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Control strategies to prevent total hip replacement-related infections: a systematic review and mixed treatment comparison

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ABSTRACT

Objective: To synthesise the available evidence and estimate the comparative efficacy of control strategies to prevent total hip replacement (THR)-related surgical site infections (SSIs) using a mixed treatment comparison.

Design: Systematic review and mixed treatment comparison.

Setting: Hospital and other healthcare settings.

Participants: Patients undergoing THR.

Primary and secondary outcome measures: The number of THR-related SSIs occurring following the surgical operation.

Results: 12 studies involving 123 788 THRs and 9 infection control strategies were identified. The strategy of 'systemic antibiotics+antibiotic-impregnated cement +conventional ventilation' significantly reduced the risk of THR-related SSI compared with the referent strategy (no systemic antibiotics+plain cement+conventional ventilation), OR 0.13 (95% credible interval (CrI) 0.03–0.35), and had the highest probability (47–64%) and highest median rank of being the most effective strategy. There was some evidence to suggest that 'systemic antibiotics+antibiotic-impregnated cement +laminar airflow' could potentially increase infection risk compared with 'systemic antibiotics+antibiotic-impregnated cement+conventional ventilation', 1.96 (95% CrI 0.52–5.37). There was no high-quality evidence that antibiotic-impregnated cement without systemic antibiotic prophylaxis was effective in reducing infection compared with plain cement with systemic antibiotics, 1.28 (95% CrI 0.38–3.38).

Conclusions: We found no convincing evidence in favour of the use of laminar airflow over conventional ventilation for prevention of THR-related SSIs, yet laminar airflow is costly and widely used. Antibiotic-impregnated cement without systemic antibiotics may not be effective in reducing THR-related SSIs. The combination with the highest confidence for reducing SSIs was 'systemic antibiotics+antibiotic-impregnated cement+conventional ventilation'. Our evidence synthesis underscores the need to review current guidelines based on the available evidence, and to conduct further high-quality double-blind randomised controlled trials to better inform the current clinical guidelines and practice for prevention of THR-related SSIs.

Strengths and limitations of this study

- This study is the first to examine the comparative effectiveness of various infection control strategies involving multiple infection control measures in preventing THR-related SSIs. Multiple sensitivity analyses contributed to the methodological rigour of the study.
- The small number of studies available for evidence synthesis reduced the statistical power and resulted in wide credible intervals for some comparisons.
- Owing to limited data available, the MTC model was unable to adjust for potential confounders such as casemix, different types of laminar airflow systems and temporal changes in clinical practices and infection control technology which may have taken place over the past several decades.

INTRODUCTION

Despite numerous advances in hip arthroplasty, surgical site infection (SSI) following total hip replacement (THR) remains a serious threat. Infection causes functional impairment, reduces quality of life and creates large costs for patients and the healthcare system. Identifying evidence based and effective infection control strategies to prevent THR-related SSI is critically important.

Evidence for the effectiveness of infection control measures in reducing THR-related SSI has been inconsistent.[1–3] Previous evidence syntheses focused on single infection control measures such as systemic antibiotic prophylaxis,[4 5] antibiotic-impregnated cement[6 7] or ventilation systems alone[8] without examining the combined effect of multiple control measures. In practice, infection control strategies combine multiple infection control measures, yet no good evidence is available on the combined comparative effectiveness of strategies involving multiple measures.

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Previous evidence syntheses relied on narrative systematic reviews or conventional pairwise meta-analysis. These do not compare the effectiveness of all trialled control measures when the evidence base of published studies does not include all possible comparisons.[9] The remedy is to define a connected network of the evidence base and combine all the available data in a single mixed treatment comparison (MTC) model.[9 10] This enables comparisons of all available infection control strategies to better inform decision making.

We conducted a MTC, also known as network meta-analysis, to synthesise the available evidence and determine the combined comparative effectiveness of infection control strategies in preventing THR-related SSI in patients undergoing THR.

METHODS

We applied the Patient, Intervention, Comparison and Outcome (PICO) framework. The population of interest was patients undergoing THR. The interventions were infection control strategies to prevent THR-related SSI. The comparison was an intervention strategy that was compared with the other intervention strategies in the MTC network. The outcome of interest was the number of THR-related SSIs. The PICO framework was specified in box 1.

Study identification

We chose antibiotic prophylaxis, antibiotic-impregnated cement and laminar airflow based on published guidelines and a survey of expert opinion.[11] We followed the systematic review guidelines in the PRISMA statement.[12] We used a two-stage search strategy. First, we used systematic reviews by Glenny and Song[4] and AlBuhairan *et al*[5] to locate studies on the efficacy of systemic antibiotic prophylaxis in preventing THR-related infection. Together, these covered the years from 1966 to 2007. Systematic reviews by Parvizi *et al*[6] and Block and Stubbs[7] were used to locate trials on the effect of antibiotic-impregnated cement in preventing THR-related SSI. These reviews covered the years from 1966 to 2004. We used the recent systematic review by Whitehead *et al*[8] to locate studies on the efficacy of operating theatre ventilation systems in preventing THR-related SSI, which covered the years from 1970 to 2007.

Box 1 Patient, Intervention, Comparison and Outcome framework

Population: Patients undergoing total hip replacement.
Intervention: Infection control strategies to prevent total hip replacement (THR)-related surgical site infection (SSI).
Comparison: An infection control strategy compared with other control strategies in the mixed treatment comparison network.
Outcome: The number of THR-related SSIs.

Second, we updated these systematic reviews by extending the search periods to June 2011. The electronic databases searched were MEDLINE, EMBASE, CINAHL and the Cochrane Central Register of Controlled Trials. Relevant journals, conference proceedings and bibliographies of retrieved papers were searched. Eleven orthopaedic surgeons and infection control experts from six hospitals were consulted. The search was limited to English-language papers (the search details are in online supplementary appendix 1).

Studies were included if they reported THR-related deep SSI or infection requiring a joint revision procedure as an outcome. While the precise definitions varied, they encompassed signs of infection involving the joint and/or fascial tissue at the site of the joint. Owing to the limited number of studies available, we included observational studies as well as randomised controlled trials (RCTs).

Studies were excluded if THR-related SSIs were not separated from knee or other joint replacement-related infections. Studies that only compared different types, doses or durations of antibiotic regimens were treated as one-arm trials and excluded from the network meta-analysis as MTC relies on there being at least two arms that can become part of the network.[10] The antibiotics were combined because there is little evidence of different efficacies in preventing THR-related SSI between antibiotics according to their type, dose or duration.[4] The two-stage search process is in the flow chart (figure 1; reasons for exclusion are shown in online supplementary appendix 2).

Data extraction

Data were extracted by two independent reviewers and discrepancies were resolved by consensus. The key data were the number of THRs performed and THR-related deep SSIs; use of antibiotic prophylaxis and its delivery mode; and operating theatre ventilation system.

Quality assessment

The quality of the included studies and their level of evidence were assessed based on the National Institute for Health and Care Excellence (NICE) public health guidelines[13] (see online supplementary appendix 3), and quality scoring systems for RCTs by the Joanna Briggs Institute[14] and observational longitudinal studies by Tooth *et al*[15] (see online supplementary appendix 4).

Statistical methods

MTC models produce estimates of the relative effects of each infection control strategy compared with every other strategy in a network, thus allowing coherent judgements to be made on which strategy is the most effective.[9] It enables simultaneous comparisons of multiple infection control strategies from trials that did not necessarily directly compare all strategies.[9 10] Bayesian methods have been developed for MTC models (see online supplementary appendix 5).[16]

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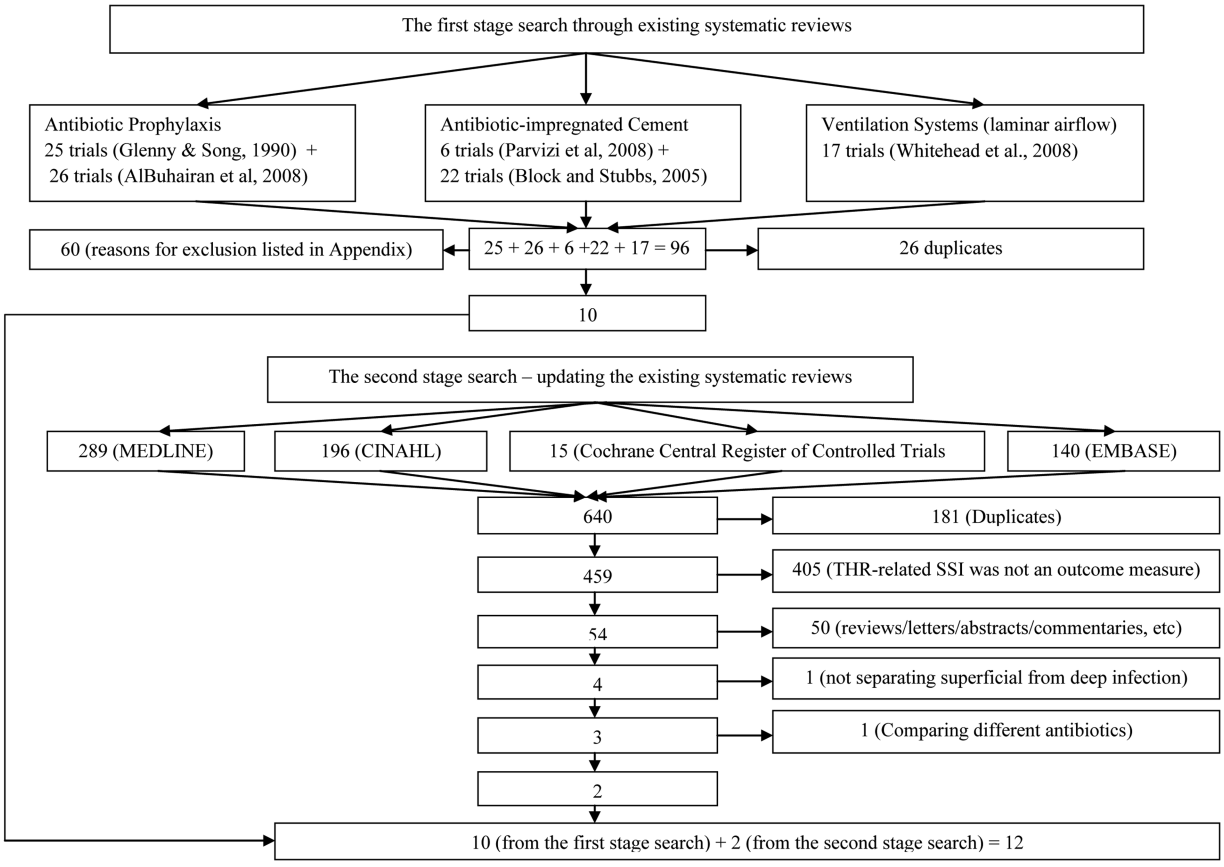


Figure 1 Two-stage literature search flow chart.

The MTC analysis was performed using a binomial random effect model allowing multiarm trials.[17] The key summary statistics were the relative infection control effects using ORs, and the probability and median rank of being the most effective strategy. Studies with longer follow-up periods were likely to find more infections; hence, we accounted for this by modelling the duration of follow-up (see online supplementary appendix 6). The models were fitted in a Bayesian framework using the WinBUGS program and code by Dias *et al*.[17]

Evaluation of model fit and evidence consistency

We assessed the models' goodness of fit (see online supplementary appendix 7). Where the model fit was poor, we explored the influence of each study on the model fit (see online supplementary appendix 8).

An assumption of MTC models is that direct and indirect sources of evidence estimate the same true treatment effect across the network. We checked this assumption by conventional pairwise meta-analyses and by removing the constraint that direct and indirect evidence estimate the same effect.[18] The latter is also known as node-splitting (see online supplementary appendix 9).

Heterogeneity and sensitivity analysis

Heterogeneity of the MTC network was quantified by using the between-study SD. We performed sensitivity analyses by removing outliers as identified through diagnostic assessment.

There may have been a difference in evidence between RCTs and observational studies. To examine this, we performed a meta-regression with study type as an interaction (see online supplementary appendix 10).[19] In further sensitivity analyses, we excluded the RCT by Hill *et al*[20] due to its reported violation of the RCT trial code, and included the RCT by Lidwell *et al*[1] which was initially excluded because it did not separate THRs from knee replacements.

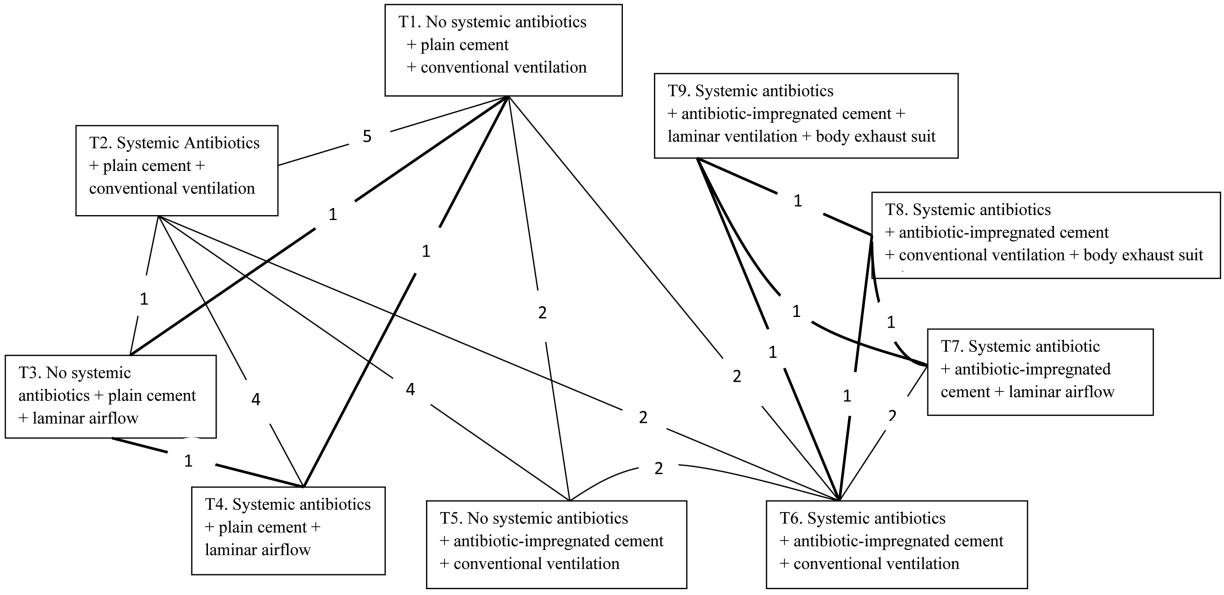
RESULTS

The two-stage search strategy yielded 529 studies, of which 12 met our inclusion criteria. Six were RCTs[20–25] and six were observational studies.[2 3 26–29] The studies included 123 788 THRs and 9 infection control strategies as mapped in the MTC network (figure 2). The raw data are in the Summary of Evidence (table 1).

The quality of evidence was mixed with the level of evidence ranging from 1 to 2 (table 1).

Five of six studies[21–25] provided no information on random sequence generation; four[22–25] provided no information on blinding assessors; and only one reported prior calculation of the sample size.[20] The statistical power for most RCTs was generally low. Only one

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Note: The lines represent direct evidence comparisons; boxes represent infection control strategies involving multiple infection control measures; the numbers on the lines represent the numbers of comparisons. The three-way loops in bold lines represent loops only formed by a multi-arm trial

Figure 2 The mixed treatment comparison network consisting of 12 studies with 9 infection control strategies.

RCT reported primary analysis based on all randomised cases[20] while the rest did not report intention to treat.

Of the six observational studies, three[3 28 29] identified and adjusted for confounding variables. One[26] reported that cases and control groups were comparable on diagnostic confounding factors, and two[28 29] described and included in the analysis the outcomes of the patients who withdrew. Four studies[2 3 28 29] used objective measures to assess the outcomes, and were adequately powered with large sample size ranging from 10 905 to 51 485.

For every infection control strategy in the connected network, a relative effect was estimated against another infection control strategy using the OR. We chose 'no systemic antibiotics, plain cement and conventional ventilation' as the referent strategy, as it was compared with the greatest number of other strategies.

Thirty-six relative effects involving nine infection control strategies were estimated in the MTC network using models that did and did not adjust for duration of follow-up (see online supplementary appendix 11 and table 2). The results from both models were almost identical, as were estimates of the model fit. Hence, the differences in follow-up duration had little effect on the effectiveness of the infection strategies. We therefore report the results of the model without adjustment for follow-up from now on (table 2). The 36 ORs for all pairwise comparisons are in the Forest Plot (figure 3).

The five infection control strategies associated with a statistically significant reduction in THR-related SSI compared with the referent strategy T1 were: T6 (systemic antibiotics+antibiotic-impregnated cement+conventional ventilation), OR 0.13 (95% credible interval (CrI) 0.03–0.35); T2 (systemic antibiotics+plain cement+conventional ventilation), 0.31 (0.12–0.65); T3 (no systemic antibiotics +plain cement+laminar airflow), 0.26 (0.03–0.95); T4 (systemic antibiotics+plain cement+laminar airflow), 0.25 (0.06–0.66); and T7 (systemic antibiotics+antibiotic-impregnated cement+laminar airflow), 0.27 (0.03–0.93; table 3).

Statistically non-significant reductions in THR-related SSIs as compared with the referent were T5 (no systemic antibiotics+antibiotic-impregnated cement+conventional ventilation), OR 0.38 (95% CrI 0.09–1.12); T8 (systemic antibiotics+antibiotic-impregnated cement+conventional ventilation+body exhaust suit), 0.52 (0.03–2.12) and T9 (systemic antibiotics+antibiotic-impregnated cement+ laminar ventilation+body exhaust suit), 0.74 (0.05–2.69).

The OR for T7 (systemic antibiotics+ antibiotic-impregnated cement+laminar airflow) compared with T6 (systemic antibiotics+antibiotic-impregnated cement +conventional ventilation) was 1.96 (95% CrI 0.52–5.37), suggesting that laminar airflow could potentially increase infection risk.

There was no high-quality evidence that antibiotic-impregnated cement without systemic antibiotics was effective in reducing infection compared with plain cement with systemic antibiotics (T2 vs T5), 1.28 (95% CrI 0.38–3.38).

Strategy T6 had the highest probability and highest median rank of being the best strategy in reducing THR-related SSI (see online supplementary appendix 12).

Model fit and evidence consistency

The model fit statistics indicated that the fit was less than adequate (table 2). This was confirmed by diagnostic plots, which showed that infection control strategies

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Table 1 Summary of evidence: comparisons of nine control strategies across the MTC network

Author/year/study design/country	Comparison of infection control strategies	Infection control strategy	Number of THR-related SSIs	Number of THRs	Evidence level and quality assessment	Study number
Carlsson *et al* (1977)[21] RCT, Sweden Schulitz *et al* (1980)[22] RCT, Germany	The referent strategy T1 (no systemic antibiotics +plain cement+conventional ventilation) vs T2 (systemic antibiotics+plain cement+conventional ventilation)	T1 T2	7 0	58 60	Evidence level: 1⁻ C1 C2 C3 C4 C5 C6 C7 C8 1 2 2 1 1 1 3 3	1
		T1 T2	8 1	89 105	Evidence level: 1⁻ C1 C2 C3 C4 C5 C6 C7 C8 1 1 1 1 2 2 3 2	2
Salvati *et al* (1982)[26] Observational study, Italy Fitzgerald (1992)[23] RCT, USA	T2 (systemic antibiotics+plain cement +conventional ventilation) vs T4 (systemic antibiotics+plain cement+laminar airflow)	T2 T4	11 13	761 1518	Evidence level: 2⁻ C1 C2 C3 C4 C5 C6 C7 C8 1 2 3 2 1 2 1 3	5
Kelly *et al* (1996)[27] Observational Study, UK		T2 T4	4 1	1739 1682	Evidence level: 1⁻ C1 C2 C3 C4 C5 C6 C7 C8 1 2 1 1 1 1 1 2	7
		T2 T4	0 3	236 207	Evidence level: 2⁻ C1 C2 C3 C4 C5 C6 C7 C8 1 1 1 1 1 3 1 2	8
Josefsson *et al* (1981)[24] RCT, Sweden McQueen *et al* (1990)[25] RCT, UK	T2 (systemic antibiotics+plain cement +conventional ventilation) vs T5 (no systemic antibiotics+antibiotic-impregnated cement +conventional ventilation)	T2 T5	10 2	812 821	Evidence level: 1⁻ C1 C2 C3 C4 C5 C6 C7 C8 1 2 1 1 1 1 3 3	4
		T2 T5	1 2	190 190	Evidence level: 1⁻ C1 C2 C3 C4 C5 C6 C7 C8 1 2 1 1 1 2 3 3	6
Brandt *et al* (2008)[3] Observational study, Germany	T6 (systemic antibiotics+antibiotic-impregnated cement+conventional ventilation) vs T7 (systemic antibiotics+antibiotic-impregnated cement+laminar airflow)	T6 T7	99 242	10 966 17 657	Evidence level: 2⁺ C1 C2 C3 C4 C5 C6 C7 C8 2 3 1 3 2 2 2 3	11
Hill *et al* (1981)[20] RCT, France	The referent strategy T1 (no systemic antibiotics +plain cement+conventional ventilation) vs T2 (systemic antibiotics+plain cement+conventional ventilation) vs T3 (no systemic antibiotics+plain cement+laminar airflow) vs T4 (systemic antibiotics+plain cement+laminar airflow)	T1 T2 T3 T4	31 4 4 6	596 590 471 480	Evidence level: 1⁻ C1 C2 C3 C4 C5 C6 C7 C8 **2 2 2 2 2 3 2 3**	3

Continued

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Table 1 Continued

Author/year/study design/country	Comparison of infection control strategies	Infection control strategy	Number of THR-related SSIs	Number of THRs	Evidence level and quality assessment	Study number
Espehaug *et al* (1997)[28] Observational study, Norway	The referent strategy T1 (no systemic antibiotics +plain cement+conventional ventilation) vs T2 (systemic antibiotics+plain cement+conventional ventilation) vs T5 (no systemic antibiotics +antibiotic-impregnated cement+conventional ventilation) vs T6 (systemic antibiotics +antibiotic-impregnated cement+conventional ventilation)	T1 T2 T5 T6	3 25 3 8	276 4586 239 5804	Evidence level: 2+ C1 C2 C3 C4 C5 C6 C7 C8 2 3 2 3 2 3 3 3	9
Engesaeter *et al* (2003)[29] Observational study, Norway		T1 T2 T5 T6	3 46 3 50	280 5960 254 15 676	Evidence level: 2+ C1 C2 C3 C4 C5 C6 C7 C8 2 3 2 3 2 3 3 3	10
Hooper *et al* (2011)[2] Observational study, New Zealand	T6 (systemic antibiotics+antibiotic-impregnated cement+conventional ventilation) vs T7 (systemic antibiotics+antibiotic-impregnated cement+laminar airflow) vs T8 (systemic antibiotics+antibiotic-impregnated cement +conventional ventilation+body exhaust suit) vs T9 (systemic antibiotics+antibiotic-impregnated cement+laminar ventilation+body exhaust suit)	T6 T7 T8 T9	17 9 4 16	31 939 8772 2696 8078	Evidence level: 2+ C1 C2 C3 C4 C5 C6 C7 C8 2 2 2 3 1 3 2 3	12

Note: 'C' denotes the quality assessment criterion as specified in online supplementary appendix 4.
RCT, randomised controlled trial; SSI, surgical site infection; THR, total hip replacement.

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Table 2 ORs with 95% credible intervals of all nine infection control strategies based on the logit link random effect MTC model

Comparison of infection control strategies			OR and 95% credible interval				
OR (1,2)							
0.31 (0.12–0.65)							
OR (1,3)	OR (2,3)						
0.26 (0.03–0.95)	0.92 (0.11–3.39)						
OR (1,4)	OR (2,4)	OR (3,4)					
0.25 (0.06–0.66)	0.84 (0.28–1.97)	1.93 (0.20–7.58)					
OR (1,5)	OR (2,5)	OR (3,5)	OR (4,5)				
0.38 (0.09–1.12)	1.28 (0.38–3.38)	3.28 (0.27–14.15)	1.96 (0.37–6.54)				
OR (1,6)	OR (2,6)	OR (3,6)	OR (4,6)	OR (5,6)			
0.13 (0.03–0.35)	0.44 (0.13–1.13)	1.12 (0.09–4.62)	0.67 (0.12–2.12)	0.43 (0.09–1.24)			
OR (1,7)	OR (2,7)	OR (3,7)	OR (4,7)	OR (5,7)	OR (6,7)		
0.27 (0.03 to 0.93)	0.90 (0.13–3.14)	2.47 (0.11–10.22)	1.41 (0.14–5.35)	0.88 (0.09–3.10)	1.96 (0.52–5.37)		
OR (1,8)	OR (2,8)	OR (3,8)	OR (4,8)	OR (5,8)	OR(6,8)	OR (7,8)	
0.52 (0.03–2.12)	1.77 (0.11–7.20)	5.78 (0.10–21.12)	2.89 (0.12–11.73)	1.71 (0.08–6.93)	3.72 (0.38–13.75)	2.26 (0.22–8.48)	
OR (1,9)	OR (2,9)	OR(3,9)	OR(4,9)	OR (5,9)	OR(6,9)	OR (7,9)	OR (8,9)
0.74 (0.05–2.69)	2.49 (0.20–9.11)	13.15 (0.18–27.4)	4.11 (0.22–14.92)	2.44 (0.15–8.62)	5.00 (0.73–16.87)	3.14 (0.42–10.41)	2.53 (0.23–10.41)
Model fit statistic (posterior mean residual deviance) 34.3*			Model fit statistic (DIC) 180.6		Heterogeneity (between-study deviation) 0.63		

*Compared with 32 data points (model fit is considered to be adequate if the posterior mean residual deviance is approximately equal to the number of total data points; see online supplementary appendix 6 for reference).
DIC, deviance information criterion; MTC, mixed treatment comparison.

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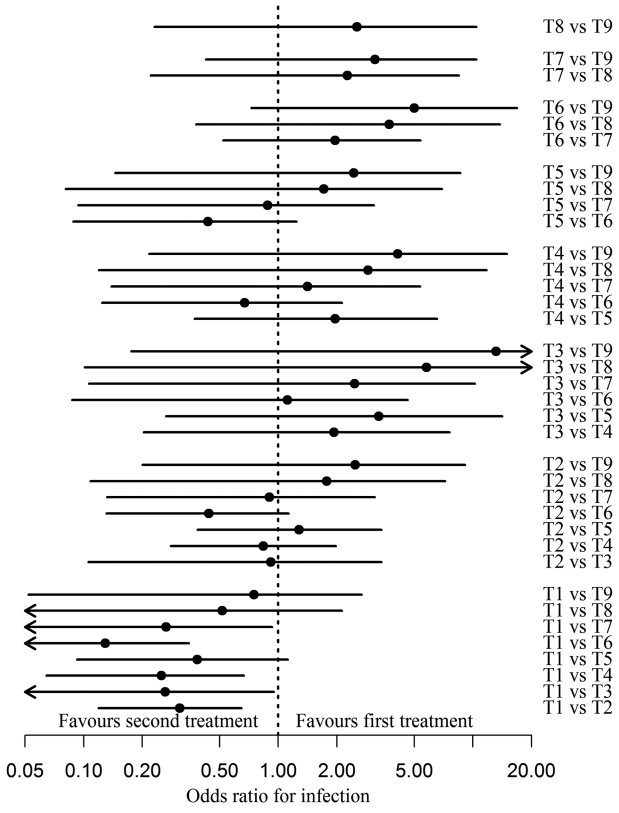


Figure 3 The forest plot of ORs of infection control strategies (random effect model).

T2 and T5 of study 4 and the referent strategy of study 10 were outliers contributing to the inadequate model fit (see online supplementary appendix 13). After exclusion of these two studies, the model fitted the data well, as indicated by model fit statistics, and the heterogeneity was significantly reduced, but the results were little changed (see online supplementary appendix 14). Infection control strategy T6 remained dominant with the highest probability (64%) and highest median rank of being the most effective strategy (see online supplementary appendix 15), and OR 0.09 (95% CrI 0.02–0.25; see online supplementary appendix 14).

The direct evidence from all conventional pairwise meta-analyses was presented in online supplementary appendix 16. There was broad agreement among the direct evidence from: conventional pairwise meta-analyses, the direct and indirect evidence from node splitting, and the evidence from the MTC model (see online supplementary appendix 16). Tests for inconsistency between direct and indirect evidence from node splitting suggested that there was no statistically significant evidence of inconsistency. The model fit statistics for the node-splitting and the MTC models were similar, implying that there was no conflict between the direct and indirect evidence (see online supplementary appendix 16). It is worth noting that the 95% CrIs for some pairwise comparisons widened greatly following node splitting. This is explained by the node splitting reducing the evidence available to inform the variance.

A test of interaction between RCTs and observational studies was not statistically significant, suggesting that combining these study types was not inappropriate (see online supplementary appendix 17).

The results were little changed by excluding the RCT by Hill *et al*[20] or including the RCT by Lidwell[1] *et al*. Strategy T6 remained dominant with the highest probability (63% and 83%, respectively) and highest median rank of being the most effective strategy (the details of the sensitivity analyses are shown in online supplementary appendix 18).

DISCUSSION

Laminar airflow has been widely used as an important infection control measure in many countries around the world. In the UK, for instance, around 98% of all hip arthroplasties are carried out in operating theatres equipped with laminar airflow systems.[30] The current infection control guidelines in the UK[31] and the USA[32] recommend the use of laminar airflow to reduce THR-related SSIs. It is an expensive technology, costing US$60 000–US$90 000 for construction and installation for each operating room.[33] However, our study showed that conventional ventilation together with systemic antibiotics and antibiotic-impregnated cement was most likely to provide the best protection against THR-related SSIs. We found no convincing evidence in favour of the use of laminar airflow over conventional ventilation for prevention of THR-related SSIs.

Although the point estimate for the infection control strategy T3 (no systemic antibiotics+plain cement +laminar airflow) compared with the referent was statistically significant, caution needs to be taken in its interpretation because it had only one RCT conducted between 1975 and 1978 by Hills and colleagues, and the study reported that about 8% of the patients (99 in the placebo group and 70 in the antibiotic group) did not follow the RCT trial protocol with unreported use of antibiotics. We therefore conducted a sensitivity analysis by excluding this RCT from the MTC network and the results for other strategies changed little, with T6 remaining the most effective.

A recent systematic review concluded that laminar airflow tended to lower infection rates as opposed to conventional ventilation, but the authors emphasised that it was difficult to draw a definite conclusion due to confounding.[8] The systematic review was descriptive, involving no statistical analysis. It cited, among others, the RCT by Lidwell *et al*[1] as the key evidence for reducing wound infection using laminar airflow. However, this RCT did not control for antibiotics as a significant confounder. Our sensitivity analysis found that the overall results changed little with the inclusion of this RCT, so it had little influence on our conclusions.

Contrary to the key early evidence in the late 1960s to early 1980s that laminar airflow and body exhaust suit reduced wound contamination and SSIs,[1 34] a number

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Table 3 Odds ratios with 95% credible intervals of infection control strategies based on the random effect MTC model

	No systemic antibiotics	Plain cement	Conventional ventilation	Systemic antibiotics	Antibiotic-impregnated cement	Laminar airflow	Body exhaust suit	OR	95% Credible interval
T1	✓	✓	✓	×	×	×	×	Referent	
T6	×	×	✓	✓	✓	×	×	0.13	0.03–0.35
T2	×	✓	✓	✓	×	×	×	0.31	0.12–0.65
T3	✓	✓	×	×	×	✓	×	0.26	0.03–0.95
T4	×	✓	×	✓	×	✓	×	0.25	0.06–0.66
T7	×	×	×	✓	✓	✓	×	0.27	0.03–0.93
T5	✓	×	✓	×	✓	×	×	0.38	0.09–1.12
T8	×	×	✓	✓	✓	×	✓	0.52	0.03–2.12
T9	×	×	×	✓	✓	✓	✓	0.74	0.05–2.69
T2 vs T5	–	–	–	–	–	–	–	1.28	0.38–3.38
T6 vs T7	–	–	–	–	–	–	–	1.96	0.52–5.37
Model fit statistic (posterior mean residual deviance) 34.3*			Model fit statistic (DIC) 180.6			Heterogeneity (between-study SD 0.63			

*Compared with 32 data points (model fit is considered to be adequate if the posterior mean residual deviance is approximately equal to the number of total data points; see online supplementary appendix 7).
Note: T1–T9: nine infection control strategies. Refer to table 1 for details.
✓: The strategy contains the infection control measure as indicated by the column heading.
×: The strategy does not contain the infection control measure as indicated by the column heading.
DIC, deviance information criterion; MTC, mixed treatment comparison.

of subsequent studies in the 1980s and 1990s found no convincing evidence that laminar airflow was effective in reducing SSIs compared with conventional ventilation.[23 26 27] Four recent large-scale observational studies of 113 183 THRs suggested that laminar airflow and body exhaust suit conferred no protective benefit against SSI and might increase the risk of SSI.[2 3 28 29]

A hypothesis of the early studies by Charnley[34] and Lidwell *et al*[1] on laminar airflow and body exhaust suits was that one of the main routes of wound contamination and infection was the air in the operating room, and laminar airflow and body exhaust suits could reduce airborne bacteria load and therefore wound contamination and infection. The studies demonstrated that laminar airflow ventilation reduced airborne organisms or colony forming units (cfu) to 10 cfu/m^3 between 150 and 300 cfu/m^3 in conventional operating theatres. To be most effective, key operating theatre staff should wear body exhaust suits while working in the ultraclean environment.[1 34] However, standard culture techniques by air sampling or landing 'mode' as a method to assess potential wound contamination do not directly correlate with wound contamination, and they are at best surrogate measures representing the degree of air contamination at the point of sampling, which might be some distance away from the implant zone.[35] There was also evidence that wound contamination was greater at the end of surgery than at the beginning.[35]

The surgeons' heads position above the surgical site and directly in the laminar airstream might facilitate pathogen-contaminating particles falling directly into the wound.[36] Laminar airflow could also result in lower intraoperative tissue temperatures in the surgical wound,[3] and systemic hypothermia is a known risk factor for SSI.[37]

Our study found no high-quality evidence that antibiotic-impregnated cement without systemic antibiotic prophylaxis was effective in reducing THR-related SSI compared with plain cement with systemic antibiotic prophylaxis. Contrary to our findings, a recent meta-analysis showed that the use of antibiotic-impregnated cement lowered the infection rate by approximately 50% compared with plain cement.[6] However, the meta-analysis failed to stratify the infection control arms according to antibiotic regimens and pool on a comparable basis. We reanalysed the data from this meta-analysis by stratifying infection control arms based on antibiotic regimens and pooling the rest of the studies on a comparable basis for summary estimation (see online supplementary appendix 19). The pooled relative risk of antibiotic-impregnated cement compared with plain cement was 0.76 (95% CI 0.46 to 1.28). So there was no high-quality evidence that antibiotic-impregnated cement without systemic antibiotic prophylaxis was effective in reducing THR-related infection compared with plain cement with systemic antibiotic prophylaxis.

A RCT showed that antibiotic-impregnated cement together with systemic antibiotic prophylaxis was

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effective in reducing knee replacement-related infection compared with plain cement with systemic antibiotic prophylaxis.[38] All the procedures were performed in a standard operating room without laminar airflow or body-exhaust suit. The authors stressed that while they did not believe that antibiotic-impregnated cement alone would prevent deep infection, it could aid in prevention of early or intermediate infection in conjunction with systemic antibiotic prophylaxis. This might be explained by the capacity of antibiotic-impregnated cement as a drug-delivery vehicle. It was suggested that the polymeric nature of polymethylmethacrylate allowed ingress of physiological fluids, which permitted elution of incorporated antibiotic, but the relative hydrophobicity of bone cement allowed only 10% of the antibiotic to elute effectively.[39]

Our evidence synthesis has limitations. The small number of studies available for evidence synthesis reduced the statistical power and resulted in wide CrIs for some comparisons. MTC can only synthesise evidence in a connected network. Consequently, one study[40] meeting our inclusion criteria could not be included as it could not be connected to the network. However, the exclusion of this study should not change our results, as the study concluded that there was no statistical difference in THR-related SSIs between plain cement and antibiotic-impregnated cement, which accorded with our findings.

Owing to the limited data available, the MTC model was unable to adjust for potential confounders such as case-mix, particularly patient comorbidity in different hospital settings, different types of laminar airflow systems used (eg, horizontal vs vertical laminar airflow systems), and temporal changes in clinical practices, infection control technology (eg, the use of ultra-high flows in modern conventional operating theatres and forced air blankets) and patient profiles which may have taken place over the past several decades.

The evidence in our study covered a period from 1966 up to June 2011 when the literature search was performed. The evidence needs to be updated when new studies become available.

CONCLUSIONS

This is the first study to examine the comparative effectiveness of various infection control strategies involving multiple infection control measures in preventing THR-related SSI. We found no convincing evidence in favour of the use of laminar airflow over conventional ventilation for prevention of THR-related SSI. Systemic antibiotic prophylaxis in conjunction with antibiotic-impregnated cement and conventional ventilation was likely to be the most effective infection control strategy for preventing THR-related SSI based on the available evidence. There was no high-quality evidence that antibiotic-impregnated cement alone without systemic antibiotic prophylaxis was effective in reducing THR-related SSI compared with plain cement with systemic antibiotics. Our evidence synthesis underscores the need to review current guidelines based on the available evidence, and to conduct further high-quality double-blind RCTs to better inform the current clinical guidelines and practice for prevention of THR-related SSI.

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