National Institute for Health and Care Excellence

Medical technologies evaluation programme

MT390 PICO negative pressure wound dressings for closed surgical incisions

Consultation comments table

Final guidance MTAC date: 22 February 2019

There were 30 consultation comments (1 duplicate) from 3 consultees:

- 1 NHS professional (n=7 including 1 duplicate)
- 1 manufacturer (sponsor) (n=1)
- 1 manufacturer (other) (n=22)

The comments are reproduced in full, including in the following themes:

Appendices included:

#	Consultee ID	Role	Section	Comments	NICE/EAC response
Theme 1: draft recommendations					
1	2	Healthcare Other	Page 3 Section 1.2	It would be helpful if you could please clarify what is meant by 'low amounts of exudate' particularly as we believe that exudate volumes may have an impact on the size of dressing used and the consequential costs.	Thank you for your comment. The committee acknowledged that the guidance did not specify the level of exudate and noted that the EAC did not identify any evidence on the assessment of levels of exudate. Clinical experts advised that there is no measure available that could be used to define the levels of exudate in practice, and one expert noted that the level of exudate could vary by different surgical wounds. Experts agreed that PICO should only be used for people with closed surgical incisions, and PICO should not be used for any open wound or wounds that are expected to require multiple dressing changes. The committee decided to make a minor amendment to the guidance to clarify that the use of PICO is only for people with closed surgical incisions and when multiple wound changes are not anticipated.
2	2	Healthcare Other	Page 10 Section 4.4	We are uncertain how the recommendation that PICO is suitable for all types of surgery can be reconciled with the committee's conclusion that the 'type of surgery' was an important factor in selecting people for PICO dressings, particularly as the statistically significant reductions in SSI were only seen when PICO was used in orthopaedic and obstetric surgery. We believe it would be helpful if the guidance were to explain more fully how, given that the evidence was believed to be too limited to make recommendations for use of a PICO dressing by	Thank you for your comment. The committee considered your comment carefully and concluded that the recommendation should be based on the pooled estimated treatment effect of PICO for preventing surgical site complications across a range of surgical specialities. The effectiveness of PICO dressings was not detected by individual specialities due to the small number of studies for the different specialities and the robustness of the evidence related to individual surgery type is less certain. Section 3.6 summarises the committee's considerations on the limitations of the evidence. The committee decided not to change the guidance.

				individual surgery type, the recommendation in para 1.2 has been made.	
3	2	Healthcare Other	Page 12 Section 4.8	We agree that training in the application and management of NPWT dressings is very important and wonder if this should be referenced in the recommendations.	Thank you for your comment. The committee's considerations on training are summarised in section 4.9. The committee considered your comment carefully and decided not to change the recommendations in section 1.
Theme 2: Patient selection and indication					
4	1	NHS professional	General	1. Needs to be stated in the first sentence that this is for closed surgical wounds only	Thank you for your comment. The first sentence in section 4.3 has been amended to state that PICO is for closed surgical incisions.
5	1	NHS professional	General	The experts also explained that PICO dressings should only be used for closed surgical incisions, and not as a treatment for open surgical wounds we also use PICO successfully on minor dehiscence in higher risk patients to aid in preventing further dehiscence. This can be cost effective in terms of time and length of stay. They state that the focus of the guidance is for closed incision management but it could still be used where appropriate on dehisced wounds with minimal depth and low exudate.	Thank you for your comment. Thank you for sharing your experience of the use of PICO dressings at preventing dehiscence in high risk patients with open surgical wounds. The committee agreed that PICO dressings should only be used for people with closed surgery incisions, and not as a treatment for open surgical wounds which are contraindicated. The use of PICO for other types of wound is not in the scope of the guidance.
6	1	NHS professional	General	Careful patient selection is important and should be informed by NICE guidance I think this is the crux of it. Whilst there is a core of high risk factors E.G obesity and diabetes there are specific factors for specific types of surgery e.g use of bilateral IMA in cardiac patients. Who makes the decisions to use or not to use? Could end up with over or under use, seems like a bit of a lottery.	Thank you for your comment. The committee considered your comment carefully and concluded that the decision to use PICO dressings should be based on the clinician's assessment of a patient's risk factors and the type of wound. Clinical experts agreed that the lead surgeon would make the decision at the time of wound closure. This has been noted in the committee discussion in section 4.2, and the committee decided not to change the guidance.

7	2	Healthcare Other	Page 9 Section 4.2	We note the committee's statement that they recognised many of the studies did not explicitly state the definition of high risk. Whilst we agree with the committee that all patients' risk of SSI should be assessed prior to surgery we believe that the lack of clarity about what constituted high-risk patients in the evaluated studies once again undermines the claimed reduction in SSI across all surgical specialties. We would like to suggest that the Sponsor is asked to provide additional data, perhaps using sub-sets, where the population who were treated with PICO, as well as those receiving standard care, can clearly be shown to meet accepted definitions of being at high risk of SSI e.g. those published by PHE.	Thank you for your comment. The committee agreed that good quality data on the use of PICO by patients' risk stratification would strengthen the evidence base for case selection for PICO dressings, but this data was not presented in the company's submission.
8	2	Healthcare Other	Page 10 Section 4.3	We understand why clinical experts have advised that PICO dressings should only be used for surgical incisions in which the amount of exudate was anticipated to be low. We have not seen any definition of what constitutes a 'low' amount of exudate and information about whether the patients in the trials included in this assessment had wounds with low exudate levels appears to be lacking from the evidence presented. We would like to suggest that a value should be given in the guidance to define the 'low amounts of exudate' that PICO can absorb as this may influence the choice and numbers of dressings used, which ultimately may impact upon costs.	Thank you for your comment. Please see the response to comment 1.
Theme 3: Technology description					
9	2	Healthcare Other	Page 4 Section 2	Section 2 - Technology It is not clear whether your recommendations apply to PICO 7 or earlier versions of this technology. As there do not appear to have been any published	Thank you for your comment. The committee considered your comment carefully and acknowledged that this guidance and its recommendations were

				studies relating to PICO 7/7Y included in this evaluation, and therefore no data about clinical or cost effectiveness is available, we assume they are not part of your recommendations.	for PICO dressings. As there are newer versions of PICO dressings available in the NHS, the committee decided to amend the guidance to further clarify the generalisability of evidence on the PICO device to the latest PICO dressings because the functional mechanism of dressings remains the same despite an improvement in pump design of the device.
10	2	Healthcare Other	Page 4 Section 2	Section 2 - Innovative Aspects We recognise that PICO is different from other negative pressure technologies, in that it does not have a canister and is therefore most likely only to be suitable for wounds with low exudate levels. We would question whether PICO's claims to be innovative due to its portability and use of a propriety dressing layer can be substantiated as there are other products available on the UK market which offer these benefits.	Thank you for your comment. The committee considered your comment carefully and, based on expert advice, concluded that PICO was innovative in terms of its design of dressing layers and portability compared to other negative pressure wound dressings. The committee decided not to change the guidance.
11	2	Healthcare Other	Page 4 Section 2	Section 2 - Intended Use We note the suggestion that PICO can be used in hospitals, communities and homes. We have not seen any evidence presented by the sponsor of its use in non-hospital settings, other than its community use in a single study focussed entirely upon colorectal surgery (Tanner 2009). We are uncertain if this suggestion can therefore be confirmed.	Thank you for your comment. The committee acknowledged that PICO dressings could be used in both secondary and primary care settings, but the evidence in the guidance was on the use of PICO dressing in secondary and tertiary care. The EAC did not identify any evidence on the use of PICO in primary care. The committee decided to make a minor amendment to section 3.1 to clarify all evidence in the guidance was for the use of PICO in secondary and tertiary care.
Theme 4: Critique of the evidence					
12	2	Healthcare Other	General	We feel it is unclear whether all of the evidence cited is relevant to the scope. This view is partly driven by comments made by both the EAC and clinical experts about the robustness of some of the studies included in the evidence review, as well as the comments about different approaches to risk assessment. These included comments such	Thank you for your comment. The committee discussed your comment carefully and the EAC confirmed that all included studies were relevant to the population, intervention, comparators and outcomes defined in the decision problem. The EAC noted that the evidence on risk profiles of study populations was weak due to a lack of data at the individual patient level, but the treatment effect was

				as ‘methodologically weak’, ‘poorly reported’ ‘population unlikely to be at high risk of SSI’. These comments have led us to question whether some of the assumptions made during the evaluation are sufficiently robust to support the recommendations made. We are unsure how the EAC and committee concluded that results from 8 RCTs and 11 observational studies, even when included in the meta-analysis, provided sufficient evidence of PICO’s ability to reduce the rate of SSIs for all types of surgery as we cannot see how these conclusions have been mapped back to the population included in the scope you issued (Patients with low to moderate levels of exudate in patients considered to be at high risk of SSC). We would like to bring your attention to a recently published paper that we believe, as a prospective RCT using PICO iNPWT in the care of orthopaedic patients, provides new evidence that you may wish to share with the committee. https://doi.org/10.1016/j.arth.2018.12.008 Whilst this study found some soft tissue benefits in the use of iNPWT, many of these were not significant. Interestingly no significant difference was found between the use PICO iNPWT and SOC dressing in the rate of either superficial (1.6% vs 2.3%, P 1â„4 .74) or deep (2.7% vs 2.8%, P 1â„4 .76) wound infection following lower extremity TJA’	consistently showing overall superiority of PICO dressings over standard surgical dressings in a wide range of surgical specialities. The EAC confirmed that all studies included patients with at least one risk factor associated with SSCs. Thank you for notification of the newly published paper. Preliminary results of this study (Keeney 2018) have been previously included in the EAC’s assessment report as academic in confidence (Stannard et al unpublished - NCT02064270). A critical appraisal of the full-text publication from Keeney 2018 was carried out by the EAC (see Appendix 2). The EAC added the additional data to the meta-analysis for surgical site infection, showing the OR of all 20 studies included in the analysis is 0.40 (95%CI 0.27 to 0.61, p<0.0001). Overall effect for SSIs based on 9 RCTs was 0.56 (95%CI 0.36-0.89), p=0.01. Both these results are in accordance with what the EAC reported in the meta-analysis based on 19 studies in the EAC assessment report. The committee discussed the new evidence and concluded that it did not change its overall conclusions on the effectiveness of PICO dressings. The committee therefore decided not to change the guidance.
13	2	Healthcare Other	Page 6 Section 3.5	We note the comments that statistical significance relating to the reductions in the rate of surgical site infection with PICO were only demonstrated in obstetric and orthopaedic surgery.	Thank you for your comment. The committee acknowledged that additional data on the use of PICO in different surgical specialities would strengthen the evidence base for the effectiveness of PICO. It was agreed that

				We would like to suggest that the Sponsor should be asked to provide additional evidence of the effectiveness of their product in the other speciality areas before such an all-encompassing recommendation is made suggesting that PICO should be considered in people who are at high risk of developing an SSI	recommendations were made based on the best available evidence. The sponsor stated that the additional data is not currently available.
14	1	NHS professional	General	2. Funders of the trials needs clearly stating I suspect that these are in the main funded by Smith and Nephew -I don't think that this is apparent in this write	Thank you for your comment. The EAC confirmed that conflicts of interest and funding sources were stated in the critical appraisal of included studies in section 3.3 of the EAC assessment report. The EAC assessment report was presented to the committee as supporting documentation when considering the draft consultation document and was available during the public consultation.
15	2	Healthcare Other	Page 5 Section 3.1	We are confused by the statement that the 15 RCTs were based on 'preventing surgical site complications in people with closed surgical incisions who were at high risk of complications after surgery'. Firstly, the EAC references 13 RCTs and included data for 11 in their report. Having carefully reviewed the referenced evidence and particularly the patient and procedure characteristics included in Table 5 of the EAC report we have been unable to confirm your statement about all patients being in a high-risk category. We note the known risk factors (based on the PHE annual SSI audit and WUWHS consensus documents) and have looked at these in the relevant studies: We have identified those occasions when declared risk factors achieve levels that equate to high risk of SSI with an asterisk, whilst noting that these are mean values and therefore will not apply to all patients.	Thank you for your comment. The EAC confirmed that evidence from 15 RCTs was considered in the assessment report. One of the RCTs was submitted as preliminary academic in confidence evidence and 3 other studies were available as abstracts only. Therefore only 11 published studies were included in the meta-analysis. The EAC confirmed that most of the evidence submitted meets the definition of a high-risk population for developing SSCs as defined by the WUWHS consensus document. Guidance on the management of closed surgical incisions is provided by both national and international guidelines, but there is local variation, especially on the categorisation of patients as high-risk. It should also be noted that there is significant variability between international and national guidelines with regards to the applied thresholds for most of these factors. The EAC noted that both the PHE and the WUWHS guidelines report also procedure-related factors not just patient-related factors as contributing to the high-risk profile. The EAC provided the committee with the following details of the risk profiles of the individual study populations:

				The data presented does not make it possible to determine whether some of the patients in the studies with high-risk factors have only one of these or whether they overlap, which increases the likelihood of some patients not being part of a high-risk group. Chaboyer Mean age =30.6, Mean BMI= 36.2*, % diabetic=28.8*, % Smokers=14.9*, ASA = not reported Galiano Mean age =35.7, Mean BMI= 30*, % diabetic=3*, % Smokers=5*, ASA = 3.5% â‰¥ 3 Tanaydin Mean age =40.9, Mean BMI= 26.5, % diabetic=0, % Smokers=6.25*, ASA = not reported Gillespie Mean age =63.2, Mean BMI= 29.9, % diabetic=NR, % Smokers=NR, ASA = 38.6%* â‰¥ 3 Svensson Mean age =71.3*, Mean BMI= 27.5, % diabetic=24.2*, % Smokers=33.3*, ASA = not reported Uchino Mean age =48.1, Mean BMI= 20, % diabetic=24.2*, % Smokers=0, ASA = 5%* â‰¥ 3 Hyldig Mean age =32, Mean BMI= 34.7*, % diabetic=17.8*, % Smokers=7.6*, ASA = not reported Karlakki Mean age =69*, Mean BMI= 30.1*, % diabetic=8.1*, % Smokers=22*, ASA = 10.5%* â‰¥ 3 Nordmeyer Mean age =52.3, Mean BMI= NR, % diabetic=NR, % Smokers=NR, ASA = NR% â‰¥ 3 O'Leary Mean age =58, BMI >30= 35*, % diabetic=12.2*, % Smokers=18.4*, ASA = Median = 2	Chaboyer: C-section in women with BMI≥30 is regarded as a high-risk procedure. 69% of patients had at least 1 co-morbidity (including diabetes, hypertension, smoking). 89% had had at least 1 previous C-section. Galiano: The study compares data for lower vs. higher BMI and breast tissue resection weight (increased BMI and tissue weight are associated with higher risk of wound complication). 80.4% of patient had BMI≥25. Tanaydin: The authors state that they "selected bilateral reduction mammoplasty patients who are at risk for postoperative wound complications", however it is unclear how the patients were categorised as such. Gillespie: Arthroplasty is a high-risk procedure. 94% of patients were grade 2 or 3 on the ASA scores i.e. had at least 1 comorbidity (e.g. diabetes, smoking, hypertension). Svensson: Among other patient related factors, abdominal surgery is regarded as a high-risk procedure. Uchino: Ileostomy closure is considered a high-risk procedure based on the WUWHS guidelines. Hyldig: C-section in women with BMI≥30 is regarded as a high-risk procedure. Karlakki: The main author was contacted and confirmed that all patients were high risk. Nordmeyer: Among other patient related factors the procedure is considered as high risk based on the WUWHS guidelines. O'Leary: Among other patient related factors the procedure is considered as high risk based on the WUWHS guidelines. Witt: Among other patient related factors the duration (>2 hours) of the surgical procedure is listed by the authors as a high-risk factor. The EAC noted that most studies included patients at risk of developing SSIs, but there is a lack of patient level data to estimate PICO treatment effect by risk stratification. Table 8 in the EAC's assessment report provides a full overview of the methodological qualities of each included study. The committee made the recommendations based on the best available evidence for the use of PICO dressings, and decided not to change the guidance.

				Witt Mean age =64.2, Mean BMI= 29.2, % diabetic=25*, % Smokers=33.8*, ASA = not reported Whilst we recognise that factors such as diabetes, age and BMI may have led to some patients in these studies falling into a 'high risk' category we are unaware of separate reporting of their surgical wound status, which may have contributed valuable data about PICO's true ability to reduce SSC. Having looked at all of the data contained in your documentation, we continue to struggle to understand how the claim that all the patients in these studies were at high risk of complications has been made.	
16	2	Healthcare Other	Page 5 Section 3.2	We are unclear how the EAC and committee have concluded that the RCT evidence shows fewer surgical site infections with PICO compared with standard wound dressings. Our uncertainty is influenced by the fact that the EAC stated only 5 of the 13 RCTs had sufficient power, and of these studies only Hyldig, showed statistical significance for reduction in SSI (cSection), Galiano for Dehiscence (Mammoplasty) and Karlakki for wound complications (Hip/Knee Arthroscopy). We understand that the EAC used 8 RCTs, and not simply the 5 with sufficient power in their own right, in the random effects metanalysis they ran. Whilst we recognise the value of this type of metanalysis in circumstances such as these, given that the studies included only C-Section, Hip and Knee Arthroscopy, CABG, laparotomy, ileostomy and mammoplasty, only 2 of which undertook any emergency procedures, we feel that the statement in para 3.2 'which showed a significant reduction in SSI	Thank you for your comment. The EAC identified and included the best available evidence on the use of PICO in a range of surgical specialities. All studies met the inclusion criteria in terms of population, intervention, comparator and outcome that were set out in the scope document. The meta-analysis was used for combining data from multiple studies to estimate the treatment effect of PICO dressings, assessing whether there was variation or consistency in the effect across different studies. Studies included in the meta-analysis may vary by quality, but statistical and clinical heterogeneity of studies were considered as the EAC used a random-effects model rather a fixed-effect model in the meta-analysis. Meta-analysis included a range of different types of surgery, which are specified in the section 3.5. The committee decided not to change the guidance.

				rates across all types of surgery' is overly strong and are unconvinced by statements of transferability. We would like to suggest that this statement should be altered so that it references only those specialties included in the meta-analysis as well as highlighting that the majority were elective procedures. We also note that prediction intervals were not used which, we believe is more usual with this type of meta-analysis and wonder why this was the case?	
17	2	Healthcare Other	Page 5 Section 3.3	We are surprised that as the EAC recognised the observational studies included in their meta-analysis may have overestimated the clinical benefits of PICO dressings they felt they could conclude that PICO was superior. We are unclear to what extent the fact that at least 2 of the studies in the meta-analysis did not draw a representative sample from the relevant population (Dingemans and Matsumoto) was taken into account and impacted upon the analysis. In addition, we would welcome clarity about why since 3 other studies (Van Der Valk, Hickson and Holt) did not assess outcomes using objective criteria or blinding they were still included in this analysis. We are concerned that all of these factors may have unduly influenced the data included in this meta-analysis and that the EAC conclusions may be invalid.	Thank you for your comment. The EAC confirmed that the meta-analyses for RCTs and observational studies were run and reported separately. Dingemans 2018 and Matsumoto 2014 were non-randomised studies and were included in the meta-analysis for observational studies. Van Der Valk 2017, Hickson 2015 and Holt 2015 were also included in the meta-analysis for observational studies but not for RCT studies. All these studies met inclusion criteria defined in the scope document and provided data on the rate of SSI. The EAC confirmed that the meta-analysis included both RCTs and observational studies but did not include any studies that were lacking enough information to ascertain methodological quality (such as those published as conference abstracts only). The EAC advised that subgroup analysis based on possible bias criteria was not carried out as frequently high bias emerges from poor reporting rather than poor study design. Also it is not possible to confidently estimate the direction of the bias.
18	2	Healthcare Other	Page Section 3.4	It is unclear which of the RCTs and observational studies were used by the EAC to evaluate seroma rates. This is of particular concern to us given the issues about some of the observational studies in particular.	Thank you for comment. The studies evaluating the rate of seroma were listed in table 8 in the EAC's assessment report. The included studies were 2 RCTs (Galiano 2008; Gillespire 2018) and 5 observational studies

				We would welcome clarity about which studies were used please.	(Fleming 2017, Pellino 2014a [colorectal], Pellino 2014a [breast]; Pellino 2014b, Selvaggi 2014) compared seroma rates between PICO and control groups.
19	2	Healthcare Other	Page 7 Section 3.6	We remain concerned by the small number of studies, and often small numbers of patients in these studies, that have been presented by the sponsor with an expectation that this evidence demonstrates statistical significance across all patients once included in a random effect meta-analysis. Our concern is once again influenced by our uncertainty that, as described by the EAC, the distribution rates of high-risk factors amongst many study participants was unclear as well as the wide variation is seen in the definitions of surgical site infections, how long the dressing was in place and the length of follow-up Given that use of PICO for high-risk patients are specifically recommended in the draft guidance we are unclear about the robustness of the sources used to develop this recommendation.	Thank you for your comment. The committee considered your comment carefully and the EAC advised that a total of 29 studies met inclusion criteria for the guidance including 15 RCTs. Of the included studies, sample size varied. The EAC critically appraised the included studies and considered the evidence on the efficacy of PICO was adequate and robust in a range of surgery. The committee concluded that the recommendations were based on the best available evidence on PICO in different surgical specialities and decided not to change the guidance.
Theme 5: Cost modelling					
20	1	NHS professional	General	I think we should express concern that neither of the cost models included clinical time for dressing change (see point 4.12) . We know that for other types of wound care, nursing time is the largest cost of care by far so this omission seems surprising, especially since the report notes that there are training needs for this intervention. Including staff costs and training costs might easily wipe out the calculation of a Â£6 per patient saving.	Thank you for your comment. The committee considered your comment carefully and discussed the impact on staff time when applying PICO dressings. The expert suggested that it took 10 minutes to teach how to apply the dressing, and an additional 2 or 3 minutes to apply PICO dressings compared with standard dressings. Therefore, the committee concluded that additional staff costs were to be negligible based on experts' clinical experience and decided not to change the guidance.
21	2	Healthcare Other	Page 4 Section 2	Section 2 - Costs There appear to be inconsistencies in the costings and parameters used to demonstrate the cost savings included in this draft guidance. For example, the use of weightings has not been applied	Thank you for your comment. The EAC made changes to the cost model presented in the sponsor's submission. This included weighting the costs in different surgical areas according to the number of procedures

				consistently throughout the cost modelling by both the sponsor and EAC. We are uncertain that the costs included in the adjusted model from EAC have taken into account the variation of the complexity of surgery in each of the surgical specialities. For this reason we do not believe that any claim of extra clinical benefit can be delivered at a similar overall costs. The use of dressing size is unclear in â€˜cohort of surgery and indications'. Therefore, it is uncertain if the averaging of all three costs for PICO is the appropriate methodology to use. It may be useful to look at a weighted average across the 3 dressing packs as a way to allocate costs. The Standard of Care (SOC) dressing items and costs, does not seem to reflect the current standards in terms of NHS treatment. This was picked up in the external expert reviews sought by NICE during this process. As NICE have already reviewed the S&N PICO product during the MIB149 (Medical Innovation Briefing) process, there has already been a precendence set in terms of SOC within the NHS. It is our understanding, from the costing model used, that EAC found some inconsistencies in terms of application. After reviewing the table used in the sponsors submission â€˜Table 19 1, Conversion of median to mean SSI cost from Jenks 2014 [18]' true page 459/sponsor section page 250. It would appear the application of the formula by Hozo 2005, has been applied incorrectly in several sections. This is referenced in more detail in our comments on section 4.10 of this response.	reported in Jenks 2014. The EAC considered that an estimate of the overall cost impact of PICO should reflect the differing volumes across different procedures. The EAC considered the cost included in the model reflects the variation of the complexity of each surgery. The impact of surgical complexity on the prevalence and cost of SSI is reflected in the data reported in Jenks (2014). In Jenks 2014 a patient record (episode) was defined as a surgical procedure with postoperative follow-up, including readmission, terminated by another surgical procedure or a lapse of 12 months. The incidence or rate of SSI was defined as the number of SSIs per 100 operations for each surgical category. All individual patient costs were accounted for by the hospital's accounting and activity systems, and included all non-duplicated costs associated with staff, diagnosis and other activities, consumables and overheads attributable to each individual episode. The EAC retained the sponsor's assumption regarding the cost of PICO. The EAC explained that the price was determined from list prices for different pack sizes combined with sales volumes and is therefore a weighted average. The EAC does not have access to sales volume data from the sponsor. The EAC assumed a standard dressing cost £2.50, based on a weighted average cost of foam dressings, and would be changed every three days. The EAC understands that there is considerable variation in practice regarding number of dressing changes and products used. The EAC subjected the cost of the comparator (the standard dressing) to sensitivity analysis and found that the cost results were not sensitive to the changes. The EAC advised that the application of the formula reported by Hozo (2005) to convert medians to means was an acceptable approach in the absence of data to calculate the mean. The EAC was able to calculate means directly from the source data in Jenks (2014). The EAC notes that the means calculated were very similar to the medians derived from the formula in Hozo (2005). It is inappropriate to estimate means from medians when the mean can be calculated from the source data. The EAC

					updated the sponsor's cost model to incorporate actual rather than estimated means. The overall impact of this change was considered small.
22	2	Healthcare Other	Page 8 Section 3.9	It is encouraging to see that the use of â€˜primary care cost data' has been used from one study to help ensure the full patient pathway is understood. We are uncertain though why it was felt appropriate to apply the 15% figure from the Tanner (2009) study across the 19 surgical areas within both the sponsor and EAC calculations. This is because the Tanner (2009) study is based solely on Colorectal surgery, as well as being described as 'an important specialty to study since it is considered to have the highest SSI rates and is among the most expensive to treat'. Having also reviewed the inclusion of the index of primary care and NHS improvement reference costs, these confirmed that colorectal costs are higher and therefore require a more significant use of resource such as district nursing. We do not agree therefore that the general logic of applying 15% across all surgical interventions in this submission is valid, as it distorts the results. Jenks (2014) also confirmed that there are cost and resource differences between the 19 specialty areas, reaffirming the fact that Colorectal surgery is the highest cost to any healthcare setting by a significant margin. Given that the use of weighted averages has been consistently applied throughout the submission and evaluation process, we are surprised that a weighting of costs in primary care has not been spread across each surgical intervention in the same way. We would urge that an appropriate weighting is applied in this part of the model, as this approach would be more reflective of the way costs are calculated in the NHS.	Thank you for your comment. The committee discussed your comment carefully. The EAC advised that they did not identify any data source that is superior to that reported in Tanner (2009) and used the best available data to estimate the primary care cost for SSIs. The committee decided not to change the guidance.

				A further reason for us suggesting that the cost statement requires attention is that the â€˜PHE 2017-18 report' referenced by both the sponsor and EAC, shows large bowel (Colorectal surgery) as having the highest dirty wound and SSI rate of 8.7%, vs the lowest of Orthopaedic at 0.2%. (Please see page 19). In other words, as the model stands, the use of the 15% uplift has been applied to all specialites, whilst it is known that the SSI rates are as low as 0.2% for Orthopaedic. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/765967/SSI_annual_report_NHS_hospitals_2017_18.pdf	
23	2	Healthcare Other	Page 8 Section 3.1	Having carefully reviewed the costs used for both PICO and standard dressings we were surprised to see that an average cost of Â£2.50 has been used to reflect the price of a standard dressing. We are surprised because the NICE approved MIB 149 (PICO) used an average price of 80p for standard dressings, basing this on the three dressings Tegaderm, Mepore and Opsite, two of which were referred to by the committee experts. We are not certain that inclusion of all foam dressings to produce the average dressing cost included in the model is appropriate as it is our understanding that these are more likely to be used for patients with higher levels of exudate. Also most foam dressings will be applied when a SSC & SSI is identified. We note the committee experts referenced other dressings as possible alternatives (Aquacel Â£1.34), but recognise the main standard as those listed in the PICO MIB 149 guidance. We would like to suggest that the average cost of standard dressings used in the model reflects that of	Thank you for your comment. The committee discussed your comment carefully and noted that the EAC retained the sponsor's assumption that the cost of a standard dressing would be £2.50. This was based on a weighted average cost of foam dressings. The committee were advised that the EAC undertook sensitivity analysis on the cost of the standard dressing and found this parameter had little impact on the overall cost difference between PICO and standard dressings. The EAC notes that the costs of PICO, and the potential cost savings from reducing SSI, are considerably higher than the cost of the standard dressing. The committee decided not to change the guidance.

				current clinical practice and draws upon those figures NICE published in MIB 149.	
24	2	Healthcare Other	Page 13 Section 4.1	It is clear that the sponsors parameters and inputs to their costing model has been accepted by both the EAC, NICE committee. We welcome the extension of the treatment areas from the proposed 7 to the full 19 by the EAC that includes data from Jenks 2014 and Tanner 2009. However, after reviewing in more detail in the sponsors submission â€˜Table 19 1, Conversion of median to mean SSI cost from Jenks 2014 [18]' true page 459/sponsor section page 250. It would appear that the process of converting from Median to Mean has been applied incorrectly according to the process used in the Hozo 2005 study This is due to 2 reasons:- â€¢ The Tanner 2009 study had already used a mean to present their findings, therefore the application of the HOZO formula (by the Sponsor and EAC) to the Tanner figure was invalid and had the effect of inflating the SSI costs. [The total additional cost incurred by the 29 patients with SSI was Â£305,173, with a mean cost of Â£10,523 per patient (Table IV)] page 3 â€“ Cost of SSIs section and not a Median as referenced in the larger Jenks 2014 study. Given this significant error in the model we believe these figures should be recalculated, especially as the level of cost savings applied have already fallen from Â£101(Sponsor supplied) to Â£6(EAC) following the EACs existing model improvements.	Thank you for your comment. The EAC stated that the sponsor used a formula from Holz (2005) to convert median cost to mean cost of SSIs, while the EAC calculated the cost of SSIs by dividing the total cost of SSIs by the number of SSIs. Although different methods were used, the estimated SSI costs were similar. The committee decided not to change the guidance.

				â€¢ Also the Hozo 2005 calculation requires the sample size to be taken into account, with 25 being a cut off point for the relevant formula to be applied. This should also be reviewed again by the EAC and recalculated and applied to the overall saving for PICO dressing.	
25	2	Healthcare Other	Page 13 Section 4.11	It is disappointing that the sponsor is unable to provide evidence on the use of PICO, as a weighted average would be more appropriate to calculate the costs for the model. Maybe with additional data this can be obtained, to support the committee members.	Thank you for your comment. The committee acknowledged and agreed that more real-world data would provide more robust evidence on the cost-effectiveness of using PICO dressings in practice. The cost of the technology in the cost model was based on a weighted average of sales volume, the detailed breakdown of which not presented by the sponsor.
26	3	Healthcare Other	General	The current draft recommendations outlined in the consultation document offers a sound and reasonable basis for the use of PICO within the NHS. Additional details reflecting product particulars are satisfactory, however there are a few inaccuracies I would like to highlight in relation to the clinical and economic interpretations and evaluations. Page 8/15 (3.8 in text) it states "the company's cost model only included people at high risk...". This is not correct, we considered all patients undergoing surgery without risk stratification and considered different risk groups in sensitivity analysis (see pg 246 of consultation document). Page 99 of the consultation document where we explained the Jenks numbers used as below. Description of factual inaccuracy Description of proposed amendment Justification for amendment Reproducing the proportions of SSI in and out of	Thank you for your comment. The description of the study population in the company base case model has been amended in the EAC assessment report to state that all patients undergoing surgery with closed incisions were considered. The sponsor used data from Jenks et al 2014 for the cost of SSI in different specialities except colorectal surgery, data for which was extracted from Tanner et al. 2009. The EAC accepted this approach but considered that post discharge costs reported in Tanner 2009 may have been based on the costs of patients being readmitted to hospital as well as those treated in the community. Therefore, this may overestimate the cost of SSI treated in the community compared with SSIs occurring during the index admission or leading to readmission. Clarification was sought from the EAC, who did not agree with this interpretation of the sensitivity analysis. The EAC did not vary 17 parameters, but varied 9 parameters. Variation in three of these parameters did not change the conclusion that PICO was cost saving: standard dressing cost; risk of SSI in primary care; and PICO effectiveness changed to meta-analysis

				hospitals Section 4.2, resource identification This is consistent with Jenks paper Table 1 in Jenks paper provides data for in patients, readmissions and post discharge SSI. We took post discharge to reflect outpatient while inpatient and readmission reflected inpatient SSI. For example Vascular 5 inpatient + 7 on readmission =12 SSI 16 SSI post discharge Total SSI =28 Inpatient =43% and outpatient 57% On page 109 and 113 of the consultation Description of factual inaccuracy Description of proposed amendment Justification for amendment Sensitivity analysis interpretation PICO was cost saving in the base case and the majority of the sensitivity analyses, suggesting that on balance it is cost saving with a small likelihood of being cost additive. The exec summary and conclusions state that on balance is it likely to be cost effective â€“ rather than cost saving. This appears to contradict the EAC's own findings and is potentially misleading. The EAC's own SA (11/17 ie 65%) and the sponsor SA shows that PICO is cost saving in the base case and the majority of sensitivity analyses. EAC notes that PICO is insensitive to the majority of parameters when 11 of the 17 parameters varied PICO remained cost saving. The main sensitivities relate to the price of PICO and the effectiveness derived from the meta-analysis. As	including observation studies. The results were sensitive to changes in the other six parameters. The EAC undertook analysis of PICO in limb amputation; reduction in long bone fracture; repair to neck of femur; cranial; spinal; abdominal hysterectomy; Bile duct, liver, pancreatic; gastric; small bowel; and multiple intra-abdominal surgery in addition to colorectal, vascular, cardiothoracic, orthopaedic, C-section, and breast, surgeries. The EAC found that PICO was cost saving in only two of the additional surgical specialties based on data in Jenks 2014: gastric and small bowel surgery. The EAC noted PICO to be cost saving when a range of surgery is combined. This was driven by large cost savings in cardiothoracic surgery, which offset the cost increase in other surgical areas. The EAC concluded that there was considerable uncertainty in this finding because the cost saving was sensitive to variation in most parameters examined in the sensitivity analysis. The EAC considered that the inclusion of observational data in the meta-analysis of effectiveness was likely to increase bias, justifying the use of trial data only in the base case analysis. The EAC found the overall estimate of cost savings with PICO to be sensitive to assumptions on PICO effectiveness, risk of inpatient SSI, cost of inpatient SSI, cost of SSI in primary care and dehiscence cost as well as the cost of PICO itself (as detailed in table 21 of the EAC's assessment report).

				indicated above, using all relevant data in the meta-analysis results in PICO remaining cost saving even in the extreme values analysis. It only becomes "marginally" cost additive when the EAC meta-analysis excluding observational data is applied. Similarly, PICO only becomes cost additive at an extreme price level of £195 50% above the list price. This is an unrealistic assumption and does not reflect prices charged to the NHS. No equality issues were determined upon review of the consultation document.	
Theme 6: Side effects					
27	2	Healthcare Other	Page 7 Section 3.7	We note the reported rates of blistering as well as the potential for skin maceration as described by one of the clinical experts and in the WHO guideline for the prevention of surgical site infections.	Thank you for your comment.
Theme 7: Other					
28	1	NHS professional	General	Who will deem a person as competent? What criteria will be used for competence?	Thank you for your comment. The committee discussed your comment and the sponsor advised that the assessor would evaluate each healthcare professional's application of PICO dressings during training but there is no criteria to evaluate the extent of the competence.
29	2	Healthcare Other	General	We are pleased to see that NICE is evaluating the evidence for use of PICO upon closed surgical incisions. We recognise the role that negative pressure wound therapy can play in reducing surgical site infections, particularly as other products available in the UK market provide additional capabilities.	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."

Appendices

1. Additional expert advice following consultation on draft guidance

Following the public consultation on the draft PICO guidance, expert advice was collected on issues raised in the consultation comments to help the committee address the comments and review the draft guidance if necessary.

Expert #1	Thomas Pinkney, Senior lecturer, Consultant colorectal surgeon, Academic Department of Surgery, University of Birmingham
Expert #2	Karlakki Sudheer, Orthopaedic surgeon, Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry
Expert #3	Fania Pagnamenta, Tissue viability nurse, Newcastle upon Tyne Hospitals NHS Foundation Trust
Expert #4	Ahmad Naseer, Consultant vascular surgeon, Manchester University Foundation Trust

Questions to experts	Comments	Experts' advice
Please can you comment on whether there are any parameters to define the levels of exudate in clinical practice?	**Comment 1** It would be helpful if you could please clarify what is meant by low amounts of exudate particularly as we believe that exudate volumes may have an	**Expert #1**: No; there is no parameter to define levels of exudate - doesn't exist And 'low exudate' from an abdominal wound might be 'high exudate' from an ankle wound I share the discomfort of the consultee on this fairly subjective assessment.

	impact on the size of dressing used and the consequential costs.	**Expert #2**: This is difficult to answer. I would suggest possibly changing the paragraph in 2.1 to 'PICO negative pressure wound dressings should be considered as an option for closed surgical incisions in people who are at high risk of developing surgical site infections. They are best suited for wounds with low volumes of exudate and do not continue to exudate after application of dressing. In high exudating wounds which repeatedly saturate the dressing, consideration should be given to canister based NPWT or surgical debridement as appropriate'
		Expert #3: There is no set definition. A working definition is that high exudate would be that a dressing needs to be changed every 24h.
		Expert #4: I would simply go with manufacturer guidelines
Please can you comment on who will decide the use of PICO dressing and the patient's eligibility to use it in clinical practice?	**Comment 6** Careful patient selection is important and should be informed by NICE guidance. I think this is the crux of it. Whilst there is a core of high risk factors E.G obesity and diabetes there are specific factors for specific types of surgery e.g use of bilateral IMA in cardiac patients. Who makes the decisions to use or not to use? Could end up with over or under use, seems like a bit of a lottery.	**Expert #1**: I don't really agree. PICO is being suggested to be used at those at high overall risk of SSI – such as obese patients and diabetics because these are global risk factors for development of SSI. We don't (yet) have any good evidence to stratify those who will versus those who will not do better with the use of a PICO
		Expert #2: Ideally the decision to use PICO dressing should be by the treating lead clinician or in conjunction with the lead clinician or by a specialised nurse in wound care. Although NICE provides a guidance on use of PICO or NPWT, further reading and literature review for the specific speciality should be undertaken by the clinician to judge the merits of use of such a dressing for a condition/situation that is being addressed. Ideally the application of a PICO/NPWT dressing should be at the end of the procedure by the clinician or an appropriately trained healthcare worker (trainee/nurse/physician assistant/advanced practitioner) to gain most out of the dressing where suitable.

		Since this is an expensive dressing, where the use is novel, the clinician and hospital should consider auditing the use and benefits
		Expert #3: If applied in theatres as it should be, then it is a surgeon decision and I agree with this comment: some will decide to use it on all the procedures they do, some not at all. Currently, there is no sufficient evidence to make recommendations in any surgical procedures.
Similar to comment 1, please can you comment whether there is any definition about the levels of exudate?	**Comment 8** We understand why clinical experts have advised that PICO dressings should only be used for surgical incisions in which the amount of exudate was anticipated to be low. We have not seen any definition of what constitutes a low amount of exudate and information about whether the patients in the trials included in this assessment had wounds with low exudate levels appears to be lacking from the evidence presented. We would like to suggest that a value should be given in the guidance to define the low amounts of exudate that PICO can absorb as this may influence the choice and numbers of dressings used, which ultimately may impact upon costs.	**Expert #1**: As above. I agree; but this evidence does not exist
		Expert #2: This depends if you want this to be evidence based or experience based. We have already suggested in our RCT that the dressing is changed if the exudate fills more than half the dressing to ensure that the dressing is functional at its best. Based on my experience I would suggest that any incisional wounds in the respective specialities where the need for dressing change based on above criteria is less than 10%, it is then perhaps be classed as low exudate wound.
		Expert #3: Agreed – see above. In my experience, high BMI patients and multiple surgical procedures will result in higher exudate levels. But I would use a different TNP product. Yes, this would make sense but I am not sure if the company will be able to answer this as exudate in the lab is not the same as real-life exudate
		Expert #4: I would simply use the manufacturer guidelines for the definition for one dressing (from memory I think it is 150mls over one week, thus <25mls per day).

Please can you comment on the innovative aspects of PICO compared with other dressings?	**Comment 10** Section 2 - Innovative Aspects We recognise that PICO is different from other negative pressure technologies, in that it does not have a canister and is therefore most likely only to be suitable for wounds with low exudate levels. We would question whether PICO's claims to be innovative due to its portability and use of a propriety dressing layer can be substantiated as there are other products available on the UK market which offer these benefits.	**Expert #1**: It's clearly innovative compared to normal dressings. It's also different to traditional negative pressure therapy devices in that there is no canister etc. Whether it is any different to the other negative pressure *wound dressing* available on the market (Pravena; made by Acelity) is a different question. The manufacturers claim that they are not synonymous due to delivering different pressures and having a different structure of the dressing. (I don't see why this is relevant really) **Expert #2**: I have previously replied to this question. There are several other products which claim to be portable and applicable to incisional wound, but not all available in the UK. All of these have advantages and disadvantages, its down to the clinician to assess them for a particular use. Some of the dressings I have used or considered are 1. KCI – produce a dressing called 'Prevena' which is a portable and cannister based dressing. Used this in practice and discontinued for reasons. 2. 'Acelity Nanova" which is based on a spring based vacuum technology. Not sure who markets them but carries limitations as the patient needs to apply negative pressure, there is very little clinical evidence. 3. A more recent addition marketed by Convatec, very similar to PICO and resembles PICO, makes use of a hydrofibre dressing, which has been in use as a standalone dressing and well established. The pump is an addition to the dressing and meant to work for 30 days, very little clinical evidence. The company although promise comparable dressing sizes, they haven't been forthcoming in supplying samples to try, therefore haven't had a chance to try.

		The advantages that I see with PICO for continued use are a. It has a sandwiched layered component in the dressing, which absorbs and evaporates exudate under continued negative pressure, which is innovative and perhaps unique to PICO and works well in clinical setting and as far as I am aware there is no other product that can claim this. Having said that it is for the company to respond not me! b. It comes in different sizes and shapes c. Pump is small and user friendly but last only a week, although I would like to see this to extended to 2 weeks d. Provided with 2 dressing, although I would like to see a price reduction with one dressing. The discussion around use of cannister system stems from traditional use of NPWT for chronic wounds and pressure sores using sponge or gauze as a surface layer where the exudate is high and continuous. In hip and knee replacement including revision hip and knee replacement, prolonged wound ooze is minimal, we use less than 10% of second dressing because the first dressing has had staining more than half of its width. When there is continued wound exudate the wounds often require surgical debridement and a cannister based system is unlikely to address this. We learnt from our experience with 'Prevena' that there was very little if any exudate in the cannister and therefore Cannister requirement for an incisional wound is minimal. This experience may be different in other surgical speciality.
		Expert #3: Prevena, which has a canister and NICE is also reviewing. More expensive but more versatile.
		Expert #4: SNAP and AVELLE are both alternatives which I have used in the NHS.

2. EAC's critique of new evidence

New evidence on PICO

A consultee noted a recently published paper using PICO in people undergoing primary or revision knee or total hip arthroplasty during public consultation. Preliminary results of this study (Keeney 2018) have been previously included in the EAC's assessment report as academic in confidence (Stannard et al unpublished - NCT02064270). The EAC critically appraised the full-text publication from Keeney 2018 and added the additional data in the meta-analysis for surgical site infection (SSI), reported in section 2.3 below.

Keeney 2018

This is a multi-centre, open-label, RCT comparing PICO with conventional dressing (Adaptic or Xeroform) in 398 people (185 in PICO vs. 213 in control group, target recruitment of 1000) undergoing elective, routine primary or revision total knee or hip arthroplasty in the US. Main risk factors were smoking, BMI, and diabetes. People were randomised 1:1 and were followed up to 5 weeks post-surgery, with dressing change scheduled to occur on day 7. There were significant differences between groups for all three main risk factors. A higher proportion of patients with smoking history were included in the PICO group, and people with a higher mean BMI and diabetes were included in the control group (Mean BMI 34.6 versus 36.5kg/m^2, p=0.04; % of diabetic patients, 21.3% versus 31.8%, p=0.37). The primary outcome was postoperative wound healing appearance and the authors did not identify any statistically significant differences between the two groups. No significant difference in late superficial or deep infection rates was identified between PICO and control (4.0% vs 3.4%, p=0.8). None of the other secondary outcomes were different between the two groups. Subgroup analysis showed that total knee arthroplasty patients with a BMI>35 experienced fewer SSCs complications (1.3% vs 21.6%, p<0.01) and fewer dressing-related concerns (1.3% vs 10.8%, p=0.02) when treated with PICO compared with a conventional dressing.

Critical appraisal

This is a US study, which means that results may not be relevant to UK practice. Due to the nature of the intervention, the study was unblinded. The study had a low consent rate (22.5%) and a high dropout rate (17.8%). The study, therefore, is at high risk for attrition bias. The authors do not report a sample size calculation for the primary or secondary outcomes and from an initial 1000 recruitment target the final analysis only includes 398 patients with uneven distribution between the two groups (185 vs 213). Despite being an RCT there were notable differences in the baseline risk characteristics between the two groups suggesting high risk for selection bias. The study is also high risk for detection bias because of the methods used to assess short and long-term outcomes. Wound healing was self-reported and with the use of digital images taken by the participants mainly through phone call follow-up. Long-term outcomes such re-operation and infection rates were extracted through the patients' clinical records. The study was partially funded by the sponsor.

Meta-analysis results

1.1 Original meta-analysis results as included in the EAC's full assessment report (3.8.2).

The calculated odds ratio (OR) of all 19 studies included in the original analysis (0.37, 95%CI 0.24-0.57, p<0.0001) is shown in table 1. The unpublished preliminary data by Stannard was excluded from the main analysis because it did not contain all necessary information.

Table 1: Pooled SSI estimate from all studies.

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect size estimate	Statistical significance
Surgical Site Infection	19	4473	Odds Ratio (M-H, Random, 95% CI)	0.37 [0.24, 0.57]	P<0.0001
RCT SSI combined	8	1804	Odds Ratio (M-H, Random, 95% CI)	0.51 [0.31, 0.82]	P=0.006
Observational SSI combined	11	2669	Odds Ratio (M-H, Random, 95% CI)	0.27 [0.14, 0.53]	P=0.0001

1.2 Original meta-analysis results for the subgroup of orthopaedic surgery as included in the EAC's full assessment report.

The analysis showed a statistically significant effect for the rate of SSI in favour of PICO (0.45, 95%CI 0.22 to 0.91, p=0.03) when all data from RCTs and observational studies were combined (Table 2). The effect was not statistically significant when data from RCTs only was combined. Karlakki 2016 (the only adequately powered RCT analysing orthopaedic surgery outcomes, did not report reduction in LOS with the use of PICO (difference 0.9 days, 95%CI -0.2 to 2.5, p = 0.07) or SSCs (2.0% PICO vs. 8.4%; p = 0.06) in comparison with standard dressing in patients undergoing elective primary knee or hip arthroplasty. The study by Karlakki 2016 was not adequately powered to detect differences in the rate of SSI between the two groups.

Table 2: Pooled SSI estimate from studies with people undergoing orthopaedic surgery.

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect size estimate	Statistical significance
Orthopaedic surgery SSI	5	607	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.22, 0.91]	P=0.03
Orthopaedic RCT SSI	2	279	Odds Ratio (M-H, Random, 95% CI)	0.36 [0.09, 1.46]	P=0.15
Orthopaedic Observational SSI	3	328	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.21, 1.11]	P=0.09

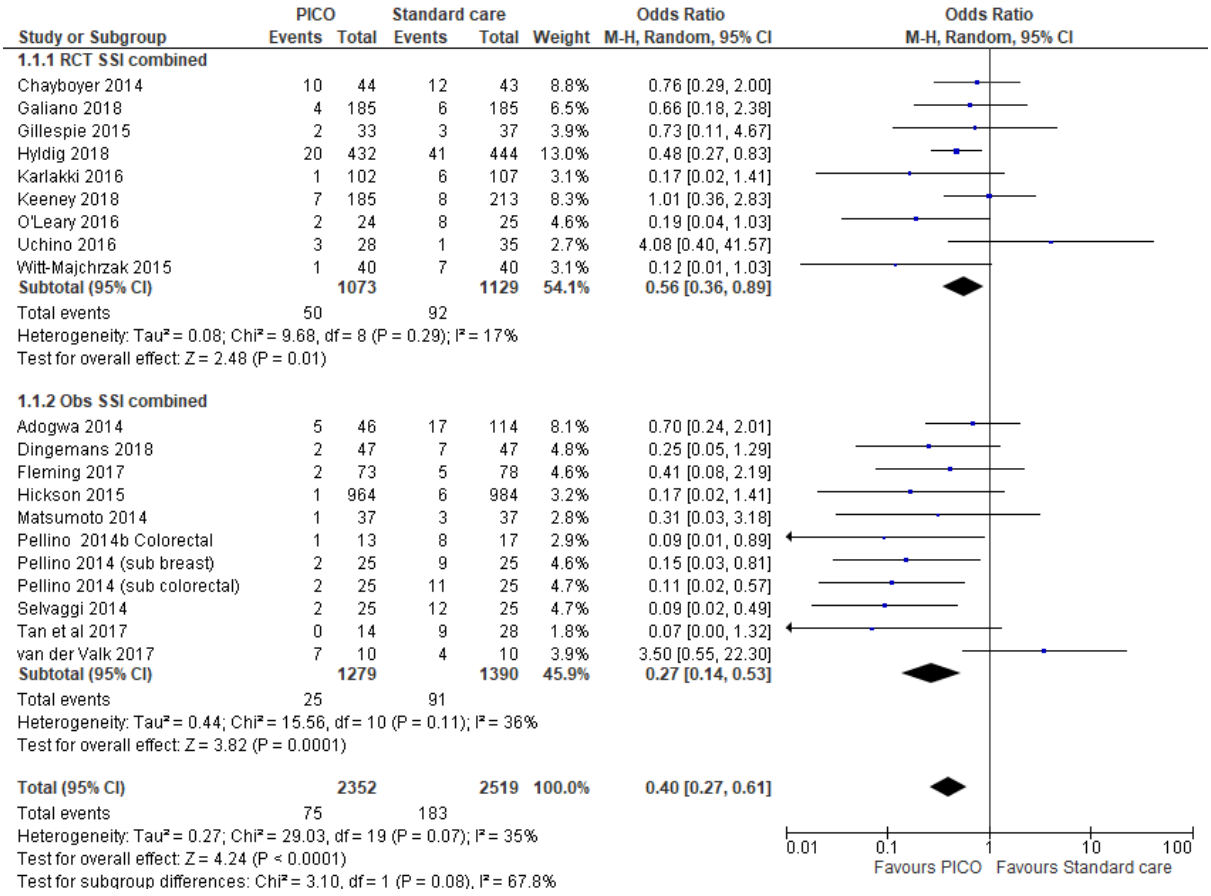
1.3 Updated meta-analysis (new evidence from Keeney 2018)

The EAC updated the meta-analysis including data from Keeney 2018. The OR of all 20 studies included in the analysis is 0.40 (95%CI 0.27 to 0.61, p<0.0001). Overall effect for SSIs based on 9 RCTs was 0.56 (95%CI 0.36-0.89), p=0.01. Both these results are in accordance with what the EAC reported in the meta-analysis reported in the full assessment report (Table 3, Figure 1).

Table 3: Pooled SSI estimate from all studies including Keeney 2018.

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect size estimate	Statistical significance
Surgical Site Infection	20	4871	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.27, 0.61]	P<0.00001
RCT SSI combined	9	2202	Odds Ratio (M-H, Random, 95% CI)	0.56 [0.36, 0.89]	P=0.01
Observational SSI combined	11	2669	Odds Ratio (M-H, Random, 95% CI)	0.27 [0.14, 0.53]	P=0.0001

Figure 1: Forest plots for all studies reporting SSIs, including the results from Keeney 2018.



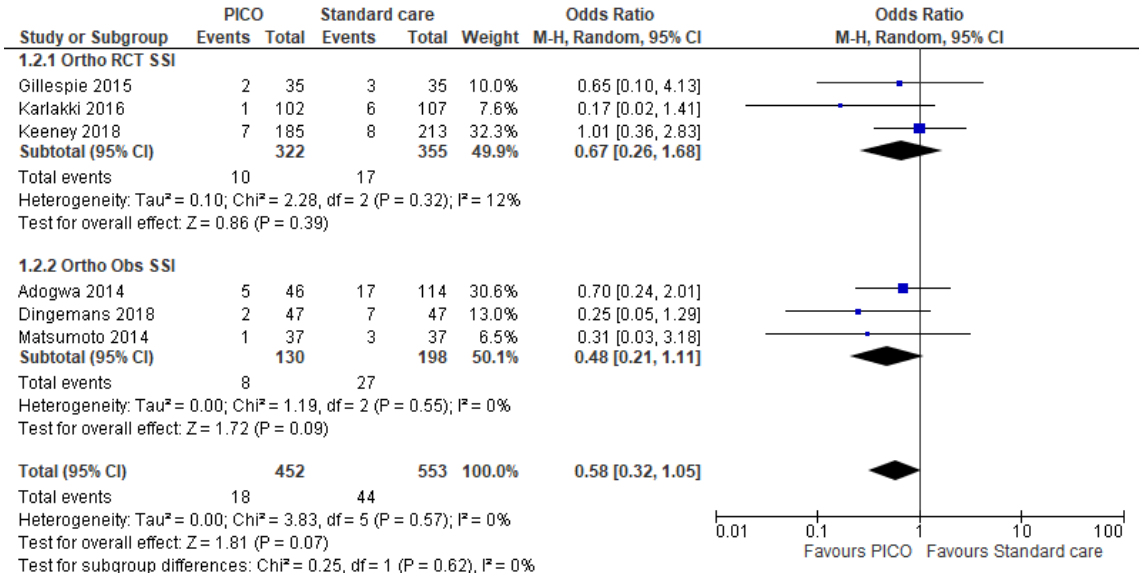
The additional data from Keeney 2018 was also added to the subgroup analysis for orthopaedic surgery. The rate of SSIs was not statistically significant when results from all studies were combined or when only

data from RCTs was pooled (Table 4, Figure 2). The EAC notes the high risk of bias associated with Keeney 2018.

Table 4: Pooled SSI estimate from studies with people undergoing orthopaedic surgery including Keeney 2018

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect size estimate	Statistical significance
Orthopaedic surgery SSI	6	1005	Odds Ratio (M-H, Random, 95% CI)	0.58 [0.32, 1.05]	P=0.07
Orthopaedic RCT SSI	3	677	Odds Ratio (M-H, Random, 95% CI)	0.67 [0.26, 1.68]	P=0.39
Orthopaedic Observational SSI	3	328	Odds Ratio (M-H, Random, 95% CI)	0.48 [0.21, 1.11]	P=0.09

Figure 2: Forest plots for all studies in orthopaedic surgery reporting SSIs including the results from Keeney 2018



References

Keeney, J. A., J. L. Cook, S. W. Clawson, et al. (2018). Incisional negative pressure wound therapy devices improve short-term wound complications, but not long-term infection rate following hip and knee arthroplasty." J Arthroplasty. Available online 15 December 2018, in Press, corrected proof https://doi.org/10.1016/j.arth.2018.12.008.