Major article

Surgical site infection prevention following total hip arthroplasty in Australia: A cost-effectiveness analysis

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Background: Surgical site infection (SSI) is associated with substantial costs for health services, reduced quality of life, and functional outcomes. The aim of this study was to evaluate the cost-effectiveness of strategies claiming to reduce the risk of SSI in hip arthroplasty in Australia.

Methods: Baseline use of antibiotic prophylaxis (AP) was compared with no antibiotic prophylaxis (no AP), antibiotic-impregnated cement (AP + ABC), and laminar air operating rooms (AP + LOR). A Markov model was used to simulate long-term health and cost outcomes of a hypothetical cohort of 30,000 total hip arthroplasty patients from a health services perspective. Model parameters were informed by the best available evidence. Uncertainty was explored in probabilistic sensitivity and scenario analyses.

Results: Stopping the routine use of AP resulted in over Australian dollars (AUD) $1.5 million extra costs and a loss of 163 quality-adjusted life years (QALYs). Using antibiotic cement in addition to AP (AP + ABC) generated an extra 32 QALYs while saving over AUD $123,000. The use of laminar air operating rooms combined with routine AP (AP + LOR) resulted in an AUD $4.59 million cost increase and 127 QALYs lost compared with the baseline comparator.

Conclusion: Preventing deep SSI with antibiotic prophylaxis and antibiotic-impregnated cement has shown to improve health outcomes among hospitalized patients, save lives, and enhance resource allocation. Based on this evidence, the use of laminar air operating rooms is not recommended.

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Total hip arthroplasty (THA) is a commonly performed procedure, and numbers are increasing with ageing populations.1 One of the most serious complications in THA is surgical site infection (SSI) caused by pathogens entering the wound during the procedure. Treatment options depend on a number of different factors besides infection type and onset of symptoms, such as condition of the implant and soft tissue; health condition of the patient; and also the preferred treatment by the head surgeon, hospital facilities, and patient preferences.2 Superficial infections do not have a big impact on quality of life and are simply treated with inexpensive oral antibiotics. Deep/organ infections on the other hand can have catastrophic consequences for the patient and typically require revision surgery or in very severe cases permanent removal of the prosthesis. Consequently, SSIs are associated with a substantial economic burden for health services, increased mortality, and reduced functional outcomes in patients.3–8

Health care facilities face pressures of providing best care at the lowest cost. Numerous strategies exist to prevent SSI, but there is no gold standard, and clinical practice varies widely. Systemic antibiotic prophylaxis is already part of standard praxis in primary THA in Australia, yet other measures such as the use of antibiotic-impregnated cement and ultraclean air systems are not well established and are controversial. Systematic reviews of some of these measures have assessed the effectiveness of individual strategies, but it is unclear which strategies or combination of strategies is not only the most effective but furthermore is cost-effective.9–21

To use scarce resources efficiently, it is important to establish a cost-effective approach to preventing deep SSI in total hip...
arthroplasty. By preventing these infections, not only costs but also unnecessary patient suffering can be reduced. The aim of this project was to evaluate the cost-effectiveness of strategies claiming to decrease the risk of deep SSI following THA in Australia.

METHODS

There are several steps preceding the actual cost-effectiveness analysis: choosing infection prevention strategies for evaluation (comparators), designing the decision model, and identifying parameters to inform model health states. The cost-effectiveness analysis consists of a baseline analysis using point estimates of parameter values, followed by analysis considering uncertainty surrounding model parameters, as well as scenario analyses.

Comparators

For the cost-effectiveness evaluation, potential prevention measures were established based on the review of clinical guidelines and through structured interviews with local orthopedic surgeons, infection control professionals, and infectious diseases physicians. Strategies were rated for importance in SSI prevention post-THA in an online survey by N = 19 experts from the same discipline areas. Selected strategies were recommended by at least one of the guidelines and classed as highly important by the majority of experts.

The baseline comparator is the routine use of preoperative antibiotic prophylaxis (AP). The 3 alternatives evaluated in the decision model are as follows: no use of antibiotic prophylaxis (No AP), additional use of antibiotic-impregnated cement (AP + ABC), and additional use of laminar air operating rooms (AP + LOR). The latter refer to operating rooms with high-efficiency particulate air (HEPA)-filtered laminar airflow ventilation using (vertical) laminar airflow supply air diffusers, as opposed to conventional operating rooms with HEPA-filtered air with turbulent ventilation.

Decision model

Decision models are a valuable tool for simplifying complex processes, in particular when clinical data are vague, to simulate long-term outcomes with existing data, to synthesize evidence, and to compare intervention alternatives. They show how a hypothetical cohort of patients moves through defined health states relevant to a decision problem.
Costs related to infection prevention strategies were derived from expert opinion, personal communication with hospital administration, and a conservative estimate of annual costs. Costs of infection treatment were calculated using treatment codes for THA patients included in routinely collected Queensland hospital data. All costs are shown in Australian dollars (AUD) (exchange rate at time of analysis 5/2011: 1 AUD = 1.067902 US dollars).

All transition probabilities used in the decision model were calculated based on Australian hospital data. Table 1 shows overall transitions, whereas these were divided into more accurate time-dependent probabilities in the model simulation reflecting time of infection onset and treatment frequency: daily cycles were used for the first month, weekly cycles for the second and third month, monthly cycles until 12 months, and yearly cycles thereafter (available from authors on request).

### Table 1

<table>
<thead>
<tr>
<th>Parameter description</th>
<th>Baseline estimate</th>
<th>Standard error</th>
<th>Distribution</th>
<th>Reference-Source</th>
</tr>
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<tbody>
<tr>
<td><strong>Clinical effect size (odds ratio)</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Antibiotic prophylaxis vs no antibiotic prophylaxis</td>
<td>0.19</td>
<td>0.2421</td>
<td>Log normal</td>
<td>(14)-Systematic review with meta-analysis</td>
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<tr>
<td>Antibiotic-impregnated cement vs standard bone cement</td>
<td>0.506</td>
<td>0.2014</td>
<td>Log normal</td>
<td>(15)-Systematic review with meta-analysis</td>
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<tr>
<td>Laminar air operating theatre vs conventional operating theatre</td>
<td>1.63</td>
<td>0.2209</td>
<td>Log normal</td>
<td>(13)-Large cohort study based on surveillance data</td>
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<tr>
<td><strong>Mortality probabilities</strong></td>
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<tr>
<td>Deep infection</td>
<td>0.119</td>
<td>0.0214</td>
<td>β</td>
<td>(6)-Retrospective review of surveillance data, UK</td>
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<tr>
<td>Revision surgery (total of DAIR, 1-stage revision, 2-stage revision, permanent resection)</td>
<td>0.01791</td>
<td>0.0042</td>
<td>β</td>
<td>(29)-Author calculation based on data from AOA NJRR</td>
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<tr>
<td>Underlying mortality (yearly transition probability)</td>
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<td>50-54</td>
<td>0.002858</td>
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<td>55-59</td>
<td>0.004308</td>
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<td>60-64</td>
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<td>85+</td>
<td>0.136947</td>
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<tr>
<td><strong>Utilities (QALY weight): range, 0-1</strong></td>
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<tr>
<td>No infection</td>
<td>0.858</td>
<td>0.0117</td>
<td>β</td>
<td>(31)-Effectiveness study, 15DHRQol</td>
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<td>≤12 months post-THA</td>
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<td>Deep infection</td>
<td>0.4</td>
<td>0.0514</td>
<td>β</td>
<td>(32)-Observational study, Aqol</td>
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<td>Revision (DAIR, 1-stage revision, 2nd stage revision)</td>
<td>0.812</td>
<td>0.0176</td>
<td>β</td>
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<td>Permanent/temporary resection</td>
<td>0.6</td>
<td>n/a</td>
<td>Uniform</td>
<td>(33)-Literature based on expert opinion</td>
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<td>Successful treatment</td>
<td>0.823</td>
<td>0.0198</td>
<td>β</td>
<td>(31)-Effectiveness study, 15DHRQol</td>
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<tr>
<td><strong>Costs (AUD)</strong></td>
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<tr>
<td>Prevention of infection</td>
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<tr>
<td>Antibiotic prophylaxis*</td>
<td>$140</td>
<td>n/a</td>
<td>Uniform</td>
<td>(Crawford R, Cost estimate. Brisbane, Australia, 3/2011, personal communication)-Expert opinion</td>
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<td>Additional costs of antibiotic cement†</td>
<td>$90</td>
<td>n/a</td>
<td>Uniform</td>
<td>(Jeynes S, Administrative records, Prince Charles Hospital, Brisbane, Australia, 3/2011, personal communication)-Hospital administration</td>
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<td>Ultraclean air system-annual capital costs</td>
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<td>n/a</td>
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<td>Conservative estimate by authors</td>
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<td>Treatment of infection</td>
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<td>DAIR</td>
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<td>$723</td>
<td>γ</td>
<td>(34)-Hospital records, AR-DRG case mix calculations</td>
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<td>1-stage revision</td>
<td>$24219</td>
<td>$1,446</td>
<td>γ</td>
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<td>2-stage revision, 1st stage</td>
<td>$20,861</td>
<td>$5,102</td>
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<td>2-stage revision, 2nd stage</td>
<td>$23,802</td>
<td>$2,309</td>
<td>γ</td>
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<td>Permanent resection</td>
<td>$16,142</td>
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<td>γ</td>
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<td>Transition probabilities</td>
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<tr>
<td>Occurrence of deep infection</td>
<td>0.0096</td>
<td>0.0008</td>
<td>β</td>
<td>(34)-Hospital records</td>
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<td>Initial treatment with:</td>
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<tr>
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<td>0.5255</td>
<td>0.0457</td>
<td>β</td>
<td>(34)-Hospital records</td>
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<td>0.0046</td>
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<td>0.0306</td>
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<td>0.1092</td>
<td>0.0000</td>
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<td>Permanent resection</td>
<td>0.0232</td>
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<td>Further treatment with:</td>
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<tr>
<td>DAIR</td>
<td>0.3195</td>
<td>0.0433</td>
<td>β</td>
<td>(34)-Hospital records</td>
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<td>0.9850</td>
<td>0.0000</td>
<td>β</td>
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<tr>
<td>Permanent resection</td>
<td>0.0444</td>
<td>0.0191</td>
<td>β</td>
<td></td>
</tr>
</tbody>
</table>

AIHW, Australian Institute of Health & Welfare; AOA NJRR, Australian Orthopaedic Association National Joint Replacement Registry; Aqol, Assessment of Quality of Life; AR-DRG, Australian Refined Diagnosis Related Group; AUD, Australian dollars; DAIR, debridement, antibiotics, and implant retention; HRQol, health-related quality of life; QALYs, quality-adjusted life years; SD, standard deviation; SE, standard error; THA, total hip arthroplasty; UK, United Kingdom.

*Based on 4 doses of cephalosporin at $35 each.
†Based on costs for either 3 × 40 g of CMW1 bone cement with 1-g Gentamycin ($165), 3 × 40 g of CMW2 bone cement with 1-g Gentamycin ($173) or 3 × 41 g of antibiotic simplex with 1-g Tobramycin ($214) compared with 40-g CMW standard bone cement ($154).
Cost-effectiveness evaluation

Baseline analysis

The health services perspective was chosen for the cost-effectiveness analysis according to the decision makers’ point of view. A hypothetical cohort of 30,000 THA patients aged 65 years was used for the model simulation, which represents the average annual rate of procedures performed in Australia. 

The baseline rate of deep SSI was 0.96% within 1 year of a primary THA, as per Queensland hospital data matched with Auslab pathology records.

In the cost-effectiveness analysis model, results for each of the infection prevention strategies (comparators) were evaluated. As patients move through different health states, outcomes are summed across all model cycles and changes to health (ΔE) and costs (ΔC) are estimated using the incremental cost-effectiveness ratio (ΔC/ΔE). Health and cost outcomes were discounted at 3%. The model was evaluated over 30 years, reflecting a lifetime evaluation of the patient cohort.

Consideration of uncertainty

Uncertainty surrounding model input parameters is accounted for in probabilistic sensitivity analysis where distributions are fitted around individual parameters. The model is then run 1,000 times, and each time a value from the parameter distribution is drawn at random using Monte Carlo simulation. The output distribution is a joint density of changes to costs and QALYs plotted on the cost-effectiveness plane. It shows 1,000 possible outcomes of incremental costs and incremental effectiveness. The results are summarized as net monetary benefits (NMB), calculated as NMB = (λ*ΔE) − ΔC. Hereby, λ is the ceiling ratio or a decision makers willingness to pay for 1 extra QALY gained. Previously, a willingness to pay of λ = $40,000 has been considered as applicable for the Australian context, whereas, currently, AUD $64,000 is the standard ceiling ratio. A positive NMB indicates that a strategy is cost-effective, and a negative NMB indicates that it is cost-ineffective.

Scenario analysis

The robustness of results was explored further in scenario analyses where model assumptions were varied and the probabilistic sensitivity analysis run each time. The effect on overall model outcomes was recorded at the standard willingness to pay of λ = AUD $64,000 and the most influential variables were identified.

RESULTS

Baseline analysis

Table 2 illustrates outcomes for the baseline comparator and alternative strategies. Compared with baseline AP, the use of additional ABC in all cemented primary THAs would prevent 46 deep SSI and save $3,909 for each QALY gained and hence be cost saving. Not using AP would increase costs by approximately $1.5 million for losing over 163 QALYs. If LOR were used in all primary THAs, costs would increase by approximately $4.6 million, and 127 QALYs are lost. Using AP + ABC clearly dominates the other alternatives.

Consideration of uncertainty

Figure 2 illustrates the probabilistic results on the cost-effectiveness plane in relation to baseline use of AP. Each point in the scatter plots represents 1 of 1,000 simulations and the blue squares the baseline point result. The proportion of simulation points being cost saving, generating extra health benefits, and being dominant, ie, resulting in both cost savings and health benefits is also given. AP + ABC clearly dominates the other strategies showing health benefits in 45.2% of simulations and also being cost saving. The alternatives No AP and AP + LOR predominately increase costs while reducing health benefits.

At a willingness-to-pay threshold of $64,000/QALY, the additional use of ABC in all cemented primary THAs is the most beneficial strategy and the only strategy with a positive mean incremental NMB (>0) of $3.3 million. If antibiotic prophylaxis was no longer undertaken, over $18 million would be lost. Similarly, the combination of AP with LOR is not beneficial and results in a mean loss of approximately $18.7 million for 30,000 procedures. At the typical willingness-to-pay values of $40,000 and $64,000, AP + ABC was the strategy with the highest probability of having the largest NMB, with a ≥98.6% probability of being cost-effective.

Scenario analysis

Table 3 summarizes the model outcomes when baseline parameters are varied. In all tested scenarios, AP + ABC remained the strategy with the highest probability of having the largest NMB. A higher initial patient age decreases the incremental mean NMB and increases the error probability slightly. Whereas higher costs of AP or lower costs of LOR did not make a big difference, additional costs of ABC had an impact on the results: the incremental mean NMB decreased by $2 million and the error probability of AP + ABC being the optimal choice increased to 19%. A higher proportion of cemented primary THAs (50% or 100%) or a higher baseline rate of deep SSI (2% or 5%) resulted in more robust outcomes and substantially higher incremental NMB.

DISCUSSION

Interpretation of findings

In the baseline and uncertainty analysis, AP + ABC clearly dominated the other 2 strategies (No AP, AP + LOR), which both showed a substantial increase in deep SSI cases, resulting in higher mortality and higher costs. If these strategies were implemented, health care providers would absurdly incur costs to harm patients. These results also verified the cost-effectiveness of routinely administering preoperative AP in primary THAs as an infection prevention measure in the absence of using antibiotic cement.
The scenario analysis confirmed the robustness of the results, and AP + ABC remained the strategy with the highest probability of having the largest NMB in all tested scenarios. The analysis showed a reduced incremental net benefit for an older patient cohort. However, data generated from a younger patient group may not reflect real transition probabilities of an older age cohort, but no information was available to consider these possible differences.

In addition, if the proportion of fully cemented or hybrid primary THAs increased, the cost-effectiveness would improve proportionally. At the current proportion of 37.3% cemented primary THAs, this would mean that 11,190 patients from the initial cohort of 30,000 could potentially be treated with ABC. With average additional cost of $90 for ABC, this would result in additional $1 million health expenditure. If all primary THAs were cemented and used ABC, health spending would increase to $2.7 million. Nevertheless, these costs are compensated by preventing SSIs and related treatment costs. Using ABC in 37.3% of primary THAs would overall save over $126,000 and in 100% of primary THAs over $330,000. Similarly, if the baseline rate of deep SSI (0.96%) was higher, the error probability of using AP + ABC would decrease, and the mean NMB would increase dramatically. These results suggest that health care facilities with higher initial infection rates would benefit even more from implementing the routine use of AP + ABC.

Our findings can be compared with results from previous studies. An economic decision analysis evaluated the cost-effectiveness of antibiotic cement in this context and reported an incremental cost-effectiveness ratio of US $37,355/QALY gained.\(^\text{39}\) Testing different scenarios showed that the cost-effectiveness of this technology was highly dependent on costs of cement and baseline patient age; its use was only recommended for a relatively young patient cohort (<71 years) and low costs of cement (<US $650).

In comparison, our results showed a better value for money when antibiotic cement was used (AUD $3,909 saved/QALY gained).

**Fig 2.** Probabilistic results on cost-effectiveness plane. \(\Delta = \text{Incremental.}\)
This might be explained by our much lower additional costs of cement employed in the analysis (AUD $90 vs US $600) reflecting international differences in costs. Furthermore, our study reported a higher initial rate of infection and higher costs of revision because of multiple treatments compared with the study by Cummins et al., which assumed 1 revision per patient. The association between the cost-effectiveness and initial patient starting age and costs of cement was confirmed by our study, yet our findings clearly favored the implementation of AP + ABC even for a high patient age (80 years) and relatively high additional costs of antibiotic cement (AUD $300) as shown in the scenario analysis. Because LOR were associated with an increased rate of deep SSI, it was to be expected that this strategy was never going to be cost-effective, even when system maintenance costs were not considered. Although older studies by Charnley and Eftekhari and later Lidwell et al. found this technology effective for infection prevention in THA, they did not adjust for some key confounding factors, in particular the use of antibiotic prophylaxis. More and more effectiveness evidence for LOR is emerging, reporting no effect or an increase of infection rates. This recent evidence from Germany, New Zealand, and the United States mainly stems from retrospective analyses of large, routinely collected data. Although supporters of laminar air systems may argue that only randomized controlled trials can give definitive answers about the effectiveness of such system, it is questionable whether the overall conclusions would change. Because of heterogeneity of definitions and outcome measures of this technology, no systematic review to date has been able to pool clinical effect sizes.

Limitations

This research has a number of limitations that should be addressed. First of all, results of model-based economic evaluations are always dependent on the model structure and assumptions made. Models consider key events related to a decision problem and represent a simplification of real events. All transition probabilities were estimated from Queensland hospital data and generalized to Australia; in reality, treatment pathways of patients may vary by region and under different infection prevention strategies. This information is unknown and could not be incorporated in the model.

Costs of treating SSIs were estimated using hospital accounting costs rather than economic costs. This considers only direct costs associated with in-hospital treatment and does not include opportunity costs, e.g., hospital bed-days or staff time that cannot be used for other purposes. The costs of antibiotic prophylaxis and annual capital costs of LOR were based on expert opinion, which is regarded as the lowest quality type of evidence. Nevertheless, scenario analysis showed that variation in these costs did not change the conclusions.

Model outcomes did not include possible future increases in resistant organisms because the mechanisms of antibiotic resistance are at present not well understood. There could be future costs in switching from common antibiotic agents to potentially more expensive agents (such as vancomycin) for the treatment of resistant strains.

Implications for decision makers

This work has shown that the use of AP combined with antibiotic cement is the cost-effective strategy for preventing deep SSI in hip arthroplasty. Currently, not all Australian hospitals use this approach in (cemented) primary THAs. If these health care facilities adopted this strategy, valuable resources could be freed and allocated to other much needed areas.

Because LOR were responsible for increased SSI rates and AUD $4.59 million higher costs, their use is not recommended. Although these systems have been shown to reduce the number of colony-forming units in the operating room, the link to SSIs remains unclear. While the presence of bacteria in the operating room is decreased, the augmented incidence of infections might be due to the top-down direction of airflow and increased air circulation, which are key characteristics of laminar air systems. The direct airflow over the heads of surgical staff onto the surgical site and a generally decreased temperature of the wound (an established risk factor for SSI) are plausible explanations.

Current evidence suggests that the use of conventional operating rooms with HEPA-filtered air with turbulent ventilation is the better alternative. Health care facilities could benefit from not utilizing these systems by potentially avoiding substantial costs while improving health outcomes.

CONCLUSION

This project contributes to a framework for decision making in infection control in Australia and possibly other countries with comparable structures. The routine use of preoperative AP is cost-effective and should be continued. Resource allocation can be
further improved by additionally using antibiotic-impregnated cement in all cemented primary THAs. Laminar air operating theaters proved harmful to patients as well as being costly. Based on this evidence, their use is not recommended. Opportunity costs of not using the best available strategy to prevent deep SSI can be avoided by implementing the routine use of AP + ABC in primary THAs in Australia.

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