NICE National Institute for Health and Care Excellence

3 April 2024

Supporting documentation pack: MTG77 Kurin Lock for blood culture collection

This pack contains additional documentation to support the publication of the final guidance.

Papers included in pack

1. Front sheet

2. Consultation comments and responses table

3. Additional information from the External Academic Group (Cedar) in response to fact check and consultation comments from the company.

4. External Assessment Report (re-published with one corrected typo)

National Institute for Health and Care Excellence

Medical technologies evaluation programme

GID-MT558 Kurin Lock for blood culture collection
Consultation comments table

There are 45 consultation comments from 2 consultees:

- 43 comments from 1 company
- 2 comments from 1 individual

The comments are reproduced in full, arranged in the following groups (**one comment containing multiple issues has been split**):

- Recommendations: comments 1 to 3
- Care pathway: comments 4 to 8
- Clinical evidence: comments 9 to 20
- Economic evidence: comments 21 to 36
- Equality considerations: comment 37
- Evidence generation: comments 38 to 39
- The technology: comments 40 to 46

#	Consultee ID	Role	Section	Comments	Chair/committee lead notes
Recommendations					
1	**2**	Company	Are the recommendations sound and a suitable basis for guidance to the NHS?	Overall the recommendations are quite conservative, they only consider the emergency departments where most blood culture contamination rates are high and do not consider the consequence of blood culture contamination in other departments such as Intensive or High Dependency Care (which were one of the scenarios modelled in the health economics) where costs are much higher and consequence to patients much greater. The recommendations should strongly recommend the use of Kurin in all NHS emergency departments, intensive care/high	Thank you for your comment. The committee's considerations about the setting recommended for use are reported in section 4.6 of the medical technologies guidance. The committee noted that the clinical evidence is limited to emergency settings and the economic modelling used for the base case is the emergency department setting. There is also no direct evidence

				dependency units and other acute departments where high risk patients are managed. It is widely reported today that nearly half of all positive blood cultures isolated are the result of a contamination and hence a false positive result. In fact, the largest proportion of false-positive blood cultures (50–85%) result from contamination with coagulase-negative staphylococci which is primarily found on the skin. Contamination creates clinical uncertainty and results in detrimental downstream effects, which can be seen in prolonged hospital stays for patients, increased risk of harm and sizeable downstream costs to a hospital. It is evident that contaminated Blood Cultures create a significant burden on the health care system and is imperative that hospital management and clinicians recognise these ongoing issues. Contamination of blood cultures and false positives create significant financial burdens to every department involved in the processing of blood cultures. Patients experience negative outcomes in the form of unnecessary antibiotic treatment, further testing and extended hospital stays, which in a currently overstretched NHS climate comes with an elevated risk. For a medical test to be revered as the 'gold standard' it needs to be upheld as having the lowest possible error rate and negative effects on patients and hospitals. By utilising Kurin for blood culture collection this can be achieved. Whilst further evidence will always be welcomed and sought Kurin has demonstrated that as a very simple and highly effective intervention which can reduce blood culture contamination rates and the commensurate consequences of a false positive blood culture. Overall improving patient outcomes and reducing the cost of healthcare to the NHS.	of how Kurin Lock affects outcomes other than blood culture contamination rates such as length of hospital stay. The EAG stated that the economic modelling is uncertain because of the lack of evidence about how Kurin Lock affects length of hospital stay compared with standard blood culture collection, which affects how cost effective Kurin Lock may be. However, the committee agreed that limiting the recommendation to the emergency department setting was appropriate due to the high blood culture contamination rates in this setting and the impact Kurin Lock can have on this. Although the economic model results are less uncertain in settings where there is a higher cost for the length of stay, the committee and clinical experts were concerned by the assumptions of the length of stay in the economic model which reduced the certainty of cost effectiveness (see section 4.2). Therefore, the recommendation has remained limited to emergency departments.
2	**2**	Company	1.1	"Kurin Lock can be used in the NHS to reduce contamination in blood culture collection in emergency departments with high blood culture contamination rates while more evidence is generated " This is very a limiting recommendation. It is unclear why the recommendation is limited to the emergency department. There is significant variation in the rates of contaminations across the various settings but also between hospitals. The submitted	Thank you for your comment. Please see NICE's response to comment 1.

				analysis demonstrates that the benefit of small reductions in length of stay for in high cost units (such as ICU, surgical wards or cancer departments) offset the cost of Kurin Lock. While in other departments that are likely to have significantly higher rates of blood culture contamination but lower bed day costs the reductions will also offset the cost of Kurin Lock. We believe the evidence available to date supports that best practice in taking blood cultures to get an accurate result requires using a Kurin device to minimise the risk of contaminated blood culture.	
3	**2**	Company	1.2	"So, it is more likely that Kurin Lock is cost saving when it is used in emergency departments with high rates of blood culture contamination. " This conclusion fails to acknowledge that other settings which may have lower rates of blood culture contamination have higher costs associated with extended length of stay. This relationship is demonstrated in Table 21 of the Supporting documentation – Committee papers.	Thank you for your comment. Please see NICE's response to comment 1.
Care pathway					
4	1	Individual	3.12	"Contamination rates of more than 9% have a high probability of Kurin Lock being cost saving " Getting contamination rates for each local NHS trust is difficult, and would probably vary from department to department. Is there a standardised way of getting data on what is a contaminant and what is not?	Thank you for your comment. The committee values comments from clinicians about their experiences. The committee concluded that there is no standardised way of collecting this data.
5	2	Company	2.3	"This requires at least 2 sets of blood culture samples to be taken within a few hours of each other." This appears to not happen very frequently in practice but is regarded as best practice.	Thank you for your comment. The clinical experts advised that standard practice comprises of collecting 2 sets of blood culture samples, which the committee accepted.
6	2	Company	2.7	"In usual practice, 2 Kurin Lock devices will be used " Our experience from working with multiple NHS Trusts is that the majority of hospitals only collect 1 set of blood cultures per patient. NHS Guidance is to collect 2 sets but this appears to be rarely done. Iskus Health have based our HE modelling on following NHS Guidance even though in our experience this is rarely followed.	Thank you for your comment. Please see NICE's response to comment 5. The committee agreed that using 2 Kurin Lock sets per person is appropriate for modelling.
7	2	Company	3.2	"Most of the studies did not specify how people were selected to have blood culture collection."	Thank you for your comment.

				The decision to take a blood culture is entirely clinical depending on the patients symptoms. Therefore patients in the studies were those that had blood cultures taken as part of their clinical diagnosis associated with their presenting symptoms. 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%. 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.	
8	2	Company	4.6	"They advised that this approach reduced blood culture contamination rates, but the change in practice needs to be regularly reinforced and may be time-consuming" Training capacity in the NHS is very limited due to high staff turnover, so constant education is required as it often not practical. Kurin is a closed system which automates the diversion of the first 0.15ml of blood passively requiring no change in the practice of taking blood cultures for the current method. Simple and easy to use	Thank you for your comment. The experts advised that all methods of taking blood samples need regular training and reinforcement to help reduce blood culture contamination. The guidance wording has been amended to reflect this.
Clinical evidence					
9	2	Company	Has all of the relevant evidence been taken into account?	We believe all the evidence for the impact of Kurin in lowering blood culture contamination has been considered as part of this report. We do believe extra consideration could be given to the huge burden and impact that blood culture contaminations have on the NHS. Blood culture contamination (BCC) that causes false positive results has consequences: • Antibiotic misuse has led to life-threatening multi-drug resistant super bugs.	Thank you for your comment. The EAG considers these consequences to have been acknowledged appropriately in the assessment report. Table 6 outlines potential impacts on patients, laboratories and hospitals of false-positive blood culture results due to contamination with skin flora. The EAG stated that all evidence relating to the

				• Contaminated blood cultures put patients at higher risk of in-hospital mortality; Davis 2019, • BCC contribute to unnecessary antibiotic use and resistance, increase length of stay and associated healthcare-acquired conditions, and create delays in proper treatment, Dorne 2019. • The cost of a false-positive blood cultures is evidenced in the published literature as being anything from £2,000 upwards and so negatively impacting hospital financial performance.	Kurin Lock device has been considered as part of this report. The committee carefully considered the evidence and concluded that, despite uncertainties, Kurin Lock can be used in the NHS to reduce contamination in blood culture collection in emergency departments with high blood culture contamination rates while more evidence is generated. The committee's considerations of the clinical evidence and cost savings can be found in sections 4.1, 4.2 and 4.3 of the medical technologies guidance.
10	2	Company	1.2	"Clinical trial evidence suggests that Kurin Lock is a safe and effective way of reducing blood culture contamination rates, compared with standard blood culture collection." Indeed it does with average an reduction of +60% in BC contamination rates when using Kurin in NHS Hospitals alone.	Thank you for your comment. The clinical evidence for the blood culture contamination rates can be found in section 3.3 of the medical technologies guidance.
11	2	Company	1.2	"It is not clear how it affects other outcomes, like length of hospital stay and antibiotic use, because the clinical trials did not formally record these outcomes." While the Kurin Lock trials do not formally record these outcomes the evidence submitted does show the association between blood contamination and the resulting waste of NHS resources including unnecessary pharmacological treatment and length of stay. With an estimated 3 million blood cultures per annum across all areas of the NHS there is always going to be uncertainty on the true impact of reduced blood culture contamination rates. However, the evidence does support that reducing the rate of blood culture contamination is beneficial to the patient and wider NHS system. Indeed there are multiple references detailing the extensive impact of contaiminated blood cultures such as Skoglund et al. 2019, Alahmadi et al. 2011, Burnie & Vining. 2021, Arnaout et al. 2021, Baxter et al. 2020, Allain. 2018, Michaelidis et al. 2014, Waltzman & Harper, 2001; Hughes, J A et al. 2018 and Doern et al. 2020 to name but a few.	Thank you for your comment. The committee carefully considered the evidence and concluded that there was uncertainty relating to the downstream impact of using Kurin Lock and the reduction in false positive blood cultures. The committee's considerations of the clinical evidence can be found in section 4.2 of the medical technologies guidance.

12	2	Company	3.3	"The UK evidence estimated baseline contaminations of between 5% and 9%. Atta (2022) reported that the contamination fell from 9% to 3.1% with Kurin Lock use, while Hodson (2022) reported a statistically significant change from 6% at baseline to 1.9%" Kurin has consistently demonstrated its ability to reduce Blood culture contamination (BCC) rates in large NHS Hospitals (ED Departments) from the baseline rates identified. • Guys & St Thomas': 66% reduction. 6% down to 1.9% BCC • Kings College: 65.5% reduction 9% down to 3% BCC • Shrewsbury & Telford: 48% reduction. 5 down to 2.6% BCC	Thank you for your comment. Please see NICE's response to comment 10.
13	2	Company	4.9	"The committee considered that the lack of evidence on the resource impact from using Kurin Lock is a significant limitation of the economic model." What would be appropriate evidence for a small medical device business? The clinical and cost consequences of Blood Culture (BC) contamination has been extremely well evidenced for many years. Kurin has demonstrated its ability to significantly reduce BC contamination rates in the real world patients in the NHS and in American Hospitals. Therefore by reducing BC contamination rates with Kurin will lead to significantly reduced clinical and cost impact from BC Contaminates. The clinical evidence demonstrates that Kurin Lock reduces the risk of blood culture contamination rates and the wider literature supports the position that blood culture contaminations have a negative impact on NHS resources (unnecessary antibiotic use and unnecessary length of stay. As per the NICE reference case modelling provides an important framework for synthesising available evidence and generating estimates of clinical and cost effectiveness. In this submission we are simply extrapolating the reduction in blood culture contamination rates to the potential NHS benefits (of reduced antibiotic use and reduced length of stay) and this is akin to extrapolating changes in HbA1c or obesity to cardiovascular outcomes."	Thank you for your comment. As noted by the EAG in the assessment report, these outcomes were not formally recorded in the Kurin Lock trials. The EAG stated that although there was evidence of how reduction in blood culture contamination affects other outcomes, most of the evidence is from outside of UK NHS setting which may affect the generalisability of results. The committee's considerations of the clinical evidence and its limitations can be found in sections 4.2 and 4.3 of the medical technologies guidance.
14	2	Company	Are the summaries of clinical and cost	We believe the summary of the clinical effectiveness and impact Kurin makes in lowering Blood culture contamination rates is broadly appropriate. Whilst much of the data is not large	Thank you for your comment.

			effectiveness reasonable interpretations of the evidence?	randomised controlled trials they are real world product impact studies on a before and after basis with Kurin being the primary intervention. We therefore believe Kurin has demonstrated in multiple clinical environments and markets its ability to significantly lower blood culture contamination. Importantly, the innovative aspects of Kurin lock, diverting and isolating the first flash (0.15 ml) of blood, which may contain contaminants that can lead to a false-positive blood culture result, applies to all blood samples collected irrespective of the hospital setting and patient.	
15	2	Company	4.2	“The committee agreed with the EAG's view that the Alahmadi (2010) study, which estimated longer hospital stays associated with false positives compared with Skoglund 2019, was not generalisable to the NHS because of the high proportion of people in intensive care.” The intensive care unit represents one aspect of the NHS where blood cultures plays a critical part of the care pathway. It is unclear why evidence on such a key part of the NHS would be excluded and disregarded. Sensitivity analysis demonstrates that although the prevalence of blood culture contamination may be lower the consequences and associated costs will be much higher than other areas of the NHS such as the emergency department.	Thank you for your comment. The wording has been amended to reflect that the evidence is not generalisable to a wider NHS setting because of the high proportion of patients in intensive care. The clinical experts and the EAG noted that 42% of the contaminated blood cultures reported in Alahmadi (2010) came from an intensive care setting, and were not matched for settings with the comparator cases. The committee agreed that it is reasonable to assume that patients in intensive care may be expected to have longer stays and higher daily stay costs compared to other settings therefore the cost saving per contaminated blood culture may be overestimated in Alahmadi (2010). The committee’s considerations of the evidence and the hospital setting that Kurin Lock may be used in can be found in sections 4.6 and 4.3 of the medical technologies guidance.
16	2	Company	4.3	“The committee considered that using Kurin Lock is not likely to have a significant impact on antibiotic stewardship “ 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.	Thank you for your comment. The committee’s considerations of the clinical evidence and the impact on antibiotic use can be found in section 4.3 of the medical technologies guidance.

				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. 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. By reducing the rates of blood culture contamination with Kurin the use of unnecessary antibiotics can support antimicrobial stewardships efforts. 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'., Kluchler: BCC associated with a 16.4% increase in Vancomycin administration compared with true negative results. Nielsen et al, found that the adoption of a diversion device resulted in a 31.4% decrease of vancomycin days of treatment.	
17	2	Company	4.3	"The committee noted that data on staff adherence is also important to determine if this reduces over time or in busy periods, and the impact on blood culture contamination rates." We believe the analysis is considered conservative, as there are several other theoretical benefits that have not been quantified within the analysis (i.e. hospital-acquired infections). In certain settings, such as cancer and renal specialisations, false positive cultures may result in unplanned removal of central venous access devices.	Thank you for your comment. Please see NICE's response to comment 29.
18	2	Company	4.2	"One clinical expert stated that a mean difference of 2 days hospital stay is not plausible in clinical practice." The literature identified by the SLR reported length of stay within a cost-benefit analysis exploring the impact of a novel blood collection device to reduce blood culture contamination in the emergency department. Alahmadi stated an average of 5 extra bed days per patient with a contaminated blood culture. Whereas Skoglung et al (2019)	Thank you for your comment. Table 13 of the assessment report summarises several studies identified by both the company and the EAG that considered the impact of contaminated blood cultures in studies that did not include Kurin Lock. The EAG noted that there was no length of stay data directly related to Kurin Lock

				identified studies which assessed the LOS in patients with false-positive blood cultures. LOS ranged from 1-22 days for patients with contaminated cultures and 1-17 days for negative cultures. Therefore, we believe this could be a conservative estimate based on US studies, and believe the LOS is likely to be higher than 2 days. Burnie and Vining showed an average extended length of stay of 2.65 days. 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. 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. Allain (2018) reported an increased length of stay of 3.2 days associated with false positive blood cultures. 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. Kurin being proven to reduce contaminated blood cultures will in turn result in reduced length of stay for patients. The LOS will vary across various hospital settings and so while the mean difference of two days may not be reflective of the clinical experts respective hospital setting the published literature supports a significant variation on this view!	that could be used in the economic model instead of the data from Skoglund (2019). The committee were uncertain if the data was generalisable to the UK NHS setting due to this study being based in the US. The committee and the clinical experts highlighted that the 2 day difference in length of stay from Skoglund (2019) may be overestimated and not representative of NHS clinical practice. As the main driver of the economic modelling is the length of stay difference, the committee highlighted the uncertainty when interpreting the base-case results. The committee's considerations of the clinical and economic evidence relating to length of stay can be found in section 4.2 and 4.8 of the medical technologies guidance.
19	2	Company	4.8	"If the difference in length of stay for people with true negative blood culture results and false-positive blood culture results is overestimated, then the cost saving is reduced " To reiterate all the published literature details extra length of stay is a significant consequence of a contaminated blood culture. Are the EAG and Committee disputing this? 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. Alahmadi et al (2011) stated an average of 5 extra days per patient with a contaminated blood culture. Atta et al (2022) at	Thank you for your comment. Please see NICE's response to comment 18.

				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. Burnie and Vining showed an average extended length of stay of 2.65 days. 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. 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. Allain (2018) reported an increased length of stay of 3.2 days associated with false positive blood cultures.	
20	2	Company	4.10	"Sensitivity analysis showed that Kurin Lock can be cost saving or cost incurring depending on the parameters used, particularly around the length and cost of hospital stay. " Skoglung et al (2019) identified studies which assessed the LOS in patients with false-positive blood cultures. LOS ranged from 1-22 days for patients with contaminated cultures and 1-17 days for negative cultures. Therefore, we believe this could be a conservative estimate based on US studies. While no published studies have directly evaluated the economic impact of Kurin Lock, the cost-effectiveness of other interventions designed to decrease the rate of blood culture contamination have been assessed. Demonstrating the benefit of using Kurin Lock as best practice when collecting blood cultures compared to current collection methods which result in blood culture contamination remaining an ongoing issue for the NHS to manage.	Thank you for your comment. Please see NICE's response to comment 18.
Economic evidence					
21	2	Company	3.9	"Alahmadi (2010) found there was a cost saving of about £5,000 per contaminated blood culture." with a range of c. £2-10k cost per contaminated blood culture so even at the lower end of cost/contamination Kurin is significantly cost saving to the NHS.	Thank you for your comment.
22	2	Company	3.9	This therefore demonstrates that contamination rates, even in the ICU, have a great impact on hospital costs.	Thank you for your comment.

23	2	Company	3.11 - This uses a daily cost of a short stay from patient-level data for 1 NHS trust.	The NHS pathway is now different (in regards to tariff perspective and costing perspective). For instance, what feeds the HRG reference costs have now changed, so we cannot apply the same logic to the costs. The value of the PLICs data is that it uses the diagnosis codes for infection, rather than the HRG result, which will include a number of other diagnoses that are not infection. Therefore, the PLICs is more accurate as it reports patient level data, so we can map the costs a lot easier, rather than apply a fix all for reference costs. We utilised PLICs data as it includes all touchpoints throughout a patient journey, so is more representative. It is also granular so will not miss out cohorts. In addition, 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 24costs from Patient Level Information and Costing System (PLICs) data, via a Head of Costing and Service-Line Reporting (SLR) for an NHS Trust. Therefore, PLICs data is representative of NHS hospital costs and is the most representative data	Thank you for your comment. The EAG agreed that PLICS can be used to identify appropriate patient costs, and that this has the potential to give more granular detail than is available through HRG groupings. The EAG, however, did not agree that the HRG groupings selected for modelling are inappropriate. The limitations with both coding approaches that the EAG and the company used were that only a partial number of appropriate groups are identified. The PLICS data used in the company submission was obtained from one provider which may not be representative of the variability observed in the NHS. The EAG agreed that there is difficulty in estimating the most relevant daily cost to apply and the alternative methods to calculate the stay cost, and these alternative costs were included in the sensitivity analysis (see Appendix D of the assessment report). The EAG provided additional analysis after the consultation period which is available in Appendix 1 using PLICS data obtained from NHS Wales. This resulted in a cost saving of £45 per person using the base case compared to £72 in the company submission. However, the committee still considered that there were too many uncertainties with the economic modelling results. Therefore, the committee agreed that having additional evidence which links the use of Kurin Lock to changes in length of stay or costs would improve the accuracy of the modelling results.

					The committee's considerations of the clinical and economic evidence relating to the model can be found in section 4.7 of the medical technologies guidance.
24	2	Company	3.11	The EAG methodology uses HRG codes associated with patients admitted with sepsis or fever of unknown origin. However, the likelihood is that the patients being tested will have been admitted for other underlying clinical reasons and that the infection will be a complication associated with this underlying admission. As such, the methodology utilised by the EAG is flawed and does not reflect the true costs associated with the incremental burden of infection. The EAG also inflated 2019/20 costs to 2021/22 using the PSSRU - However, 2021/22 figures are available directly. In light of current levels of inflation these are also likely to be conservative with current levels of inflation – the UK Consumer Price Index rose by 6.3% for the 12 months to November 2023	Thank you for your comment. The EAG stated that their methodology is unlikely to capture all the appropriate patient groups. However, it argues that the methods used by the company are also unlikely to capture all appropriate patient groups. The EAG used 2019/20 costs to avoid the impact of COVID-19. The EAG provided additional analysis after the consultation period using costs from 2021/22 which is available in Appendix 1. The length of stay costs calculated by the EAG were lower than the company's results, therefore, the cost saving would not be as high as the company submission. The committee concluded that the EAG modelling was appropriate but that there is uncertainty on which costs to apply which affect the cost saving potential of Kurin Lock.
25	2	Company	3.11	One cannot have an excess bed day for a short stay, as this would be a long stay and excess bed days are intended for when there are minimal interventions. As excess bed days only kick-in after a patient is deemed medically fit for discharge, there are also other factors stopping them from being discharged from hospital. Therefore, the calculation of the cost for an excess bed day does not account for any clinical interventions (which would be included in a short stay tariff). Furthermore, excess bed days are not counted for in PLICs based National cost collection anymore, so the excess bed days cost would not be reflective of current NHS costs. The value of the PLICs data is that it uses the diagnosis codes for infection,	Thank you for your comment. The EAG stated that the short stay method was inappropriate as it assumes all interventions are performed daily, which was supported by the clinical experts.

				rather than the HRG result, which will include a number of other diagnoses that are not infection.	
26	2	Company	3.11	The last reference costs are for 2017/2018, and how they were calculated then are different to how they are calculated now (due to different grouper costs). If we were to match current activity to inflated costs, there would be gaps in the data. Therefore, we cannot apply the same logic to older data. By inference, the EAG analysis is considering those patients with infections ((WHO7A-G) for non-elective short-stay) 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.	Thank you for your comment. The EAG agreed there were limitations to inflating old cost data. The EAG stated that having additional evidence linking the use of Kurin Lock to costs would improve the accuracy of the modelling results. The EAG provided additional costings after the consultation period which are available in Appendix 1. This showed the range and the weighted mean costings for patients with the codes WH07A-G. WH07A-G refers to 'Infections or Other Complications of Procedures, including with and without intervention'. The weighted mean value was £730.84 which was lower than the company submission. Therefore, the cost saving would not be as high as the company submission. The committee concluded that the EAG modelling was appropriate.
27	2	Company	3.12	The EAGs own analysis of length of stay cost (Appendix D) reports three alternative approaches all resulting in higher bed day costs than the EAG base case (ranging from £440 to £953 from a preferred base case of £329). Therefore including a negative variance of 20% on this parameter will significantly and inappropriately reduce the probability of Kurin Lock being cost saving in the PSA.	Thank you for your comment. The EAG agreed that there was difficulty in estimating the most relevant daily cost to apply and the alternative methods to calculate the stay cost. Alternative costs were included in the sensitivity analysis (see Appendix D of the assessment report). The EAG provided additional costs after the consultation period, which are available in Appendix 1. The committee concluded that the EAG modelling was appropriate but that there is uncertainty about which costs to apply and this impacts the cost saving potential of Kurin Lock.

28	2	Company	3.12	"A one-way sensitivity analysis showed that the length and cost of stay, rate of blood culture contamination at baseline and reduction in rate of blood culture contamination from using Kurin Lock all have the potential to make Kurin Lock cost incurring or cost neutral." This is only true at the EAGs preferred daily bed day cost.	Thank you for your comment. Section 3.12 of the medical technologies guidance describes the EAG's model.
29	2	Company	4.5	We believe the analysis is considered conservative, as there are several other theoretical benefits that have not been quantified within the analysis (i.e. hospital-acquired infections, staff adherence). In certain settings, such as cancer and renal specialisations, false positive cultures may result in unplanned removal of central venous access devices. Therefore, Kurin Lock would result in further benefits, not reported.	Thank you for your comment. As noted by the EAG in the assessment report, these outcomes were not formally recorded in the Kurin Lock trials. The EAG noted that, although there is evidence of how reduction in blood culture contamination affects other outcomes, most of the evidence is from outside of UK NHS setting which may affect the generalisability of results. The committee concluded that having additional evidence linking the use of Kurin Lock to changes in these clinical outcomes and the costs associated with these changes would improve the accuracy of the modelling results. The committee's considerations of the clinical evidence and its limitations can be found in sections 4.2 and 4.3 of the medical technologies guidance.
30	2	Company	4.5	Rather narrow view: Also consider, Kurin would be cost saving where the bed day cost is high, where the cost consequence of a contaminated blood culture is high (ICU/HDU/CCU/Cancer/GI etc) and the impact on the patient could be significant. Also with the current pressures the NHS is facing with significant capacity issues every bed day saved can support better downstream resource efficiencies.	Thank you for your comment. The EAG stated that although the model results indicate that the Kurin Lock would be cost saving when the bed day cost is high, there was uncertainty whether the cost savings would be realised in settings such as intensive care. The committee's considerations of the clinical and economic evidence relating to hospital setting can be found in section 4.6 of the medical technologies guidance.

31	2	Company	4.7	As previously noted, the methodology employed by the EAG has many significant limitations. - EAG used the HRG for sepsis admissions but patients will be admitted for various indications and the infection would be deemed a complication. As such the HRG selected is inappropriate - The EAG used 2017/18 data and inflated this to 2021/22 but 2021/2022 figures are already available - The methodology to estimate first day and excess say costs is flawed. The EAG attempted three alternative methods for determining the bed day costs and all resulted in higher daily costs than the EAG base case (Appendix D: Table 23). In	Thank you for your comment. Please see NICE's response to comments 23 and 24.
32	2	Company	4.7	"It considered that the lower daily hospital stay cost used by the EAG was appropriate." Why? It is unclear why this cost is deemed appropriate other than it being the cheapest.	Thank you for your comment. The EAG agreed that there is difficulty in estimating the most relevant daily cost to apply and the alternative methods to calculate the stay cost, and these alternative costs were included in the sensitivity analysis (see Appendix D of the assessment report). The EAG provided additional costs after the consultation period, which are available in Appendix 1. The committee's considerations of the evidence relating to economic model can be found in section 4.7 of the medical technologies guidance.
33	2	Company	4.7	This is critical of course and has been a large element of this health economic submission. Patient Level Information and Costing System (PLICS) data represents the most accurate resource and current costing information for the NHS, while we acknowledge the provided data set reflects a single NHS trust we feel it is significantly more accurate and reflective of current costs than other sources. The EAG methodology assumes all patients have sepsis and links to the associated tariff code. Instead of using the HRG result, like the EAG have done with the NHS reference cost, the PLICS data	Thank you for your comment. Please see NICE's response to comments 23 and 24.

				uses the diagnosis codes for infection and therefore more accurately reflects the various underlying conditions that the patient will have been originally admitted for. The data shared by the Company is therefore the most accurate costing data available from the NHS.	
34	2	Company	4.8	As per the title the length of stay AND the associated cost are the main drivers. The EAG have selected a low base case value (As noted by their own analysis of alternative bed day costs - See Appendix D, Table 23). All submitted evidence and the EAGs own analysis suggest that the cost per bed day is much higher than their base-case which will increase the likelihood of Kurin Lock being cost-saving. In settings where the bed day cost is high (ICU, cancer wards etc.) the length of stay benefit doesn't need to be as long, nor the reduction in false-positive blood contaminations as high for Kurin Lock to be cost-saving.	Thank you for your comment. Please see NICE's response to comments 23 and 24.
35	2	Company	4.9	As noted previously this analysis is flawed - The EAG varied their cost parameters by +/- 20%. In the base case the cost of a hospital bed day is £377 as such the associated range would be £302 - £452. However, the EAG note that their alternative assessment of bed day costs is much higher. As such the implementation by the EAG will significantly under report the probability that Kurin Lock would be cost saving.	Thank you for your comment. The EAG also noted that +/- 20% variance is commonly used for sensitivity analysis and reflects the uncertainty of the inputs. The committee concluded that the EAG modelling, and sensitivity analysis was appropriate. The committee also agreed that having additional evidence which links the use of Kurin Lock to changes in length of stay and the costs associated with the length of stay would improve the accuracy of the modelling results.
36			Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?	We believe the summary of the clinical effectiveness and impact Kurin makes in lowering Blood culture contamination rates is broadly appropriate. Whilst much of the data is not large randomised controlled trials they are real world product impact studies on a before and after basis with Kurin being the primary intervention. We therefore believe Kurin has demonstrated in multiple clinical environments and markets its ability to significantly lower blood culture contamination. Importantly, the innovative aspects of Kurin lock, diverting and isolating the first flash (0.15 ml) of blood, which may contain contaminants that can lead to a false-positive blood culture result, applies to all blood samples collected irrespective of the hospital setting and patient.	Thank you for your comment. Please see NICE's response to comments 1, 9, 15, 23 and 24. The EAG and committee agreed that there is insufficient robust economic evidence to assume £2,000 is a conservative minimum cost saving for avoided BCC. The committee concluded that having additional evidence linking the use of Kurin Lock to changes in length of stay or costs would improve the

				We do however believe the cost effectiveness from the health economic modelling has been unreasonably interpreted. The submitted cost-consequence analysis selected specific hospital settings to illustrate the potential cost savings the EAG have limited their conclusions to the emergency department only, the base case setting presented by the manufacturer, citing the higher blood culture contamination rates typically seen in this setting. In the submitted evidence multiple settings were presented and setting agnostic analysis was also considered demonstrating that there is a relationship between contamination rates and costs that often results in Kurin Lock being cost saving. For example, the Alahmadi (2010) paper is critiqued for overestimating potential costs associated with blood contamination due to the high number of patients in the intensive care setting rather than recognising that despite having potentially lower rates of blood culture contamination the associated cost impact of a blood culture contamination is significantly more costly in this setting. The EAG note that there is uncertainty with regards to Kurin lock demonstrating cost savings however we feel this is predominantly due to flawed methodology in deriving the bed day costs for excess bed days (occuring as a consequence of contaminated blood cultures) which significantly underestimates the associated costs. Issues with the methodology include; using old costs and inflating rather than using the latest costs; using the HRG code for sepsis when in clinical practice the blood stream infection would likely be a complication in addition to their original reason for hospital admission, using non-elective short stay data to determine the cost of the first day of stay cost and then calculating excess costs using other unclear methods. In addition, the EAG have biased their analysis against Kurin lock by assuming a +/- 20% variance on their assumed base case hospital bed day cost of £377 (£302 - £452). The EAG themselves try three alternative approaches to estimate the bed day cost, all of which are higher than their own base case. As such, at a minimum the current base case cost should act as a floor cost with uncertainty looking at higher bed day costs which will increase the probability of Kurin Lock being cost effective.	accuracy of the modelling results and reduce uncertainty.

				As noted above, by assuming the costs are based on the HRG for sepsis the EAG also fail to recognise and consider the varying bed day costs associated with other hospital settings such as intensive care which have previously been shown to be costly (Alahmadi et al). While we agree with the recommendation for Kurin Lock use in the emergency department, which is associated with high blood culture contamination rates, we would urge that the recommendation be expanded to include all services where contamination rates are above the current accepted contamination rate standard of 3%, and where the cost associated with an unnecessary length of stay is also high (such as in intensive care). Finally the NHS Macro level impact of contaminated blood cultures is quite stark! The NHS performs approximately 3M blood cultures per year. The average Blood Culture Contamination rate is 5%. That's 150,000 false positive blood cultures annually. Whilst there is clearly a lack of consensus on what the actual cost of blood culture contamination is in the NHS, even the most conservative of costs in the published literature are recording it at +£2,000 and 2 extra days in hospital. That cost alone to the NHS is +£300M per year in downstream costs and potentially +300,000 extra beds. Kurin is proven to reduce blood culture contamination rates consistently by over 60%. Which potentially means that over 90,000 false positives could be prevented. Even if 100% of blood culture sets had a Kurin used the total spend would be less that £60M in total, and the potential savings generated would in excess of £180M, a net benefit to the NHS of +£120M, with the added benefit of +180,000 bed days saved. That's appears to be a great return on investment for patients and the Tax payer!	
Equality considerations					
37	2	Company	Are there any equality issues that need special consideration and are not covered	No. Kurin is very easy to use and can be used on any patient of any age to take a blood culture.	Thank you for your comment.

			in the medical technology consultation document?		
Evidence generation					
38	2	Company	1.2	1.2 - B2: Agree that this data would be useful however it is unclear why the burden of such data should fall on the suppliers of Kurin, Iskus Health UK Ltd. Current contamination rates (which are well documented within the NHS) reflect the challenges with adherence to current blood culture collection techniques. The Kurin lock is a simple to use device that helps simplify the process of taking a blood cultures and ensuring the 1st flash of blood where potential contaminates are is 'locked away' and so lead to improved blood blood culture accuracy.	Thank you for your comment. Please see NICE's response to comments 1, 9, 11, 13, 29 and 36.
39	2	Company	1.2	1.2 - B3: 12 Studies have been submitted to NICE. All demonstrate a reduction in BC Contamination rates using Kurin. Whilst Iskus Health will continue to support NHS Hospitals in proving Kurin works in lowering their contamination rates this should not be an indefinite.	Thank you for your comment. Please see NICE's response to comments 9 and 10. NICE expects to review the guidance in 3 years or sooner if evidence becomes available.
Technology					
40	1	Individual	2.6	Patients with implanted cardiac devices or prosthetic valves would also be in this group as organisms that would normally be considered contaminants (i.e. Staphylococcus epidermidis) may be a causative pathogen in this group of patients. Therefore false positives can lead to uncertainty about treatment and often patients are given lengthy courses of treatment because of this uncertainty.	Thank you for your comment. The committee values comments from clinicians about their experiences. Section 2.7 of the guidance has been amended to include these population groups.
41	2	Company	2.4	Passively diverts and sidelines the 1st flash of blood. This is important as it means there is no change in practice and does not require blood culture takers to take additional steps during the procedure.	Thank you for your comment. Section 2.5 of the guidance has been amended to include 'passively diverts'.
42	2	Company	2.5	Not Can... 'do' have ... Any false positive blood culture has a consequence and downstream cost to the healthcare system.	Thank you for your comment.
43	2	Company	4.4	It is complementary to CVC blood cultures as a Peripheral Blood Culture set should always be taken when taking line cultures.	Thank you for your comment.
44	2	Company	4.4	NHS England B0686-improving-the-blood-culture-pathway--executive-summary.pdf (england.nhs.uk) recommends implementing 'Best Practice' for blood culture taking. Kurin supports best practice 100% and can be used in all patients having blood cultures taken in all departments to avoid the	Thank you for your comment.

				consequences of any contaminated blood culture and improve patient outcomes.	
45	2	Company	4.6	Much of the NHS product evaluations with Kurin had blood cultures taken from freshly inserted peripheral IV cannulas. Significant reductions in blood culture contaminations were achieved in all cases both using an IV Cannula Connect Kurin and a fresh venipuncture Kurin.	Thank you for your comment.
46	2	Company	4.6	This is very plausible. However is still open to cross contamination and a manual intervention to achieve an initial blood volume discard. Kurin passively diverts the 1st flash of blood in a very small volume (only 0.15ml) and is a closed system so takes blood from vein to bottle without breaking the circuit once its in place.	Thank you for your comment.

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."

MTG582 Kurin Lock

Additional information in response to fact check and consultation comments from company, updated 2024 following NICE queries

PLICS and National Cost Collection

Patient Level Information and Costing System (PLICS) will show the total cost for each patient for an episode of care, and this can be related to diagnostic and procedural codes. This information is fed into a national database and used to create the National Cost Collection which is published online each year for NHS England. Therefore, the costs are nominally the same in each system, however the PLICS allows a greater level of granular interrogation than the publicly available information.

ICD10 codes and HRG codes

ICD10 codes are for specific diagnoses (either as the primary diagnosis, or occurring in secondary diagnostic codes). These and procedure codes are grouped together and used to create health resource group (HRG) codes that with costs for episodes that are similar in resource use. The NHS Grouper tool can be used to interrogate the relationship between the diagnostic, procedural and HRG codes.

The ICD10 codes used by the company for adult ward costs are:

T808	Other complications following infusion, transfusion and therapeutic injection
T809	Unspecified complication following infusion, transfusion and therapeutic injection

Using the NHS grouper tool these would result in the following HRG groups (although for most patients the HRG group would be determined first by any relevant procedure)

SA09	Other Red Blood Cell Disorders (with or without complications)
WH07	Infections or Other Complications of Procedures (with or without interventions or complications)

The HRG codes used by the EAG for adult ward costs are:

WJ06	Sepsis (with or without interventions or complications)
WJ07	Fever of unknown origin (with or without interventions or complications)

The EAG agree that PLICS can be used to identify appropriate patient costs, and this has potential to give more granular detail than is available through HRG groupings, however in this case the EAG do not agree that the HRG groups selected are inappropriate. Both coding approaches are likely to only partially identify the appropriate groups, and therefore additional evidence that links the use of Kurin Lock to changes in length of stay or costs would improve the accuracy.

Variation in daily costs and use of 21/22 data

The submission used daily length of stay costs that were based on PLICS costs for the 2020-21 period (adults) and 2021-22 (paediatric):

Table 1 Daily ward 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
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 /
EAG cost for excess bed day	£322	Weighted mean, HRG groups WJ06 and WJ07

The company queried the use of previous year's data, and also supplied National Cost Collection costs for 2021/22, highlighting the range of values.

The EAG used excess bed day costs inflated from 2017/18 as they are unavailable in more recent years. Other HRG costs were inflated from 2019/20 to avoid the impact of COVID19, however the EAG considered 2021/22 costs in response to this query. Rather than looking at the range of values the EAG preferred a weighted mean, which is the approach usual in economic model inputs. Table 2 shows the weighted mean for non-elective short stays using 2021/22 costs. This demonstrates that they are lower than the company daily rate, and they are also lower than the inflated 2019/20 costs when looking at adult data.

Table 2 Costs for non-elective short stay NCC 2021/22

Costs for non-elective short stay NCC 2021/22	Range of values	Weighted mean for all	Weighted mean for those with complications only
Sepsis (WJ06A-J) including with and without intervention	£646 to £1,840	£731.49	£753.07
Fever of Unknown Origin (WJ07A-D) including with and without intervention	£374 - £617	£562.21	£610.49
Infections or Other Complications of Procedures, (WH07A-G) including with and without intervention	£538 to £2,061	£575.27	£730.84

Alternative sources of PLICS data

The EAG requested a PLICS extract from NHS Wales, for the ICD10 codes used by the company, and also for codes A40X and A41X, which relate to sepsis, and R50X which relate to fever. The information received is summarised in Table 3

Table 3 PLICS request from NHS Wales

PLICS data NHS Wales 21/22		No. FCE	Cost per FCE	Mean cost per day
Adult, General ward: ICD10 T808,T809	Non elective short stay	26	£588	£588
	Non elective long stay	40	£6,573	£697
Adult, General ward: ICD10 A40X, A41X and R50X	Non elective short stay	5,144	£719	£719
	Non elective long stay	13,249	£6,829	£563
18 and under, General ward: ICD10 T808,T809	Non elective short stay	5	£639	£639
	Non elective long stay	6	£23,895	£2,043
18 and under, General ward: A40X, A41X and R50X	Non elective short stay	2,069	£916	£916
	Non elective long stay	638	£5,279	£1,217
Footnote from NHS Wales: All costs are NHS Wales patient level costs which are fully absorbed, and thus contain direct, indirect and overhead elements. The costs are an indication of resource				

use, but are not fully releasable and thus are not applicable as an indicator of savings potential. NHS Wales PLICS data is compiled on similar principles and calculated on the same basis as NHS England Reference Costs, which are also fully absorbed.

These are taken for patients who were admitted as non-elective patients, where the stated diagnostic codes occur at any coding position, but excludes all those who spent any time in critical care during their hospital stay.

The EAG applied the same methodology as used in the assessment report base case, [(total FCE cost – short stay cost) / (length of stay – 1)] and applied this to the diagnostic codes for A40X and R50X, resulting in an average daily cost of £549 for adults (19 and over) and £1,307 for 18 and under. This has been entered into the model and results in a weighted total daily cost of £692. Alternative calculation methods result in slightly lower costs (between £599 and £692)

Using this in the model results in a cost saving of £45 per patient, however the following should be noted:

- We cannot be sure if the correct population is being selected in costing (for example 76% of those 18 and under are treated as short stay in the data).
- There may still be impacts of COVID-19 in 2021/22 costs.
- The method of calculating daily cost is unlikely to reflect the cost of an additional day of monitoring a patient due to BCC, however a more accurate costing is not currently available.
- The base case uses a reduction of 2 days stay and baseline contamination rates of 9%, there remains uncertainty around these.

Table 4 demonstrates that when varying the length of stay and baseline contamination rate, even with this higher cost of £692, a baseline contamination rate of 5% would require 2 days saved due to the introduction of Kurin Lock to be cost neutral.

Table 4 Additional scenario: NHS Wales PLICS cost for A40X, A41X and R50X, showing variation in background bacteraemia rate, and the number of days saved, updated to include 0.25 and 0.5 bed days

		Baseline risk of BC contamination with SoC									
	£45	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%
Additional bed days per BCC	0.25	-£37	-£35	-£34	-£33	-£32	-£30	-£29	-£28	-£26	-£25
	0.50	-£36	-£33	-£31	-£28	-£26	-£23	-£21	-£19	-£16	-£14
	1.00	-£33	-£29	-£24	-£19	-£15	-£10	-£5	£0	£4	£9
	1.50	-£31	-£24	-£17	-£10	-£3	£4	£11	£18	£25	£32
	2.00	-£29	-£20	-£10	-£1	£8	£17	£27	£36	**£45**	£54
	2.50	-£27	-£15	-£4	£8	£19	£31	£42	£54	£65	£77
	3.00	-£24	-£11	£3	£17	£31	£45	£58	£72	£86	£100
	3.50	-£22	-£6	£10	£26	£42	£58	£74	£90	£106	£122
	4.00	-£20	-£1	£17	£35	£53	£72	£90	£108	£127	£145

Table 5 has been requested following the second MTAC. It continues the scenario where the bed day cost is £692, and also assumes an increase of 0.5 bed days per false positive result. This demonstrates that in this particular scenario a lower cost per device would be needed to show cost savings than the £19.50 used for the submission.

Table 5 Additional scenario: NHS Wales PLICS cost for A40X, A41X and R50X, showing variation in background bacteraemia rate, and the cost of a single Kurin lock device, including the assumption of 0.5 bed days per false positive blood culture result.

		Baseline risk of BC contamination with SoC (LOS set at 0.5 days per false positive)									
	£45	1%	2%	3%	4%	5%	6%	7%	8%	9%	10%
Cost of Kurin Lock (per device)	£6	-£9	-£6	-£4	-£1	£1	£4	£6	£8	£11	£13
	£8	-£13	-£10	-£8	-£5	-£3	£0	£2	£4	£7	£9
	£10	-£17	-£14	-£12	-£9	-£7	-£4	-£2	£0	£3	£5
	£12	-£21	-£18	-£16	-£13	-£11	-£8	-£6	-£4	-£1	£1
	£14	-£25	-£22	-£20	-£17	-£15	-£12	-£10	-£8	-£5	-£3
	£16	-£29	-£26	-£24	-£21	-£19	-£16	-£14	-£12	-£9	-£7
	£18	-£33	-£30	-£28	-£25	-£23	-£20	-£18	-£16	-£13	-£11
	£20	-£37	-£34	-£32	-£29	-£27	-£24	-£22	-£20	-£17	-£15
	£22	-£41	-£38	-£36	-£33	-£31	-£28	-£26	-£24	-£21	-£19

Sensitivity analysis

The EAG changed the PSA variance from 10% to 20%, due to the uncertainty of the inputs. The company queried the use of 20% lower than the EAG bed day cost, and the EAG therefore explored the impact of using 10% for that cost, while leaving the remainder at 20%. This changed the probability of Kurin Lock being cost saving from 62 to 63%.

The EAG also re-ran the PSA at 20% using the alternative bed day cost of £692 (with 20% range of £554 to £830) resulting in a probability of Kurin Lock being cost saving of 87%. However a 20% variation in length of stay is only 1.6 to 2.4 bed days, and a baseline contamination rate of 7% to 11%.

The EAG feel that the uncertainty in daily cost, length of stay and baseline contamination rates is potentially much greater than 20%, and that in this case the two way sensitivity analysis, as presented in the report and table 4 of this addendum, is more appropriate.

Previous MTEP assessment reports

The EAG have considered the last 5 assessment reports completed that included bed days, and described the method and cost used, in Table 6, and are satisfied

that the costs and methods used are in accordance with normal practice accepted by MTEP.

Table 6 Summary of daily costs used in previous assessments

Assessment report	Method	Daily cost
MTG64 KardiaMobile		Not included
AposHealth		Not included
UrgoStart	Weighted average of non elective excess bed day cost	Not included
Memokath-051		£51 for 4 hours, equates to £306 per 24 hours
Optilume		Not included
Greenlight	PbR Tariff LB25F, but not included in EAG model	£294
MagTrace		Not included
Faecal microbiota transplant	Quotes NCC 2021, currency code: SD01A)however no further information available	£371
iFUSE	NHS CC weighted average for excess days, inflated to current costs	In 2018: £272 in submission, £381 in EAG model In 2022 update: £415.44
SecurAcath		Not included
Pleurex	Excess bed days, inflated to current costs	£312 in 2011, £355 in 2028, £368 in 2022
MiraQ		Not included
Peristeen		Not included
Thopaz	Using Excess bed days and inflated	£365.93
Sleepio		Not included
MyCOPD		Not included
Uroshield		Not included
Prontosan		Not included
3C Patch		Not included
Sedaconda		Not included
Endosponge	Company referenced "http://www.wales.nhs.uk/documents/delivery-plan-for-thecritically-ill.pdf"	£413 from company, not included by EAG
Clear guard	LOS discussed but no value found for cost.	Not stated

Curos	(included because referenced in Clear Guard	

Additional papers identified by the Company in consultation comments

The company referenced a number of additional papers during these comments, some of which had not been submitted or discussed in the assessment process, although none were within the scope for Kurin Lock. The EAG have attempted to identify these and briefly summarised any relevant points in Table 7 below.

Additional References:

Doern, G. V., Carroll, K. C., Diekema, D. J., Garey, K. W., Rupp, M. E., Weinstein, M. P., & Sexton, D. J. (2019). A comprehensive update on the problem of blood culture contamination and a discussion of methods for addressing the problem. Clin Microbiol Rev, 33(1), e00009-19.

Hughes, J. A., Cabilan, C. J., Williams, J., Ray, M., & Coyer, F. (2018). The effectiveness of interventions to reduce peripheral blood culture contamination in acute care: a systematic review protocol. Systematic Reviews, 7(1), 1-6.

Hughes, J. A., Cabilan, C. J., Williams, J., Ray, M., & Coyer, F. (2023). Interventions to reduce peripheral blood culture contamination in acute care settings: A systematic review and meta-analysis. medRxiv, 2023-07.

Michaelidis, C. I., Fine, M. J., Lin, C. J., Linder, J. A., Nowalk, M. P., Shields, R. K., ... & Smith, K. J. (2016). The hidden societal cost of antibiotic resistance per antibiotic prescribed in the United States: an exploratory analysis. BMC infectious diseases, 16, 1-8.

Michaelidis, C. I., Zimmerman, R. K., Nowalk, M. P., Fine, M. J., & Smith, K. J. (2014). Cost-effectiveness of procalcitonin-guided antibiotic therapy for outpatient management of acute respiratory tract infections in adults. Journal of general internal medicine, 29, 579-586.

Table 7 Summary of additional papers

Study	Used for company model?	Used for EAG model?	Baseline BCC	BCC change	Change in LOS	Key results	Comments
Skoglund 2019						Already included in table 13, EAG report	
Alahmadi 2011						Already included in table 13, EAG report	
Burnie & Vinning 2021						Already included in table 12, EAG report	
Arnaout 2021						Already included in table 12, EAG report	
Baxter 2020						Already included in table 12, EAG report	
Allain 2018						Already included in table 12, EAG report	
Michaelidis 2014	No	No	n/a	n/a	n/a	None	The EAG identified two possible papers, one addresses cost-effectiveness of procalcitonin guided antibiotic therapy, and the other addresses costs of antibiotic resistance. Neither are directly relevant to the EAG report.
Waltzman and Harper 2001						Already included in table 13, EAG report	
Hughes, JA 2018	No	No	1.8 – 4.7% for diversion devices	57% decrease for diversion devices	Not reported	The authors identified 34 studies across all methods of reducing blood contamination that could be included in quantitative synthesis. A total of 5 studies were for diversion devices, of which 4 were suitable for quantitative synthesis..They reported the greatest reduction where there was a dedicated phlebotomy team (RR 0.40 95%CI 0.21 – 0.76). The second largest reduction was for diversion devices (RR 0.43, 95% CI 0.31-0.58)	The EAG have identified a protocol for a systematic review and meta-analysis which matches this description. Following this, a full systematic review and meta-analysis was identified as a pre-print online, prior to peer review. Note that this has not yet been peer reviewed or published. Two of the studies are already included in the EAG assessment Sutton and Rupp)
Doern 2020	No	No	n/a	n/a	n/a	None	This is a discussion paper based on published work and the authors' opinions. It includes numerous references for the work but is not a systematic review.

Document cover sheet

Assessment report: Kurin Lock for Blood Culture Collection

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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

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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.

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- 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.

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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 • People at increased risk of infections such as those who are immunocompromised • 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, but the following indicators should be taken into account when assessing a patient for signs of bacteraemia or sepsis: • core temperature out of normal range; • focal signs of infection; • abnormal heart rate (raised), blood pressure (low or raised) or respiratory rate (raised); • chills or rigors; • raised or very low white blood cell count; and • new or worsening confusion. • 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: • Blood culture contamination rate • Positive and negative predictive values • Rates of antimicrobial prescriptions • Use of unneeded antibiotic treatment • Unnecessary further interventions such as laboratory tests to rule out suspected bacteraemia • Treatment delays • Length of hospital stay • Rates of hospital-acquired infection • Patient-reported outcome measures such as health-related quality of life • Patient-reported experience measures • 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 • Long-term indwelling lines and/or catheters removed unnecessarily in an attempt to eliminate cause of suspected infection • 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 • 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 • 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 Step 1: With clean hands clean tray according to local policy Step 2: Gather equipment and place around tray Step 3: Clean hands with alcohol hand rub or soap and water Step 4: Prepare equipment using a non-touch technique (NTT) Step 5: Apply disposable apron and label bottles Step 6: Clean hands with alcohol hand rub or soap and water Step 7: Scrub bottle ports for 15 seconds using 2% chlorhexidine & 70% alcohol wipe Step 8: Position arm on drape and pillow Step 9: Apply disposable tourniquet, identify a vein, relax tourniquet Step 10: Clean hands with alcohol hand rub or soap and water Step 11: Re-tighten tourniquet Step 12: Apply non-sterilised gloves Step 13: Clean skin – 2% chlorhexidine / 70% alcohol applicator, back and forth & left to right strokes for 30 seconds. Allow to dry Step 14: Puncture vein (DO NOT RE-PALPATE). Draw blood Step 15: Inoculate blood into bottles using a NTT. Release tourniquet Step 16: Apply an appropriate dressing to the puncture site Step 17: Dispose of sharps Step 18: Clean tray according to local policy Step 19: Dispose of gloves 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:** **DO:** • 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') • use one pair of non-sterile gloves per procedure or patient • use a single-use device for blood sampling and drawing • disinfect the skin at the venepuncture site • discard the used device (a needle and syringe is a single unit) immediately into a robust sharps container • use the one-hand scoop technique, where recapping of a needle is unavoidable • seal the sharps container with a tamper-proof lid • place laboratory sample tubes in a sturdy rack before injecting into the rubber stopper • immediately report any incident or accident linked to a needle or sharp injury, and seek assistance; start PEP as soon as possible, following protocols **DO NOT:** • forget to clean your hands • use the same pair of gloves for more than one patient • wash gloves for reuse • use a syringe, needle or lancet for more than one patient • touch the puncture site after disinfecting it • leave an unprotected needle lying outside the sharps container • recap a needle using both hands • overfill or decant a sharps container • inject into a laboratory tube while holding it with the other hand • delay post-exposure prophylaxis (PEP) after exposure to potentially contaminated material; beyond 72 hours, PEP is NOT effective **Monitoring and evaluation** A monitoring and evaluation system should be in place to offer surveillance of management of phlebotomy services and adverse events, and to document improvements. One indicator to be included would be the number (and percentage) of laboratory test results lost due to errors or poor quality; for example: • blood culture contamination rate • blood transfusion adverse events • haemolysis • 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** **Clinical:** Method of collection • 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 • Changing needles between venepuncture and inoculation of the bottles is not recommended because this carries a risk of needle stick injury. Number and timing of samples: • 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 • 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. Previous antimicrobial therapy • 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. Volume of blood • 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. **Contamination** • 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 **Location:** USA **Duration: Unclear.** 3 months with Kurin Lock analysed. **Aims:** to investigate the impact of introducing Kurin Lock into blood culture sampling processes. **Green:** meets scope	**Design:** Before/after study. **Intervention:** Kurin Lock **Green:** meets scope	**Participants:** Emergency department patients requiring blood culture samples (n = not reported). **Exclusions:** None reported. **Setting:** Emergency department in USA hospital. **Green:** meets scope	• Blood culture contamination rate • Estimated associated impact on costs **Green:** meets scope	Abstract with limited study details. Estimated cost savings of implementing Kurin Lock calculated, based on assumed costs associated with false positive blood culture results.
Arenas 2021 **Location**: USA **Duration:** 16 months **Aims**: to test 2 commercially available devices to reduce the blood culture contamination rate in an emergency department.	**Design**: Prospective and retrospective trial. **Intervention**: 2 different blood diversion devices (device A and device B). **Green**: meets scope	**Participants**: Emergency department patients requiring blood culture samples (n = 4030 samples). **Exclusions**: None reported. **Setting**: Emergency department in USA hospital. **Green**: meets scope	• Blood culture contamination rate **Green**: meets scope	Full text peer reviewed publication. 2 devices not identified in publication. Company submission indicated that device B is Kurin Lock. 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 **Location**: USA **Duration**: 10 week period at one site, followed by second 10 week period at a second site. Washout phase in-between. **Aims**: to assess the effectiveness of a blood diversion device **Green**: meets scope	**Design**: Multi-phase prospective crossover trial **Intervention**: Kurin Lock **Green**: meets scope	**Participants**: Emergency department patients requiring blood culture samples (n = 5675 samples taken, 5661 analysed). **Exclusions**: None reported. **Setting**: 2 emergency departments in USA hospital. **Green**: meets scope	• Blood culture contamination rate **Green**: meets scope	Abstract with limited study details. Device not named in abstract, company submission indicates the device is Kurin Lock. Authors noted that second emergency department site had both a level 1 trauma centre and transplant program.
Atta 2022 **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 **Aims**: to determine, if the introduction of Kurin Lock will reduce the number of false-positive blood cultures. **Green**: meets scope	**Intervention**: Kurin Lock **Green**: meets scope	blood culture samples (n = 381 samples). **Exclusions**: None reported. **Setting**: Emergency department in NHS hospital. **Green**: meets scope	• Estimated impact on length of stay • Estimated associated impact on costs • Staff adherence **Green**: meets scope	Number of patients from whom samples were taken is unclear.
Baxter 2020 **Location**: USA **Duration**: Not reported. **Aims**: to investigate the impact of introducing Kurin Lock on blood culture contamination rates. **Green**: meets scope	**Design**: Before/after study. **Intervention**: Kurin Lock **Green**: meets scope	**Participants**: Emergency department patients requiring blood culture samples (n = not reported). **Exclusions**: None reported. **Setting**: Emergency department in USA hospital. **Green**: meets scope	• Blood culture contamination rate • Length of stay • Antibiotic provision • Estimated associated impact on cost • Staff adherence **Green**: meets scope	Abstract with limited study details. Device not named in abstract, company submission indicates the device is Kurin Lock.
Burnie 2021 **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. **Aims**: to investigate the impact of introducing Kurin Lock on blood culture contamination rates. **Green**: meets scope	**Intervention**: Kurin Lock **Green**: meets scope	blood culture samples (n = not reported). **Exclusions**: None reported. **Setting**: Emergency department in USA hospital. **Green**: meets scope	• Estimated associated impact on costs **Green**: meets scope	Impact of BCC on length of stay and associated cost of admission reported, not results linked to Kurin Lock implementation. 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 **Location**: UK **Duration**: 5 months. **Aims**: to determine if the introduction of Kurin Lock reduces the number of contamination rates in an A&E department. **Green**: meets scope	**Design**: Before/after study. **Intervention**: Kurin Lock **Green**: meets scope	**Participants**: Emergency department patients requiring blood culture samples (n = 533). **Exclusions**: None reported. **Setting**: A&E department in NHS hospital. **Green**: meets scope	• Blood culture contamination rate • Estimated associated impact on costs **Green**: meets scope	Poster with limited study details.

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Ostwald 2021a Ostwald 2021b **Location**: USA **Duration**: 2 months (initial study period) and 3 months (second study period with revised device). **Aims**: to investigate the impact of introducing Kurin Lock on blood culture contamination rates in a paediatric emergency department. **Green**: meets scope	**Design**: Before/after study. **Intervention**: Kurin Lock **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). Exclusions: None reported. Setting: USA paediatric emergency department. **Green**: meets scope	• Blood culture contamination rate • Mean cost of recall or admission due to false positive blood culture • Estimated associated impact on costs **Green**: meets scope	Abstract and poster with supplementary information identified. Data extracted from poster with supplementary information. Downstream impacts such as reduced length of stay and antibiotic use mentioned, but not quantified. 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 **Location**: USA **Duration**: 3 months. **Aims**: to evaluate if a minimal-risk blood	**Design**: Before/after study. **Intervention**: Kurin Lock **Green**: meets scope	**Participants**: Emergency department patients requiring blood culture samples (n = not reported). **Exclusions**: None reported.	• Blood culture contamination rate • Estimated impact on associated costs **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. **Green**: meets scope		**Setting**: Emergency department in USA hospital. **Green**: meets scope		
Parsons 2023 **Location**: UK. **Duration**: Not reported. **Aims**: to determine if the introduction Kurin Lock will reduce the number of false positives in an emergency department. **Green**: meets scope	**Design**: Before/after study. **Intervention**: Kurin Lock **Green**: meets scope	**Participants**: Emergency department patients requiring blood culture samples (n = 464 samples). **Exclusions**: None reported. **Setting**: Emergency department in NHS hospital. **Green**: meets scope	• Blood culture contamination rate • Estimated impact on length of stay • Estimated associated impact on costs **Green**: meets scope	Poster with limited study details.
Rhew 2021 **Location**: USA. **Duration**: Not explicitly stated. Graphs suggest 1 year.	**Design**: Implementation study (before/after). **Intervention**: Kurin Lock (peripheral IV blood draws)	**Participants**: Emergency department patients requiring blood culture samples (n = not reported). **Exclusions**: None reported.	• Blood culture contamination rate **Green**: meets scope	Full text peer reviewed publication. 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. **Green**: meets scope	**Green**: meets scope	**Setting**: 4 USA emergency departments based in one integrated hospital system. **Green**: meets scope		Kurin lock was introduced as part of wider improvement measures at the same point in time.
Sutton 2018a Sutton 2018b **Location**: USA **Duration**: 9 months total (4 with intervention, 5 without). **Aims**: to investigate the efficacy of an engineered passive	**Design**: Before/after study. **Intervention**: Kurin Lock **Green**: meets scope	**Participants**: Emergency department patients requiring blood culture samples (n = 4220 samples). **Exclusions**: None reported. **Setting**: Phlebotomy and emergency department in single USA hospital. **Green**: meets scope	• Blood culture contamination rate • Estimated associated impact on costs **Green**: meets scope	Abstract and poster with supplementary information identified. 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. **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% • Annual average BCC rate pre-Kurin in 2016: 1.6% (99 contaminations) • BCC rate 3 months post-Kurin Lock in 2017: 0.8% (8 contaminations) Number of samples included in each rate calculation not reported.
Arenas 2021 (USA ED)	4030 samples included in total (device A and device B). At baseline, the emergency department had contamination rates of between 3% to 4.7%. <u>Device B (Kurin Lock) results</u> • BCC rate in control group: 5.2% (1293 samples) • BCC rate with Kurin Lock: 0.3% (1312 samples) • 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> • Standard procedure: 2.9% • With Kurin Lock: 1.9% p = 0.018 <u>Emergency department 1 BCC rates (1719 samples)</u> • Standard procedure: 1.4% • With Kurin Lock: 1.1% p = 0.57 <u>Emergency department 2 BCC rates (3942 samples)</u> • Pre-Kurin Lock: 3.5% • With Kurin Lock: 2.3% p = 0.024 BCC rates reduced by 1% overall, with a 34% relative reduction. 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) • BCC with Kurin Lock (381 samples included): 3.1% (3.19% in graph) • An overall relative reduction of 65.5%
Baxter 2020 (USA ED)	• BCC rate without Kurin Lock: 4.93% • BCC rate with Kurin Lock: 1.66% • Overall reduction in BCC rates of 66%.

Study (setting)	Blood culture contamination (BCC) rate
Burnie 2021 (USA ED)	BCC rate at baseline: • 2.92% in 2018 BCC rate with Kurin Lock: • 1.42% in 2019 • 1.51% in 2020 (48% improvement from 2018 rate) Introduction at a second site for 6 months (additional data, not associated with the original study period) • BCC rate at baseline: 4.96% • BCC rate with Kurin Lock: 1.6%
Hodson 2022 (UK A&E)	• BCC rate pre-Kurin Lock: 6% (1343 samples) • BCC rate with Kurin Lock: 1.9% (2% reported in text) (533 samples) Statistically significant difference between 2 rates, p=0.045
Ostwald 2021a **Ostwald 2021b** (USA Paediatric ED)	Retrospective analysis of BCC rates in department ranged from 0.45 to 5.63%. <u>First study period:</u> Overall BCC rate: 1.5% (stated by authors, figures suggest rate is 1.17%) • 0 instances of contamination observed in 303 samples drawn with Kurin Lock (0%) • 4 instances of contamination observed in 38 samples drawn without Kurin Lock (10.5%) p=0.0001, significant difference in BCC rate observed post-Kurin Lock introduction. <u>Second study period (modified tubing):</u> Overall BCC rate: 0.22% • 0 instances of contamination observed in 872 samples drawn with Kurin Lock (0%) • 2 instances of contamination observed in 33 samples drawn without Kurin Lock (6.06%) 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: • March 2017: 1.4% • February 2017: 1.6% • January 2017: 2.1% BCC rates in 3 most recent months where Kurin Lock was implemented: • June 2017: 0.4% • May 2017: 0.5% • April 2017: 0.4% 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). 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% • BCC rate with Kurin Lock: 2.6% • Overall reduction of 48%
Rhew 2021 (USA EDs)	*Monthly BCC rates for 4 hospitals not extracted from bar graphs, values not reported in text.* 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 **Sutton 2018b** (USA ED)	• Pre-intervention BCC rate (1953 samples): 0.025 (2.6%), 95% CI (0.019-0.033) • Post-Kurin Lock BCC rate (2267 samples): 0.012 (1.2%), 95% CI (0.008-0.017) 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) 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. 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 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. 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. 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 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. 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. 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) 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. 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 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 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.

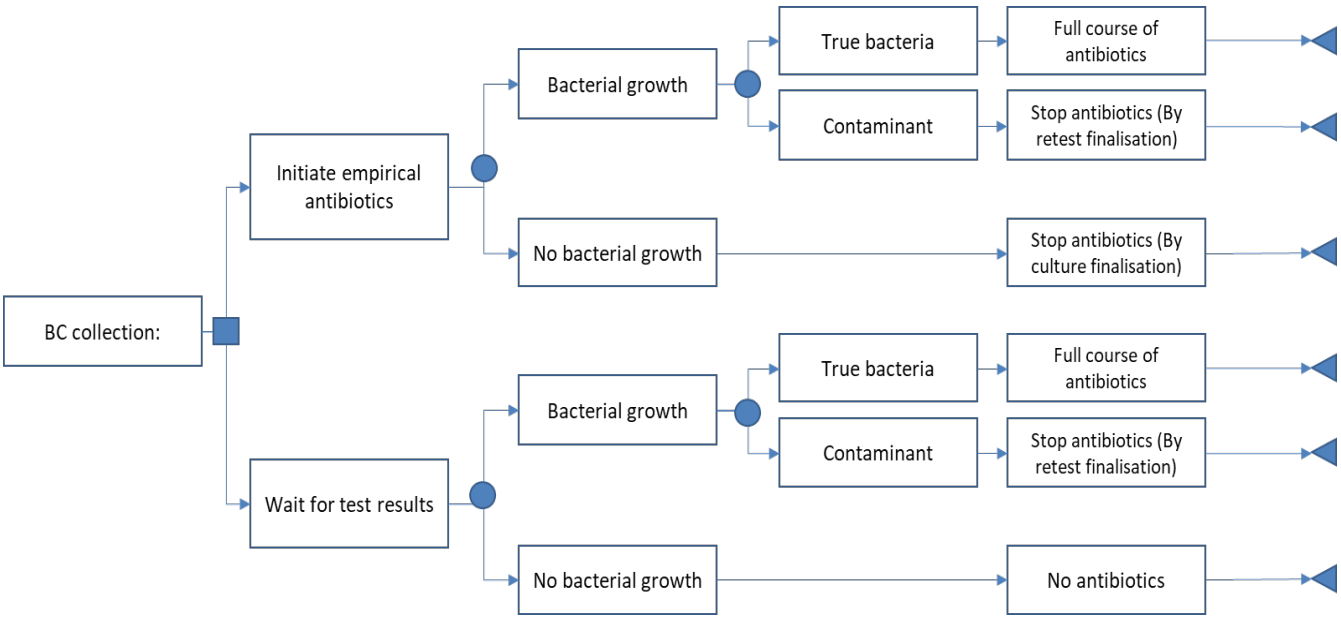

Figure 1 Economic model structure (taken from company model)

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. 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 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 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***.

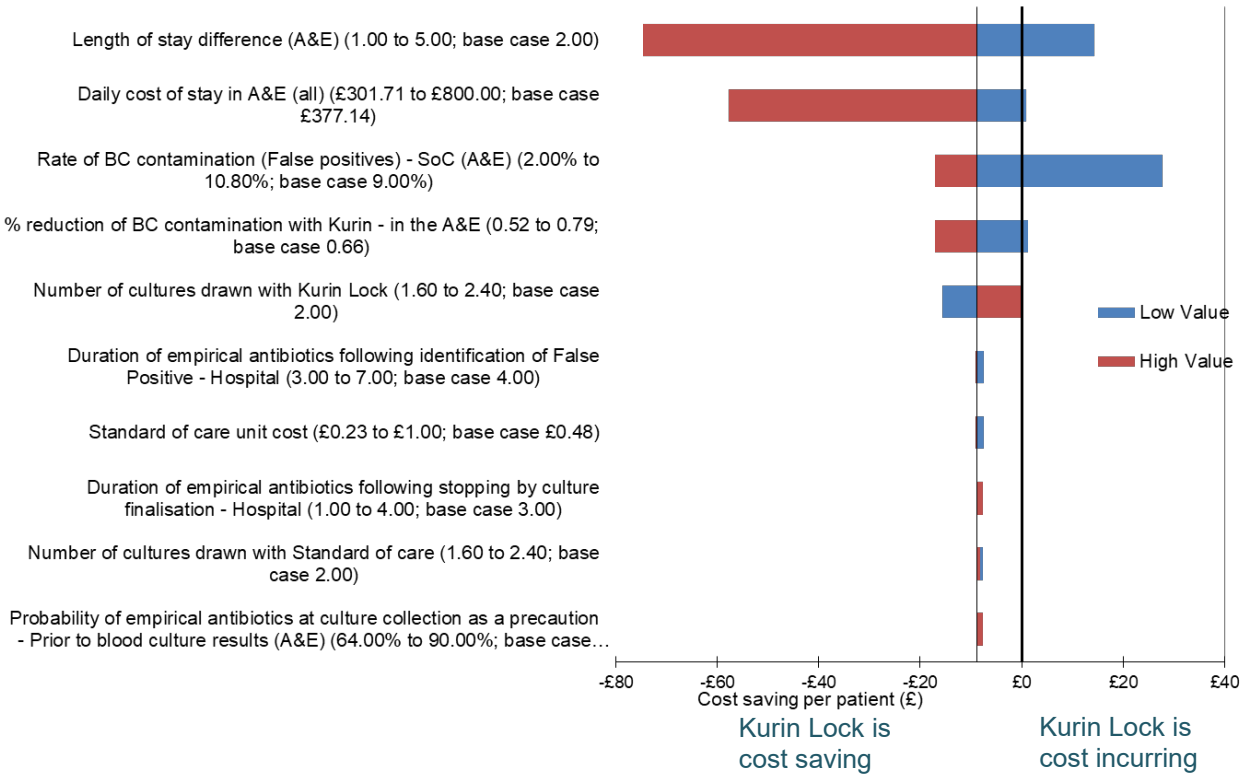

Figure 2 Tornado diagram for EAG base case, A&E setting

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 £880 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.

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17. Appendices

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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 CDSR CENTRAL	 0 29	
12/06/23	CRD (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

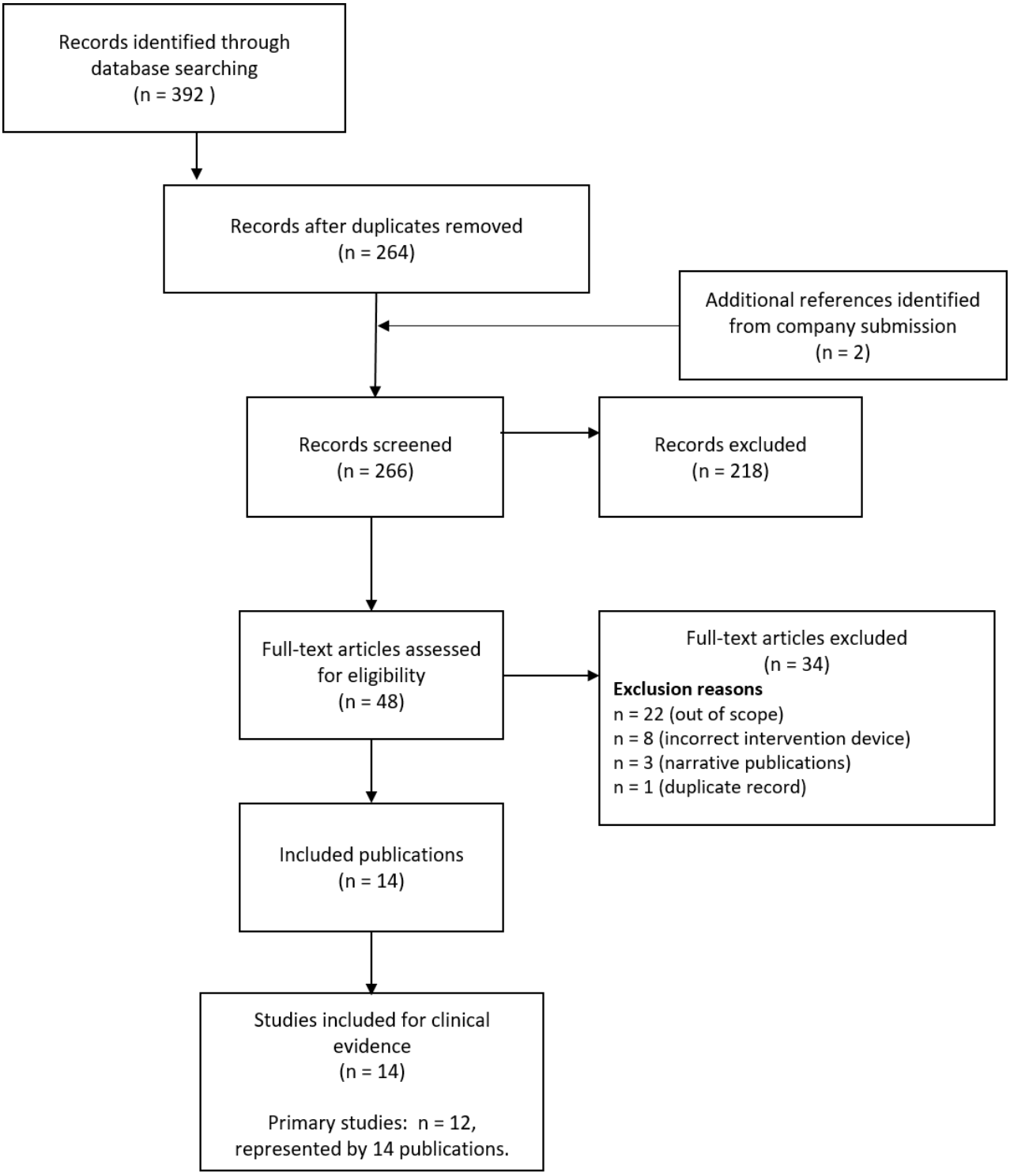
MHRA

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 (USA ED)	• Overall contamination rate from 2013-2016 ranged from 2.1% to 1.6% • Annual average BCC rate pre-Kurin in 2016: 1.6% • BCC rate 3 months post-Kurin Lock in 2017: 0.8% 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. • 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 (USA ED)	4030 samples included in total. At baseline, the emergency department had contamination rates of 3% to 4.7%. <u>Device A results</u> • BCC rate in control group: 2.2% (761 samples) • BCC rate with device A: 0% (664 samples) • 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) <u>Device B results</u> • BCC rate in control group: 5.2% (1293 samples) • BCC rate with Kurin Lock: 0.3% (1312 samples) • 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 (USA EDs)	Overall BCC rate (5661 samples) • Standard procedure: 2.9% • With Kurin Lock: 1.9% p = 0.018 Emergency department 1 BCC rates (1719 samples) • Standard procedure: 1.4% • With Kurin Lock: 1.1% p = 0.57 Emergency department 2 BCC rates (3942 samples) • Pre-Kurin Lock: 3.5% • With Kurin Lock: 2.3% p = 0.024 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 (UK A&E)	• Baseline BCC in emergency department: 9% (8.91% in graph) • BCC with Kurin Lock (381 samples included): 3.1% (3.19% stated in graph) • 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: • 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% • BCC rate with Kurin Lock: 1.66% • Overall reduction in BCC rates of 66%.	• Authors state 144 patients spared from receiving unnecessary antibiotics as a result of a false-positive BCC • 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: • 2.92% in 2018 BCC rate with Kurin Lock: • 1.42% in 2019 • 1.51% in 2020 (48% improvement from 2018 rate) Introduction at a second site for 6 months (additional data, not associated with the original study period) • BCC rate at baseline:4.96% • 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) • 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 (UK A&E)	• BCC rate pre-Kurin Lock: 6% (1343 samples) • BCC rate with Kurin Lock: 1.9% (2% reported in text) (533 samples) 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 **Ostwald 2021b** (USA Paediatric ED)	Retrospective analysis of BCC rates in department ranged from 0.45 to 5.63%. <u>First study period:</u> Overall BCC rate: 1.5% (stated by authors, figures suggest rate is 1.17%) • 0 instances of contamination observed in 303 samples drawn with Kurin Lock (0%) • 4 instances of contamination observed in 38 samples drawn without Kurin Lock (10.5%) p=0.0001, significant difference in BCC rate observed post-Kurin Lock introduction. <u>Second study period (modified tubing):</u> Overall BCC rate: 0.22% • 0 instances of contamination observed in 872 samples drawn with Kurin Lock (0%) • 2 instances of contamination observed in 33 samples drawn without Kurin Lock (6.06%) 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) • 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: • 45% of nurses found the device to be easy to use • 85% of nurses said the device made sense 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: • March 2017: 1.4% • February 2017: 1.6% • January 2017: 2.1% BCC rates in 3 most recent months where Kurin Lock was implemented: • June 2017: 0.4% • May 2017: 0.5% • April 2017: 0.4% 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). 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. • Above calculated on how many BCC events occurred during 3 months without Kurin Lock and 3 months with Kurin Lock: <u>Without Kurin Lock</u> – March 2017: 20 – February 2017: 24 – January 2017: 33 <u>With Kurin Lock</u> – June 2017: 4 – May 2017: 5 – 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% • BCC rate with Kurin Lock: 2.6% • 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.* 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: • Visibility of data – for all staff • Visibility of resources • Using workshops, sills fairs and educational material • Clear objectives and expectations • Communications – encouraging collaboration
Sutton 2018a **Sutton 2018b** (USA ED)	• Pre-intervention BCC rate (1953 samples): 0.025 (2.6%), 95% CI (0.019-0.033) • Post-Kurin Lock BCC rate (2267 samples): 0.012 (1.2%), 95% CI (0.008-0.017) 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: • Costs associated with BCC pre-intervention: $814,512 • 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 (£[redacted] to £[redacted]; 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 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 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 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