunction? | No |
| 3. | Are there cost differences between the different versions of the device, and if so, which one is represented by the cost of £19.50? | No, all Kurin blood culture device configurations are the same price. |
| 4. | Does the cost of £19.50 per unit vary depending on the configuration of bottles/methods shown in Fig.1 of the submission? | No - As above |
| 5. | In section 1.2 of the submission: *"The technology"*, it is stated that an alternative name for the Kurin Lock device is 'blood culture collection division device'. Can we check, is this supposed to say '**diversion** device'? | Yes. Typo, should be diversion device not division. |
| 6. | Please could you explain how the pressure-rated extension set is used, and if it is relevant to the submission? | Not relevant to the submission, but effectively a free component added for those that choose to take a BC from a winged IV Cannula. They can then leave the extension set in situ once the BC is complete. More of a convenience offering from Kurin. |
| **Use of the technology** | | |
| 7. | Are you aware of any issues or barriers relating to staff adherence to using the Kurin Lock device? | Stock being available to hand. No issues with actually being able to use it. |
| 8. | When using Kurin Lock, is preparation of the skin (cleaning) intended to be the same as standard of care? Is this carried out in practice? | Yes and Yes. |

| No. | EAG Question | Company response |
|---|---|---|
| 9. | Is Kurin Lock compatible with any type of collection bottle or only specific bottles provided as part of the Kurin Lock system? | Yes. Kurin compatible with BD and BioM who are the only manufacturers used in the UK. |
| **Evidence and benefits** | | |
| 10. | How widespread is the use of Kurin Lock in the NHS? Which settings is it most commonly used in? | As detailed in the submission document, GSTT uses it as there BC collection device throughout the Trust.<br>HCA group have started its introduction. |
| 11. | In section 4.3 of the submission 'Decision model structure', it states: *"For **false positive** patients with a contaminated blood culture, there will be an unnecessary increased length of stay (LOS) which will be greater than that of **true negative** patients and less than that of **false positive** patients."*<br><br>Please can you clarify this statement? | Apologies, this sentence should read: *"For **false positive** patients with a contaminated blood culture, there will be an unnecessary increased length of stay (LOS) which will be greater than that of **true negative** patients and less than that of **true positive** patients."*<br><br>In essence a **true negative** patient (i.e. someone without an infection) will stay in hospital for a period of time linked to their underlying health condition. A **true positive** patient (i.e. some with an infection), will remain in hospital for an increased length of time (beyond that for the underlying health condition) while the infection is treated. A **false positive** patient (i.e. someone who initially tests positive for an infection but is later shown not to), will likely have an increase in their LoS while the initial positive result is assessed, and this is likely to be an increase on that for a true negative patient (due to additional tests being run etc.) but less than that of a false positive as their will be no infection to actually treat. |

| No. | EAG Question | Company response |
|---|---|---|
| 12. | Please could you explain how the costs for daily stay on an adult or paediatric ward were obtained and where the data can be accessed? | The ward costs were obtained from Patient Level Information and Costing System (PLICs) data via a Head of Costing and Service-Line Reporting (SLR) for an NHS Trust (*Maidstone and Tunbridge Wells (MTW) NHS Trust*). The data provided is specific to the local NHS trust, but we hope reflective of the other trusts withing the UK.<br><br>The referenced link (https://digital.nhs.uk/data-and-information/publications/statistical/patient-level-activity-and-costing/2020-21/relationship-to-national-cost-collection) is to the NHS Digital explanation of the process of collecting the National cost collection that underpins the PLICS portal. The PLICS data for MTW was accessed via the following link: ACUTE PLICS PORTAL: Select your peers - Tableau Server (england.nhs.uk)<br>However, this is restricted to authorised users only. |
| 13. | Does the model assume that all blood collection is via venepuncture and does that reflect standard practice? | It is assumed that venepuncture reflects the most frequent method of blood sample collection in the NHS but the model is agnostic of the method of blood collection. It is assumed that the blood collection method with Kurin Lock would be identical to SoC. Therefore, if a patient was not suitable for venepuncture and an alternative method was used, such as arterial puncture, then the same alternative method would be used with Kurin Lock or SoC. |

| No. | EAG Question | Company response |
|---|---|---|
| 14. | The economic model uses length of stay data from Skoglund, which is based in the USA. Is there any evidence that compares this to normal practice within the NHS? | We are not aware of any studies that have compared length of stay (LoS) associated with blood contamination in the US and UK. While we recognise that the (LoS) can often be considered longer in the US than the UK we wanted to use a single reference for the majority of data points in our base case and explore these in sensitivity analysis. The studies we identified that report LoS illustrate that there is a large variation in the LoS and more importantly, as noted in the report, the incremental length of stay associated with the false positive blood contamination which ranged from 1.3 to 5 days. Our sensitivity analysis demonstrated that, assuming all other inputs in the base case hold, that the incremental LoS associated with a false positive needs to 0.6 days or more to achieve cost neutrality for Kurin Lock.<br><br>The Alahmadi (2011) paper which is from an NHS hospital in Northern Ireland details 5.1 Extra days stay. |
| 15. | Vancomycin serum concentration assay cost is based on the High Drugs list from NHS Cost collection. Can you explain more about this please? | [Need to just check this and will revert ASAP)<br><br>It appears that the source cost of the Vancomycin serum concentration assay may have been in error. As noted in the submission the cost of the serum concentration assay was excluded from the base case analysis and only included in a scenario analysis where it was shown to have minimal impact on the cost savings realised with Kurin Lock (In the scenario including the cost of the assay increased the cost saving with Kurin Lock by £5.55) |

## Appendix 2. Notes from clinical experts engagement meeting.

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

Medical Technologies Evaluation Programme

**Clinical Expert Engagement Meeting**

**MTG582 Kurin Lock for Blood Collection**

This document summarises the discussions that took place at the Kurin Lock Expert Engagement meeting for MTG582, which took place on Monday 19th June from 10:00am to 12:00pm. A list of questions was shared with the clinical experts in advance of the meeting to allow them to prepare some responses where appropriate (**Error! Reference source not found.**).

**Attendees:**

**NICE:**

- Aamer Jawed
- Amy Barr
- Bernice Dillon
- Edgar Masanga

**EAG**

- Ayesha Rahim
- Megan Dale
- Susan O'Connell

**Clinical Experts**

- David Partridge
- Jane Hodson

**Observers**

- Sophie Hughes (HTW)
- Katie McDermott (HTW)

**Welcome and introductions**

NICE briefly introduced everyone on the call and outlined the format for the meeting.

Discussion centred around some key topic areas including:

- The care pathway
- The technology
- Use of the technology
- Evidence and benefits

**The care pathway**

1) **In which settings is Kurin Lock most commonly used?**

One expert stated that Kurin Lock is not currently used in their Trust but that if it were to be introduced, accident and emergency (A&E) would be the setting of choice as this is where blood contamination rates (BCC) are highest.

Another expert stated that Kurin Lock is used across their Trust, in A&E and in ward settings.

NICE sought clarification on whether Kurin Lock would be used in primary care at all.

One expert stated that blood cultures are very rarely received from primary care.

2) **Are there any care pathways or patient populations in which Kurin Lock would be particularly helpful?**

One expert stated that it would be particularly helpful in groups where blood sampling is challenging and where the risk for sample contamination is higher, such as intravenous (IV) drug users, and for use with children.

A second expert agreed with this, and said Kurin Lock is useful where gaining access for blood draws is challenging which includes haematology and oncology, cardiac and renal patients.

Experts clarified that the reason is that there is a higher risk of contaminating blood samples when obtaining the blood sample is difficult.

3) **What are the currently used measures to prevent contamination, and how well are they adhered to?**

One expert described current measures as including good aseptic technique, decontaminating the skin before venepuncture, using direct blood sampling rather than through a cannula, having a blood culture policy in place, and education/training people on best practice. Adherence is variable, with time pressures playing a big part in this.

A second expert agreed and added that the introduction of 'blood culture packs' have improved adherence, as all equipment needed to take a blood culture sample is in one package. The Kurin Lock device is not currently part of this pack in their Trust.

4) **Does this vary across different settings?**

One expert advised there is no solid evidence of this but it is assumed that adherence to the above processes is reduced in busier environments such as A&E.

NICE queried on whether BCC rates were broken down into departments to enable trends to be identified.

The expert confirmed this data was available in their Trust, and that A&E has the highest rates of BCC, at around 10%.

A second expert agreed that A&E is where most contamination occurs, and commented that 10% would be considered a high rate of contamination.

5) **How long would it normally take to receive a blood culture test result?**

One expert stated that typically, most true pathogens will normally grow within 12-16 hours, and certainly within 24 hours. Some organisms are slower at growing. All blood cultures are grown for at least 5 days, and a negative result would therefore not be confirmed until the end of the 5 days. Interim negative results are provided within 48 hours. Positive result turnaround times are heavily patient/organism-dependent.

6) **How would contamination in the sample be detected? Would a second test be done, and if so, when?**

One expert stated that this largely depends on the organism being cultured. If it is an organism which is low virulence i.e. not one that normally causes infections, and is a common organism on the skin then it will be assumed that it is most likely to be a contaminant. Most of the contaminants that grow on the skin are not pathogenic. However, those same germs are the ones that are the cause of infections in certain groups such as immunocompromised people. Some of these germs are also the same ones that commonly cause infections of the heart. When a positive blood culture result occurs, how quickly it grows and clinical details of the patient are considered and then a decision of whether it's a contaminant, or whether it is "real" pathogen is made. There is a subset of patients where this decision is not clear-cut and therefore a repeat sample will be requested. The urgency of this repeat sample depends on the clinical situation. Often the person has already been started on antibiotics which complicates things as the pathogens are suppressed in the second sample. It is now recommended that 2 blood samples for cultures are taken at the initial test request.

A second expert agreed that the above description is reflective of processes in their Trust.

NICE queried if it is standard procedure to do 2 blood culture samples.

One expert confirmed that it is recommended but it does not always happen in practice.

The second expert stated that in most cases a second culture sample would be taken, and Kurin Lock is used both times in their Trust.

NICE queried if both aerobic and anaerobic cultures were grown in practice.

One expert commented that this is standard practice and that it depends on the type of organism but some will only grow in one environment. A lot of organisms would expect to grow in both environments.

There is an exception to the recommendation of 2 blood samples for smaller paediatric patients where only one sample is taken due to the volume of blood required.

**The technology**

7) **Is Kurin Lock unique in its mechanism of action? Are you aware of an alternatives in use?**

One expert commented that the mechanism is unique, and very simple. There is another company making a similar device which is available in the USA, which is a more involved, manual device in comparison to Kurin Lock.

8) **Are there any safety concerns or risks to the patient with the technology?**

No safety concerns or risks were raised by the experts.

**Use of the technology**

9) **Would Kurin Lock be suitable for taking blood from peripheral IV cannulas? Is blood taken from PIVs in standard practice?**

One expert commented that Kurin Lock was used to take blood from PIVs during a trial period of the device in their Trust. There is evidence that there is more risk of sample contamination with PIV samples, but their use does occur in practice.

A second expert agreed with the above statement regarding a higher risk of contamination with PIV sampling but it occurring in practice, particularly in an A&E setting where most patients would have a PIV.

**Evidence and benefits**

10) **Are the proposed downstream system benefits of Kurin Lock, which include reduced length of stay (LOS) and reduced use of antibiotics, reasonable assumptions?**

One expert expressed belief that the assumptions are reasonable. If a patient is started on antibiotics when infection is indicated, they can be stopped very quickly if their blood culture turns out to be a false positive. However, if Kurin Lock is used, it does not get to this point as false positives are reduced. Another benefit which could arise from Kurin Lock is the ability to sustain and maintain use of central lines in patients that rely on them. Often when a patient has suspected blood infection, their long-term lines are removed as they are assumed to be the root cause of infection. This can be quite traumatic and have severe knock-on effects such as thrombosis and even death. Reducing the incidence of unnecessary line removal would be hugely beneficial. The expert stated it is too early to tell if these benefits are occurring as a result of Kurin Lock, and they may not be seen until Kurin Lock is added to the Trust's blood culture packs as standard.

Another expert agreed that those would be the potential benefits and they can recollect times when patients' lines have been removed and then it is discovered it was unnecessary. The expert also stated that there would be benefits in reducing blood culture contamination rates for patients who have blood cultures taken but are then discharged home before the culture is deemed positive. These patients may be called back for repeat sampling unnecessarily if the isolate turns out to be a false positive.

NICE stated that the patients with long-term lines could be a potential subgroup, where the technology would be particularly helpful. Queried with the experts if they have any data on how reduced contamination rates translate to LOS/ reduced antibiotic use.

One expert confirmed that acquiring this data is something that is being worked on.

NICE queried whether staff require more time to use in Kurin Lock, to inform the resource impact assessment.

The experts stated that the time for using Kurin Lock is exactly the same as standard practice without Kurin Lock.

11) **In an intensive care setting, what interventions would be triggered by**
    **a) clinical indications of infection**
    **b) positive test result**

One expert stated that antibiotics would be commenced and as the patient will most likely have at least one central line in, it may be removed and a new one put in. The patient would be treated according to the signs and symptoms being shown. If the patient has sepsis, this would include ventilation etc.

The EAG queried whether blood culture samples would be taken if there are no clinical signs of infection.

One expert stated that only if clinical signs of infection are present would treatment start and blood samples for culture be taken.

NICE queried how quick the turnaround of test results for white blood cell count is.

One expert stated a couple of hours, and this could be an initial indication of infection, but often antibiotics would be started first and a blood culture test requested.

After a positive blood culture result, the antibiotics given might change. If the patient hasn't responded to antibiotics they are on, the antibiotic may be changed either by narrowing the spectrum if appropriate or broadening.

**12) If a second test was negative, how would these interventions change?**

One expert described an example patient pathway in the ICU. Normally there will be 2, or even 3, samples for blood culture, one from a peripheral site and one from an arterial/central line. If the organism that is cultured from both samples is staphylococcus, for example, that would indicate that the line is infected and removal would be advised. If the peripheral culture was negative then it might make recommending removal of the line less likely. Staphylococcus is a common skin flora and also a common line infection.

NICE highlighted that this could be an area where resources are saved, if line removals are reduced.

The expert stated that this would be the case, but it would be hard to quantify the amount of resources saved as there would be little evidence on how many lines are unnecessarily removed.

**13) Would this be different in other settings, such as A&E?**

One expert provided an example patient pathway, in A&E. In A&E, blood cultures would only be recommended if there is clinical indication such as fever and rapid pulse. Antibiotics are usually started if there is clinical indication, the impact of the positive blood culture result is to refine the antibiotics chosen. There are 2 potential consequences of a contaminant being present, one is inappropriate antibiotics being prescribed, and the other consequence is when patients who have had a culture and have not been started on antibiotics. Some of those patients will have gone home and then get called back. Around 10% of patients who have a culture taken do not have antibiotics started immediately. This is more frequent through flu pandemics or when Covid was circulating heavily etc.

Another expert commented that they would say the figure is less than 10%.

The EAG queried if the patients who are started on antibiotics are always admitted.

One expert stated that if there is someone with suspected infection and a fever, the vast majority are admitted. Occasionally people are discharged and then an infection is identified on their blood cultures so they are called back in to hospital.

**14) What would the antibiotics given typically be (type and dose)?**

One expert stated that it is really variable, it depends on site of infection, patient allergies, how sick they are (and therefore broader spectrum antibiotics are chosen), it also depends on what pathogens have been identified in previous cultures in addition to potential resistances.

**15) Would the antibiotics be supplied as a vial normally? And if less than a whole vial is required, what happens to the remaining portion?**

One expert commented that vials are single doses only.

**16) Are there additional tests required when using these antibiotics?**

One expert stated that the most commonly prescribed antibiotics do not require further tests, but level monitoring is required with some antibiotics such as vancomycin.

NICE queried if there are any typical first line antibiotics that could be named to aid the EAG with costings.

One expert commented that most common infections to present via A&E will be urinary tract infections (UTIs).

For UTIs the antibiotic may be co-amoxiclav, for respiratory infections it depends on severity but potentially amoxicillin or co-amoxiclav with or without clarithromycin. For abdominal infections it varies with age but possibly cefuroxime and metronidazole or piperacillin-tazobactam. For skin or soft tissue infections it would be flucloxacillin. It is tremendously variable and also dependent on allergies and local resistance rates.

**Concluding comments:**

One expert stated that the crux of this assessment will be that the contamination rate will be easy to quantify, but the downstream events will be difficult to quantify. It will be difficult to know the true impact of the Kurin Lock device.

A second expert claimed the results of the Kurin Lock trial in their trust were promising, but it has been difficult to get the data post-implementation, mainly because they are undergoing changes to their electronic patient record system. Data will be easier to get once Kurin Lock.is added to the standard blood culture packs.

*Table 2: Questions for clinical experts provided by the EAG in advance of the meeting.*

| No. | EAG Question | Response |
|---|---|---|
| **The care pathway** | | |
| 1. | In which settings is Kurin Lock most commonly used? | |
| 2. | Are there any care pathways or patient populations in which Kurin Lock would be particularly helpful? | |
| 3. | What are the currently used measures to prevent contamination, and how well are they adhered to? | |
| 4. | Does this vary across different settings? | |
| 5. | How long would it normally take to receive a blood culture test result? | |
| 6. | How would contamination in the sample be detected? Would a second test be done, and if so, when? | |
| **The technology** | | |
| 7. | Is Kurin Lock unique in its mechanism of action? Are you aware of an alternatives in use? | |
| 8. | Are there any safety concerns or risks to the patient with the technology? | |
| **Use of the technology** | | |
| 9. | Would Kurin Lock be suitable for taking blood from peripheral IV cannulas? Is blood taken from PIVs in standard practice? | |
| **Evidence and benefits** | | |
| 10. | Are the proposed downstream system benefits of Kurin Lock, which include reduced length of stay and reduced use of antibiotics, reasonable assumptions? | |
| 11. | In an intensive care setting, what interventions would be triggered by<br>a. clinical indications of infection<br>b. positive test result | |
| 12. | If a second test was negative, how would these interventions change? | |
| 13. | Would this be different in other settings, such as A&E? | |
| 14. | What would the antibiotics given typically be (type and dose)? | |
| 15. | Would the antibiotics be supplied as a vial normally? And if less than a whole vial is required, what happens to the remaining portion? | |
| 16. | Are there additional tests required when using these antibiotics? | |

## Appendix 3. Written responses from additional clinical experts to EAG's initial list of questions.

*Table 3: Written responses to initial list of EAG questions from clinical expert: Mr Andrew Barton.*

| No. | EAG Question | Response |
|---|---|---|
| The Care Pathway | | |
| 1. | In which settings is Kurin Lock most commonly used? | In any clinical area where blood cultures are taken |
| 2. | Are there any care pathways or patient populations in which Kurin Lock would be particularly helpful? | In a clinical rea such as ED and critical care where patients with suspected sepsis need blood cultures to be taken and the risk of false positive results needs to be eliminated, this would be applicable to any clinical area but ED and critical care probably take the most blood cultures. ED are more likely to use a peripheral cannula for a blood draw which increases the risk of contamination and critical care are likely to use CVC for blood drawn which is also a risk for contamination. |
| 3. | What are the currently used measures to prevent contamination, and how well are they adhered to? | ANTT, blood culture packs and using a fresh venepuncture stab instead of a VAD indwelling to take the culture. Instead of using Kurin a blood bottle could be used to take a 2ml sample before the blood culture using the same vacutainer and this would remove the first 2mls of blood which is likely to be contaminated much in the same way as Kurin diverts the first few mls. |
| 4. | Does this vary across different settings? | Is shouldn't do because this is a national standard, but it Does. ED for instance will always place a peripheral cannula and draw bloods and blood cultures instead of a dedicated fresh venepuncture, this increase contamination risk. |
| 5. | How long would it normally take to receive a blood culture test result? | 3 to 5 days |
| 6. | How would contamination in the sample be detected? Would a second test be done, and if so, when? | The level of contamination would be a deciding factor as would the type of bacteria, if it was a skin colonisation type this is Lilley to be a contaminant also if the patient has a positive culture and they are totally well this would also be suspicious. |
| The Technology | | |

| No. | EAG Question | Response |
|---|---|---|
| 7. | Is Kurin Lock unique in its mechanism of action? Are you aware of an alternatives in use? | It is unique however the use of a blood bottle to diverted first few mls before attaching the blood culture bottles. While this isn't the same device idea it is the same concept of diverting the first part of the blood draw. |
| 8. | Are there any safety concerns or risks to the patient with the technology? | No risks to the patient |
| Use of the technology | | |
| 9. | Would Kurin Lock be suitable for taking blood from peripheral IV cannulas? Is blood taken from PIVs in standard practice? | Yes this would be an attractive feature as it is cultures taken for peripheral cannula that are Haigh risk of contamination. |
| Evidence and benefits | | |
| 10. | Are the proposed downstream system benefits of Kurin Lock, which include reduced length of stay and reduced use of antibiotics, reasonable assumptions? | Yes and no, if the device stopped a false positive blood culture result you could argue it will save the patient having antibiotics and an extended stay in hospital however, microbiology labs are very good at detecting if the blood culture is a false positive so this statement is a bit over exaggerated in my opinion |
| 11. | In an intensive care setting, what interventions would be triggered by<br>a. clinical indications of infection<br>b. positive test result | Signs of sepsis, indwelling invasive devices and positive blood culture results from indwelling devices from all lumens of a vascular access device and a set of positive peripheral blood cultures plus positive results from swabbing of all wounds and catheters for MC&S |
| 12. | If a second test was negative, how would these interventions change? | If antibiotics has started the results may be negative, if the patient is well and has not physical signs of sepsis it may be a false positive and treatment would likely be stopped. |
| 13. | Would this be different in other settings, such as A&E? | no |
| 14. | What would the antibiotics given typically be (type and dose)? | This would depend on local microbiology guidelines which is different for each hospital |
| 15. | Would the antibiotics be supplied as a vial normally? And if less than a whole vial is required, what happens to the remaining portion? | Depends on the manufacturer and dose, any remaining antibiotic solutions would be discarded as they would be single use items. |
| 16. | Are there additional tests required when using these antibiotics? | Blood plasma levels, renal function and liver enzymes, FNC CRP etc would all be monitored |

*Table 4: Written responses to initial list of EAG questions from clinical expert: Dr Mustafa Atta.*

| No. | EAG Question | Response |
|---|---|---|
| **The Care Pathway** | | |
| 1. | In which settings is Kurin Lock most commonly used? | In-patient setting |
| 2. | Are there any care pathways or patient populations in which Kurin Lock would be particularly helpful? | Sepsis pathways, Infective endocarditis: Blood cultures are essential samples to diagnose these life threatening conditions |
| 3. | What are the currently used measures to prevent contamination, and how well are they adhered to? | Blood culture collected by using vacutainer device after decontamination of the skin with Chlorhexidine containing products, following ANTT technique. Adherence varies depends the level of training, experience and environment. Adherence is often compromised in busy environment such as ED. Training improve adherence but with time the adherence is reduces as contamination rates rise again. |
| 4. | Does this vary across different settings? | no variation for most patients. |
| 5. | How long would it normally take to receive a blood culture test result? | This depends on many factors, including the species of bacteria/fungus, the level of bacteraemia/fungaemia, length of time to transport to the lab, condition of the transport, volume of blood inoculated into the bottle, and whether a rapid identification method (e.g. MALDI) is available.<br><br>In general most Blood cultures flag positive within 24-48 hours of incubation. Another 48 hours is needed to have the final Identification and sensitivity results. |
| 6. | How would contamination in the sample be detected? Would a second test be done, and if so, when? | Contamination is suspected from the clinical background of the patient and the type of the isolate. In some cases it is difficult to decide if the isolate is a contaminant or significant. |
| **The Technology** | | |
| 7. | Is Kurin Lock unique in its mechanism of action? Are you aware of an alternatives in use? | Steripath uses same principle. |
| 8. | Are there any safety concerns or risks to the patient with the technology? | I am not aware of risks to patient with Kurin |
| **Use of the technology** | | |

| No. | EAG Question | Response |
|---|---|---|
| 9. | Would Kurin Lock be suitable for taking blood from peripheral IV cannulas? Is blood taken from PIVs in standard practice? | I don't think so and we do not recommend taking blood cultures from a peripheral cannulas. |
| **Evidence and benefits** | | |
| 10. | Are the proposed downstream system benefits of Kurin Lock, which include reduced length of stay and reduced use of antibiotics, reasonable assumptions? | All these will improve patient experience and safety |
| 11. | In an intensive care setting, what interventions would be triggered by<br>a. clinical indications of infection<br>b. positive test result | They might start antibiotics, do additional investigation, repeat blood culture, and possibly un-necessary procedure e.g. remove/replace a central line. |
| 12. | If a second test was negative, how would these interventions change? | Blood culture are incubated for 5 days before reported finally as negative, or at least 48hours for provisional result, by then most of the above interventions could have been completed |
| 13. | Would this be different in other settings, such as A&E? | It depends if the patient was admitted or discharged from A&E. if discharged from A&E the clinician usually contact the patient to assess the likelihood of significance and act accordingly until ID results are ready (usually after 24-48hours), if they are well enough to stay at home no further action will be taken. If they were already admitted or called back to be admitted, the actions could be similar to those for critical care patients. |
| 14. | What would the antibiotics given typically be (type and dose)? | This would be according to the suspected infection site and the Gram stain results of the blood culture. Possibly, Vancomycin, or Flucloxacillin or co-amoxicillin plus/minus gentamicin |
| 15. | Would the antibiotics be supplied as a vial normally? And if less than a whole vial is required, what happens to the remaining portion? | If Vancomycin or gentamicin were used then part of a vial could be used and the rest is discarded. |
| 16. | Are there additional tests required when using these antibiotics? | Vancomycin and gentamicin require therapeutic drug monitoring |

## Appendix 4. Written responses from Iskus Health LTD to additional questions from EAG.

**Date:** 30/6/23

**Company:** Iskus Health UK LTD

*Table 5: Written responses from the company to additional questions from the EAG following the first meeting.*

| No. | EAG Question | Company response |
|---|---|---|
| Economic modelling | | |
| 1. | Email 20/6/23<br>Could I please check that in the submitted model, the worksheet named "English population estimates" is only used to inform the proportion of adults in the population (cell C24, model setup), which is then used to calculate antibiotic costs.<br>And that the paediatric population is defined as 0-12, with the adult population defined as 13 – 95-99? | Yes, you are correct.<br>The "English population estimates" tab provides the data to estimate the proportion that are adults (currently assumed to be >12 years) which in turn is used to calculate the antibiotic costs. |
| 2. | To follow up Q4, is there a reason to exclude those over 99? (although there is almost no impact to this, but just to understand). | There is no rationale for excluding patients aged over 99. This appears to have been a typo in cell c42 in the "English population estimates" tab. However, including those aged 100 and over was found to have little to no impact on the results. |

| No. | EAG Question | Company response |
|---|---|---|
| 3. | Please could you explain the choice of non-elective short stay costs for patients admitted to hospital from A&E, given that these are multiplied by the number of days stay? | In the base case, the A&E setting was selected as it is associated with a high contamination rate, and reflected available clinical data for Kurin Lock which was derived from a trial at the A&E department of King's Princess Royal Hospital.[1]<br><br>We recognise that there is significant variability in the hospital bed day costs depending on the associated setting. In the National schedule of NHS costs (Year 2021/22) mean costs associated with sepsis (WJ06A-J) for non-elective short-stay range from £646 to £1,840 and non-elective long stay range from £2,878-£10,034. Similarly, mean costs associated with infections (WHO7A-G) for non-elective short-stay range from £538 to £2,061 and non-elective long stay range from £2,599-£11,420. By inference, the analysis is considering those patients with infections incremental to their original reason for hospitalisation and it can therefore be assumed that these patients would be considered those with a complication. As such, the costs are likely to be at the higher end of the cost range. The figures from the National schedule of NHS costs are for the entirety of the stay and so could not be used to estimate a per day cost. We therefore obtained per day ward costs from Patient Level Information and Costing System (PLICs) data, via a Head of Costing and Service-Line Reporting (SLR) for an NHS Trust.<br><br>1. Atta M, Mcguire R. Reducing False Positive Blood Cultures in an Adult NHS Emergency Department using a Kurin Lock Blood Culture Collection Device. King's College Hospital. 2022 |
| 4. | Were any other reference costs considered for length of stay, such as excess days, in either A&E or hospital settings, and if so what was the reason they were not used? | While specific reference costs weren't considered in the submission, the cost per day was considered in threshold analysis. This demonstrated, assuming all other baseline parameters remained constant, that the cost per day could drop to £122.46 and use of Kurin Lock would remain cost neutral. |

| No. | EAG Question | Company response |
|---|---|---|
| 5. | Did you consider the inclusion of costs for removal and replacement of central line catheters due to a false positive blood culture result? | The model did not consider the cost of removal and replacement of central line catheters as the literature review did not identify data to quantify the associated rates. It is anticipated that a reduced false-positive rate will lead to the reduction of unnecessary tests and procedures, including central line replacement, and as such, excluding these associated costs could be considered conservative. |

## Appendix 5: Written responses from clinical experts to additional questions from EAG.

*Table 6: Written responses to additional list of EAG questions from clinical expert: Mr Andrew Barton.*

| No. | EAG Question | Clinical Expert Response |
|---|---|---|
| **Use of antibiotics** | | |
| 1. | What proportion of patients that have blood culture tests would be started on antibiotics at the point of sample taking? | Most patients have blood cultures taken as part of a septic screen because they are displaying signs of sepsis, this means they would usually be started on an antibiotic while waiting or the septic screen results to become available or the patients' symptoms recovered, with this in mind as much as 90% of patients could be given antibiotics. |
| 2. | Does this differ between A&E, ICU and general hospital settings? | The same is likely. |
| 3. | Is Vancomycin (20mg/Kg for patients over 12) twice a day a plausible estimate for a patient in A&E with suspected infection? We understand that this will be very variable in practice. | Until source of sepsis known and antibiotic sensitivities to pathogen known:<br>First line sepsis we use IV Gentamycin:<br>Adult<br>3–5 mg/kg daily in 3 divided doses, to be given in a multiple daily dose regimen, divided doses to be given every 8 hours, intravenous injection to be administered over at least 3 minutes.<br>By intravenous infusion<br>Adult<br>Initially 5–7 mg/kg, subsequent doses adjusted according to serum-gentamicin concentration, to be given in a once daily dose regimen.<br><br>With additional Amoxicillin 1-2g TDS<br><br>Or in sever sepsis C0-amoxiclav 1.2g TDS plus Gentamycin IV<br><br>If penicillin allergic we would give gentamycin with metronidazole or teicoplanin. |
| **Taking two samples for blood culture** | | |

| No. | EAG Question | Clinical Expert Response |
|---|---|---|
| 4. | We understand that two samples are taken when blood cultures are ordered, to increase the chance of identifying infection-causing organisms, but also to determine if either sample was contaminated by skin flora.<br><br>In your opinion, is this an effective method of identifying false positives that occur as a result of skin flora contamination? | Taking 2 samples also identifies if an indwelling device is a likely source. This practice is affective in identifying false positive samples. |
| 5. | Would the presence of skin flora contamination in only one of the two samples be interpreted as a negative result in terms of stopping antibiotics/treatment for infection? | If the patient was well with no other clinical signs of sepsis it might. |
| 6. | How would the one sample with positive growth impact care and healthcare resource, when the second sample result identifies it as a false positive? | If the patient had other clinical signs of sepsis it would indicate further cultures could be taken and antibiotic treatment continued. |
| 7. | Would the addition of Kurin Lock change the blood culture sampling process in any way i.e. would two samples still be taken? | It would |
| 8. | Where studies report the rate of false positive blood cultures, is this counting the number of false positive *samples* or false positive *patients*?<br><br>Essentially, would a false positive result that occurs in tandem with a true negative result from the same patient's two samples be incorporated into the false positive blood culture rate calculation? | This is unclear in all cases but is likely to be the samples.<br><br>A false positive sample would be reported in isolation to the others. |
| **Downstream events post-blood culture sampling** | | |
| 9. | If a contaminant is suspected to be present in a blood culture sample, what action is taken?<br>e.g. Are additional blood culture samples taken from the patient? Are further investigations/tests ordered? Which ones? | The patients overall clinical condition and other sings of sepsis should be considered. A blood culture is not the sole, definitive marker of sepsis. The blood culture is hopefully going to identify the pathogen so a targeted antibiotic treatment can be given, the septic patient should be treated either way. |

| No. | EAG Question | Clinical Expert Response |
|---|---|---|
| 10. | Would it be feasible to collect data on the downstream outcomes that are claimed to be associated with introducing Kurin Lock?<br>e.g. reduced length of hospital stay, reduction in use of unnecessary antibiotics. | Not really, there are so many other variables that can affect the patient length of stay etc..<br><br>A false positive blood culture is still a reportable positive plod culture if the pathogen is MRSA, MSSA, Ecoli etc.. these carry financial penalties so if you reduce the number of false positives you might should a saving to the organisation, also reputationally, part of a hospitals safety profile is judged on the number of reportable blood stream bacteraemia's, reducing false positive blood culture results can have a positive impact on the organisation reputation. |

*Table 7: Written responses to additional list of EAG questions from clinical expert: Dr David Partridge.*

| No. | EAG Question | Clinical Expert Response |
|---|---|---|
| **Use of antibiotics** | | |
| 1. | What proportion of patients that have blood culture tests would be started on antibiotics at the point of sample taking? | Very much a guess but I would estimate 90% |
| 2. | Does this differ between A&E, ICU and general hospital settings? | More likely in ITU and general wards where fever (which is the primary indication for sampling) is more likely to represent bacterial infection |
| 3. | Is Vancomycin (20mg/Kg for patients over 12) twice a day a plausible estimate for a patient in A&E with suspected infection? We understand that this will be very variable in practice. | Vancomycin would be an unusual drug to start in A+E except in patients with long term lines. I am not sure that I understand the question. |
| **Taking two samples for blood culture** | | |
| 4. | We understand that two samples are taken when blood cultures are ordered, to increase the chance of identifying infection-causing organisms, but also to determine if either sample was contaminated by skin flora.<br><br>In your opinion, is this an effective method of identifying false positives that occur as a result of skin flora contamination? | It certainly helps to define whether an isolated organism is a contaminant or not but of course it is not 100% accurate. |
| 5. | Would the presence of skin flora contamination in only one of the two samples be interpreted as a negative result in terms of stopping antibiotics/treatment for infection? | If clinically consistent with contamination then yes. |
| 6. | How would the one sample with positive growth impact care and healthcare resource, when the second sample result identifies it as a false positive? | This depends upon the Gram stain result, the time to positivity and the clinical context. It may lead to starting of antibiotics initially, which would then be discontinued; in some cases it could lead to unnecessary investigations e.g. echocardiogram or to the patient being called back for review. |
| 7. | Would the addition of Kurin Lock change the blood culture sampling process in any way i.e. would two samples still be taken? | Yes 2 samples would still be taken to improve sensitivity even if Kurin improved the specificity of the test. |

| No. | EAG Question | Clinical Expert Response |
|---|---|---|
| 8. | Where studies report the rate of false positive blood cultures, is this counting the number of false positive *samples* or false positive *patients*?<br><br>Essentially, would a false positive result that occurs in tandem with a true negative result from the same patient's two samples be incorporated into the false positive blood culture rate calculation? | This depends on the study but it would usually be samples not patients. If you provide me an example study that you are using to define rate then I can help to interpret if needed. |
| **Downstream events post-blood culture sampling** | | |
| 9. | If a contaminant is suspected to be present in a blood culture sample, what action is taken?<br>e.g. Are additional blood culture samples taken from the patient? Are further investigations/tests ordered? Which ones? | Unless it is clearly a contaminant because it is inconsistent with the clinical findings then repeat cultures would often be requested and other tests may also follow e.g. echocardiogram or other imaging tests e.g. abdominal imaging. Streptococci and Staph aureus (when a contaminant) are most challenging in this regard. |
| 10. | Would it be feasible to collect data on the downstream outcomes that are claimed to be associated with introducing Kurin Lock?<br>e.g. reduced length of hospital stay, reduction in use of unnecessary antibiotics. | This would be feasible though variations between units in terms of practice would need to be reflected in study design |

*Table 8: Written responses to additional list of EAG questions from clinical expert: Dr Mustafa Atta.*

| No. | EAG Question | Clinical Expert Response |
|---|---|---|
| **Use of antibiotics** | | |
| 1. | What proportion of patients that have blood culture tests would be started on antibiotics at the point of sample taking? | All Patient with suspected sepsis should have Antibiotic started after blood culture collection. |
| 2. | Does this differ between A&E, ICU and general hospital settings? | No |
| 3. | Is Vancomycin (20mg/Kg for patients over 12) twice a day a plausible estimate for a patient in A&E with suspected infection? We understand that this will be very variable in practice. | The empirical Antibiotic treatment aims to treat the suspected source of sepsis. The choice of antibiotic depends on the source.<br>Vancomycin is not the standard first line treatment choice. |
| **Taking two samples for blood culture** | | |
| 4. | We understand that two samples are taken when blood cultures are ordered, to increase the chance of identifying infection-causing organisms, but also to determine if either sample was contaminated by skin flora.<br><br>In your opinion, is this an effective method of identifying false positives that occur as a result of skin flora contamination? | Taking two sets of blood cultures may not always effective in identifying contaminant e.g both sets of blood cultures could be contaminated with exactly the same organism from the patient's skin. |
| 5. | Would the presence of skin flora contamination in only one of the two samples be interpreted as a negative result in terms of stopping antibiotics/treatment for infection? | This would be one of the factors for the influence the decision of stopping the antibiotics. The clinical background of the patient should always be taken into account. |
| 6. | How would the one sample with positive growth impact care and healthcare resource, when the second sample result identifies it as a false positive? | The second result will not necessarily identify it as false positive.<br>Blood cultures are incubated for 5 days before reported as negative. So if one set flagged positive on day 2 after collection, we have to wait for the final result of the second set. |
| 7. | Would the addition of Kurin Lock change the blood culture sampling process in any way i.e. would two samples still be taken? | In some cases yes will continue taking two or three sets, e,g IE. |

| No. | EAG Question | Clinical Expert Response |
|---|---|---|
| 8. | Where studies report the rate of false positive blood cultures, is this counting the number of false positive *samples* or false positive *patients*?<br><br>Essentially, would a false positive result that occurs in tandem with a true negative result from the same patient's two samples be incorporated into the false positive blood culture rate calculation? | Which studies you are referring to, I think they should be counting False positive samples.<br><br>the false positive rates (contamination) is counting the false positive samples not patients as you are checking for error in collection process for each sample independent of other sampes collected from the same patient.. |
| **Downstream events post-blood culture sampling** | | |
| 9. | If a contaminant is suspected to be present in a blood culture sample, what action is taken?<br>e.g. Are additional blood culture samples taken from the patient? Are further investigations/tests ordered? Which ones? | This depends on patient clinical condition and how likely the patient is having an infections.<br>Based on clinical background of teh patient We do not always request further blood culture or other investigations. |
| 10. | Would it be feasible to collect data on the downstream outcomes that are claimed to be associated with introducing Kurin Lock?<br>e.g. reduced length of hospital stay, reduction in use of unnecessary antibiotics. | It may be possible, but need the resource to recruit personnel to collect and analyse the data. |

## Appendix 6: Study author (MA) written responses to queries on information reported in poster publication included in evidence base (Atta 2022)

1) **EAG:** Along the X-axis of the graph, it lists 'wk1, wk3, wk4, wk2'. Could you indicate why these weeks are in non-consecutive order? Additionally, there is a 0.00% contamination rate reported in week 2, is this accurate?

   **MA:** The X-axis is set in order of level of compliance with using Kurin against contamination rates. It was not intended to show compliance with time, hence data appeared in non-consecutive order, the reason for putting it in this was is to make it visually easier to see the relationship between the compliance using Kurin and the subsequent drop in contaminant levels. The 0.00% contamination rate in Wk2 was accurate. No contaminants were recorded in wk2 (see table below)

| | Wk1 | Wk2 | Wk3 | Wk4 | Total |
|---|---|---|---|---|---|
| **Samples** | 101 | 88 | 101 | 94 | 384 |
| **Contaminants** | 9 | 0 | 5 | 3 | 17 |
| **Contamination %** | 8.91% | 0.00% | 4.95% | 3.19% | 4.43% |
| **Units used** | 57 | 81 | 79 | 80 | 297 |
| **Compliance** | 56.44% | 92.05% | 78.22% | 85.11% | 77.95% |

2) **EAG:** In the poster, it is stated that adoption of the device "could potentially free up 1,444 bed-days at the PRUH, and 5,041 trust-wide". Do you have any further detail on how these figures were calculated?

   **MA:** This was based on data from the Alahmadi paper (https://www.journalofhospitalinfection.com/article/S0195-6701(10)00454-8/fulltext). A contaminated blood culture can cost add 5.1 days to a patients stay in hospital. Please see attached health economic models.

3) **EAG:** The text reports that data was collected for 381 blood culture samples that utilised a Kurin device. Do you know how many patients these 381 samples were obtained from?

   **MA:** All samples were taken from patients at the time of their attendance to ED, no sample was a repeat to exclude contamination in a previous sample. 3 samples were removed from the process due to data coming from paediatric A&E. It was known that a Kurin device will not have been used in obtaining those samples.

NICE National Institute for Health and Care Excellence

# National Institute for Health and Care Excellence
# Centre for Health Technology Evaluation

## Pro-forma Response

## External Assessment Report factual check

## MTG582 Kurin Lock

Please find enclosed the external assessment report prepared for this assessment by the External Assessment Group (EAG).

You are asked to check the external assessment report from CEDAR to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 12pm, **4th Aug 2023** using the below proforma comments table. All your comments on factual inaccuracies will receive a response from the EAG and when appropriate, will be amended in the external assessment report. This table, including EAG responses will be presented to the Medical Technologies Advisory Committee and will subsequently be published on the NICE website with the external assessment report.

**1ST August 2023**

NICE National Institute for Health and Care Excellence

## Issue 1

| Description of factual inaccuracy | Description of proposed amendment | Justification for amendment | EAG response |
|---|---|---|---|
| Title Page Update | MT582 Kurin Lock for Blood Culture Collection | Kurin is for Blood culture collection not blood collection which is an important distinction to make for accuracy purposes. | The EAG have changed this to the proposed amendment and agree this is an important distinction. |

## Issue 2

| Description of factual inaccuracy | Description of proposed amendment | Justification for amendment | EAG response |
|---|---|---|---|
| P39 | 3rd paragraph. Hodson (UK Study) reference attached reported a p=0.045 statistically significant reduction in BCC. Therefore statement is not correct | Incorrect facts detailed. Statistical significance was reported in Hodson paper. | Thank you for highlighting this. The EAG have added this information to the text on P39, into Table 10 and Appendix C. |

## Issue 3

| Description of factual inaccuracy | Description of proposed amendment | Justification for amendment | EAG response |
|---|---|---|---|
| Section 1.3.2 (page 10): No acceptable UK alternative for length of stay was identified | Current text: "no acceptable UK alternative was identified" (for length of stay)<br><br>Suggested amend: "no acceptable UK alternative was identified for the A&E base case setting". | This amend is proposed as Alahmadi et al (2011) is a UK based study (conducted in Northern Ireland) which reported the length of stay in a hospital setting. | Amended as suggested, although the EAG have reservations about the suitability of Alahmadi length of stay data for any setting due to the high proportion of ICU patients in the intervention arm. |

### Issue 4

| Description of factual inaccuracy | Description of proposed amendment | Justification for amendment | EAG response |
|---|---|---|---|
| Section 11.2, Table 14 (page 55). Missing date and reference for Patel. | Current text: "The model assumed no adverse events of vancomycin (Patel)"<br><br>Proposed text: "The model assumed no adverse events of vancomycin (Patel, 2022)"<br><br>Reference to include: Patel S, Preuss CV, Bernice F. Vancomycin. StatPearls [internet]: StatPearls Publishing; 2022. | No reference or date was included for this model assumption. | Amended as suggested in table, and added to reference list. |

### Issue 5

| Description of factual inaccuracy | Description of proposed amendment | Justification for amendment | EAG response |
|---|---|---|---|
| Section 11.2, Table 14 (page 56). Wording is unclear | Current text: "No impact hospital acquired infection and/or on associated mortality" | The text was previously unclear. | Amended as suggested |

| | | | |
|---|---|---|---|
| | Proposed text: "No impact **on** hospital acquired infection and/ or on **the** associated mortality **is assumed**" | | |

### Issue 6

| Description of factual inaccuracy | Description of proposed amendment | Justification for amendment | EAG response |
|---|---|---|---|
| Section 11.2, Table 16 (Page 58) | Current text does not include dates for he references.<br><br>Proposed amend: (Hodson 2022, Parsons 2023), (Rupp, 2017) (Atta, 2022) | This is for consistency in the reporting of references. | Amended as suggested |

### Issue 7

| Description of factual inaccuracy | Description of proposed amendment | Justification for amendment | EAG response |
|---|---|---|---|
| Section 11.2, Table 16 (Page 59) | Current text: "up to 90% in an A%E setting"<br><br>Proposed amend: "up to 90% in an A&E setting" | There was a typo in how A&E was spelt. | Amended as suggested |

### Issue 8

| Description of factual inaccuracy | Description of proposed amendment | Justification for amendment | EAG response |
|---|---|---|---|
| Sensitivity analysis (page 64). Clarification of fixed amounts in the one-way sensitivity analysis. | Current text: "the majority of length of stay inputs were varied by a fixed amount rather than 10%".<br><br>Proposed text: "the majority of length of stay inputs were varied by a fixed amount, which were derived from literature, rather than 10%." | The company would like to clarify the fixed variance was derived from literature. | Amended to read:<br>the majority of length of stay inputs were varied by a fixed amount, which the company reported as based on literature, rather than 10%. |

### Issue 9

| Description of factual inaccuracy | Description of proposed amendment | Justification for amendment | EAG response |
|---|---|---|---|
| | | | |

### Issue 10