Laminar airflow and surgical site infections: the evidence is blowing in the wind

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More than a million joint arthroplasties are done each year; with an ageing population, numbers of arthroplasties might grow two to six times by 2030.[1] A major concern is the risk of operating room-acquired prosthetic joint infections, which cause substantial morbidity, prolonged treatment in hospital, repeat surgeries, prolonged antibiotic use, and patient, family, and societal stresses—all at great cost.[2]

Several factors contribute to the risk of prosthetic joint infections, including patient age and co-morbidities, especially diabetes and obesity, skill of the surgeon, extent of the operating team's attention to principles of asepsis, and contamination of the surgical site by bacteria shed from patient and staff skin and mucosal microbiomes and by airborne microbes in the operating room.

Interventions that are recommended to reduce infection risks—when possible, on the basis of randomised controlled trials—include administration of intravenous perioperative antibiotic prophylaxis; ensuring of proper surgical site preparation and, in some instances, preoperative nasal decolonisation for patients who carry *Staphylococcus aureus*; prohibition of extraneous operating room conversations and movements, to limit concentrations of shed and airborne bacteria; maintenance of the operating room architectural infrastructure and hygienic environment; and reporting infection rates.[3] Interventions often are bundled into surgical care checklists, without clear delineation of the relative importance of the components. With skilled surgeons and adherence to infection control recommendations, risk of prosthetic joint infections has decreased considerably in the past 40 years from 10% to 0·5–1%.[4]

Concern about infection control in the hospital environment has been subject to swings in opinion in the past 60 years. In the landmark study of Lidwell and colleagues,[4] done in the 1970s, laminar airflow (LAF) filtration that provided ultraclean air in operating rooms was associated with a reduction of prosthetic joint infections from 1·5% to 0·6%. Although revolutionary at the time, this and other studies had methodological problems and might no longer apply to present-day operating rooms, designed with high efficiency particulate air filtration; and LAF technology might have reduced potential to affect risks of prosthetic joint infection in light of other current interventions. More recent studies of the efficacy of LAF for infection control also had major design drawbacks—eg, no randomisation or no control population, confounded by the robust inventory of other interventions, and yielded conflicting results. However, despite the grading of LAF for preventing surgical site infections (SSIs) as "of indeterminate benefit" in international guidelines,[3,5] LAF is widely used.

In *The Lancet Infectious Diseases*, Peter Bischoff and colleagues[6] provide important support for infection control decision making by expanding on their previous meta-analysis of the effect of LAF on SSIs. Bischoff and colleagues review total hip and knee arthroplasties and abdominal and open vascular surgery studies that evaluated LAF technology and were done since 1990. Because abdominal and vascular procedures are an unusual combination for joint replacement surgery, we comment here only on the role of LAF for arthroplasties.

Bischoff and colleagues' extensive systemic review yielded information about 464 514 joint replacement procedures from 12 studies, mostly using large observational cohorts. None of the studies had a randomised study design. Meta-analyses were once proposed as a method to derive precise estimates of efficacy from studies testing similar interventions, under reasonably similar conditions, in comparable patient populations (ie, low clinical heterogeneity, for which an objectively quantifiable measure is absent), and yielding effect estimates of individual studies pointing in the same direction (ie, revealing low statistical heterogeneity, quantified by the inconsistency index [I^2]). However, the 12 studies in Bischoff and colleagues' review had both high clinical heterogeneity (based on study designs, definitions of infections, air handling policies in the control populations, and infection control settings) and high statistical heterogeneity in the meta-analyses (based on the derived I^2). Some observers might question the scientific appropriateness of pooling data with so much heterogeneity.[7] Nevertheless,

the pooled data did not find a protective effect of LAF on prosthetic joint infection risk (odds ratio *vs* conventional ventilation for total hip arthroplasties 1·29 [95% CI 0·98–1·71] and for total knee arthroplasty 1·08 [0·77–1·52]), even in extensive sensitivity analyses. And creation and maintenance of LAF in the operating room, including regular validation tests to document adherence to arbitrarily chosen air contamination thresholds, is more expensive than use of conventional operating room ventilation strategies. Thus, this study adds another layer of so-called failing evidence for an intervention heavily debated by infection control experts, surgeons, and anaesthesiologists in the past 25 years.

What is the take home message for medical leadership and hospital administrators? Effort and money should be directed at implementation and monitoring of adherence to the successful interventions that have been subjected to carefully designed randomised controlled trials,[3] and that have benefitted patients by reducing infection risks. Until evidence is truly provided, the recommendations should not include LAF technology in operating rooms for the prevention of SSIs.

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1 Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007; **89:** 780–85.
2 Darouiche RO. Treatment of infections associated with surgical implants. *N Engl J Med* 2004; **350:** 1422–29.
3 Anderson DJ, Podgorny K, Berríos-Torres SI, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014; **35:** 605–27.
4 Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomised study. *BMJ* 1982; **285:** 10–14.
5 Sehulster L, Chinn RY, for CDC and HICPAC. Guidelines for environmental infection control in health-care facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR Recomm Rep* 2003; **52:** 1–42.
6 Bischoff P, Zeynep Kubilay N, Allegranzi B, Egger M, Gastmeier P. Effect of laminar airflow ventilation on surgical site infections: a systematic review and meta-analysis. *Lancet Infect Dis* 2017; published online Feb 16. http://dx.doi.org/10.1016/S1473-3099(17)30059-2.
7 Melsen WG, Bootsma MC, Rovers MM, Bonten MJ. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. *Clin Microbiol Infect* 2014; **20:** 123–29.

Effect of laminar airflow ventilation on surgical site infections: a systematic review and meta-analysis

Peter Bischoff, N Zeynep Kubilay, Benedetta Allegranzi, Matthias Egger, Petra Gastmeier

Summary

Background The role of the operating room's ventilation system in the prevention of surgical site infections (SSIs) is widely discussed, and existing guidelines do not reflect current evidence. In this context, laminar airflow ventilation was compared with conventional ventilation to assess their effectiveness in reducing the risk of SSIs.

Methods We searched MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and WHO regional medical databases from Jan 1, 1990, to Jan 31, 2014. We updated the search for MEDLINE for the period between Feb 1, 2014, and May 25, 2016. We included studies most relevant to our predefined question: is the use of laminar airflow in the operating room associated with the reduction of overall or deep SSI as outcomes in patients of any age undergoing surgical operations? We excluded studies not relevant to the study question, studies not in the selected languages, studies published before Jan 1, 1990, or after May 25, 2016, meeting or conference abstracts, and studies of which the full text was not available. Data were extracted by two independent investigators, with disagreements resolved through further discussion. Authors were contacted if the full-text article was not available, or if important data or information on the paper's content was absent. Studies were assessed for publication bias. Grading of recommendations assessment, development, and evaluation was used to assess the quality of the identified evidence. Meta-analyses were done with RevMan (version 5.3).

Findings We identified 1947 records of which 12 observational studies were comparing laminar airflow ventilation with conventional turbulent ventilation in orthopaedic, abdominal, and vascular surgery. The meta-analysis of eight cohort studies showed no difference in risk for deep SSIs following total hip arthroplasty (330 146 procedures, odds ratio [OR] 1·29, 95% CI 0·98–1·71; p=0·07, I^2=83%). For total knee arthroplasty, the meta-analysis of six cohort studies showed no difference in risk for deep SSIs (134 368 procedures, OR 1·08, 95% CI 0·77–1·52; p=0·65, I^2=71%). For abdominal and open vascular surgery, the meta-analysis of three cohort studies found no difference in risk for overall SSIs (63 472 procedures, OR 0·75, 95% CI 0·43–1·33; p=0·33, I^2=95%).

Interpretation The available evidence shows no benefit for laminar airflow compared with conventional turbulent ventilation of the operating room in reducing the risk of SSIs in total hip and knee arthroplasties, and abdominal surgery. Decision makers, medical and administrative, should not regard laminar airflow as a preventive measure to reduce the risk of SSIs. Consequently, this equipment should not be installed in new operating rooms.

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Introduction

Surgical site infections (SSIs) range between the leading and the second most commonly reported health-care-associated infections worldwide, and are associated with increased morbidity, length of stay in hospital, and costs.[1–5] The role of the operating room's ventilation system in preventing SSIs has been discussed for many decades.[6]

Numerous studies have shown a reduction of air contamination associated with the use of laminar airflow, often referred to as ultraclean ventilation systems, compared with other types of operating room ventilation assessed by bacterial and particle counts.[7–11] However, recent evidence suggests that air contamination might not be associated with wound contamination.[7] Even more important, the association of microbial air contamination with SSIs has not been shown so far. In some countries, terminal high efficiency particulate air (HEPA) filters are recommended for laminar airflow only.[12,13] In other countries, their use is recommended for conventional ventilation systems and based on national regulations or technical standards.[14]

The keystone study investigating the effect of operating room ventilation systems on SSIs was done from 1974 to 1979 in the UK and Sweden.[15] The investigators found a significant reduction of deep SSIs in total hip and knee arthroplasties associated with the use of ultraclean ventilation in the operating room by comparison with procedures done in conventionally ventilated operating rooms. The use of body-exhaust suits was left to the discretion of the surgical team. It is not clear whether the modern positive-pressure air supply of the operating rooms in the control group of the study compares with conventional turbulent ventilation systems used in operating rooms today. Furthermore, there was no uniform method for random allocation and the study did not control for the administration of surgical antibiotic prophylaxis, which was given in about 60% of patients.

Research in context

Evidence before this study

Surgical site infections (SSIs) range between the leading and the second most commonly reported category of health-care-associated infections worldwide. The role of the laminar airflow ventilation system in preventing SSIs has been discussed for many decades, especially regarding orthopaedic implant surgery. A randomised trial done in the 1970s, which did not control for the administration of prophylactic antibiotics, showed a reduction of deep SSIs in total hip and knee arthroplasties associated with the use of laminar airflow in the operating room by comparison with procedures done in conventionally ventilated operating rooms; however, these findings could not be reproduced in large studies published thereafter. A 2012 systematic review found laminar airflow to be associated with an increased risk of deep SSIs following total hip and knee arthroplasties. We searched MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and WHO regional medical databases from Jan 1, 1990, to Jan 31, 2014, with a combination of search terms of "ventilation", "surgical wound infection", and "operating rooms". The search was updated for MEDLINE for the period between Feb 1, 2014, and May 25, 2016.

Added value of this study

By contrast with the 2012 systematic review, the search strategy was extended for this study including broader time limits, more databases, and a more rigorous hand search. We could include seven additional studies leading to a substantially increased number of procedures used for the meta-analyses. By adding data from several countries, we could decrease the risk of indirectness. We show that after total hip and knee arthroplasties and abdominal surgery there is no difference in SSIs whether the operations are done in operating rooms equipped with laminar airflow or with conventional ventilation systems. Our study makes an important contribution to understanding the effects of laminar airflow ventilation on clinical outcomes. We are now more confident in saying that laminar airflow does not reduce the risk of SSIs after total hip and knee arthroplasties, which implies that we can save the resources, rather than saying that laminar airflow increases or even decreases the risk.

Implications of all the available evidence

Given the available evidence shown by this systematic review and previous cost-effectiveness analyses, which found laminar airflow systems to be more expensive than conventional ventilation systems, operating rooms equipped with laminar airflow should not be used as a preventive measure to reduce the risk of SSIs. Because randomised trials are not likely to be done, national surveillance systems and registries would need to provide internationally standardised information about risk factors and confounders, and should use internationally standardised SSI definitions to increase our confidence in the results of further cohort studies.

From 1974 to 1985, a non-randomised, single centre study comparing the association of laminar airflow in a tent-like enclosure within the operating room and HEPA-filtered conventional ventilation on deep SSI after various arthroplasties, mainly total hip arthroplasty, found no difference in risk.[16] Surgical antibiotic prophylaxis, which was introduced in this hospital in 1979, resulted in a significant decrease in SSIs in both settings. The first published study in which patients were randomly assigned to operating rooms equipped with horizontal laminar airflow or to conventional airflow and in which all patients received appropriate surgical antibiotic prophylaxis was done from 1981 to 1990.[17] The investigators found no difference in risk of deep SSIs following total hip and knee arthroplasties.

Investigators of a systematic review published in 2012 on the effect of laminar airflow on prosthetic joint infections found laminar airflow ventilation to be a risk factor for the development of severe SSIs.[18] There are only a few current guidelines that have provided recommendations regarding ventilation systems in the operating room. The US Centers for Disease Control and Prevention guidelines for environmental infection control in health-care facilities issued in 2003 offer no recommendation for doing orthopaedic implant operations in operating rooms supplied with laminar airflow because of inadequate evidence.[19] The SSI prevention guidelines published by the Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America in 2014 support the American Institute of Architects' recommendations for air handling in the operating room.[20] The Royal College of Anaesthetists' guidelines for the provision of anaesthesia services issued in 2016 recommend that major joint replacements are done in an operating room with multiple air changes per hour, not necessarily equipped with laminar airflow, to reduce the risks of wound infection.[21]

The purpose of this systematic review was to assess the effectiveness of ventilation systems in the operating room for the prevention of SSI. In this context, laminar airflow ventilation was compared with conventional ventilation in any type of surgery. We did this review within the framework of developing WHO Global Guidelines for the Prevention of Surgical Site Infections issued in 2016.

For the **WHO Global Guidelines and SSI Series** see http://www.thelancet.com/series/surgical-site-infection

Methods

Search strategy and selection criteria

To evaluate the evidence on this topic, we assessed the literature according to a predefined question: is the use

of laminar airflow in the operating room associated with the reduction of overall or deep SSI?

The population was inpatients and outpatients of any age undergoing surgical operations. Ventilation systems of operating rooms without laminar airflow technology were considered as the comparator. In most cases, these systems would be classified as conventional, ordinary, mixed, or turbulent ventilation systems with or without HEPA-filtered air. Superficial, deep, and overall SSIs were considered outcomes. SSIs referred to in primary studies as severe SSI, periprosthetic infection, or deep infection requiring revision were considered deep SSIs.

We searched MEDLINE, Embase, Cochrane Central Register of Controlled Trials, and WHO regional medical databases. We used a comprehensive list of search terms—ie, "ventilation", "surgical wound infection", and "operating rooms"—including Medical Subject Headings (appendix pp 1, 2), for studies published between Jan 1, 1990, and Jan 31, 2014. We updated the search for MEDLINE for the period between Feb 1, 2014, and May 25, 2016. We restricted the language to English, French, German, and Spanish. Two independent reviewers (PB and PG) screened the titles and abstracts of retrieved references for potentially relevant studies. The full text of all potentially eligible articles was obtained and then reviewed independently by two authors (PB and PG) for eligibility. Exclusion criteria were studies not relevant to the predefined study question, studies not in the selected languages, studies published before Jan 1, 1990, or after May 25, 2016, meeting or conference abstracts, and studies of which the full text was not available for review. Duplicate studies were also excluded. We systematically screened the reference lists of all reviewed studies and of literature reviews for further eligible publications. Authors were contacted if the full-text article was not available, or if important data or information on the paper's content were missing. We reported this systematic review and meta-analysis in accordance with the PRISMA statement.[22]

Data analysis

The two investigators (PB and PG) extracted data and populated a predefined evidence table (including information about year of publication, study design, setting, scope, location, population, type of surgery, SSI definitions, statistical method, and limitations; appendix pp 3–17), and critically appraised the retrieved studies. Quality was assessed with the Newcastle–Ottawa Quality Assessment Scale (NOS) for cohort studies (appendix p 18).[23] Any disagreements were resolved through discussion or after consultation with NZK, when necessary. Meta-analyses of available comparisons were done with RevMan (version 5.3) as appropriate.[24] Crude estimates were pooled as odds ratios (ORs) with 95% CIs by use of a DerSimonian and Laird random effect model for each comparison (appendix pp 19–24).[25] Sensitivity analyses were completed to test the robustness of our findings. Heterogeneity in studies was tested with use of the inconsistency index (I^2).[26] Funnel plots were created to assess whether publication bias occurred (appendix pp 19, 21, 23).[27] The Grading of Recommendations Assessment, Development and Evaluation (GRADE) method (GRADEpro software) was used to assess the quality of evidence retrieved as appropriate.[28]

For the **GRADEpro guideline development tool** see http://www.gradepro.org

Role of the funding source

There was no funding source for this study. The corresponding author had full access to all study data and had final responsibility for the decision to submit the manuscript for publication.

Results

The figure shows the study selection process. The initial search identified 1947 records. After removal of duplicates and screening, 109 full-text articles were assessed for eligibility. Of those assessed, 12 observational cohort studies[29–40] comparing laminar airflow with conventional ventilation in the operating room were identified. Few investigators reported the use of conventional turbulent ventilation with HEPA-filtered air,[30,36,37] whereas most investigators described the ventilation system used in the control group as conventional (plenum) or ordinary—ie, without the notion of HEPA filters.[29,31,35,38,39] In

See **Online** for appendix

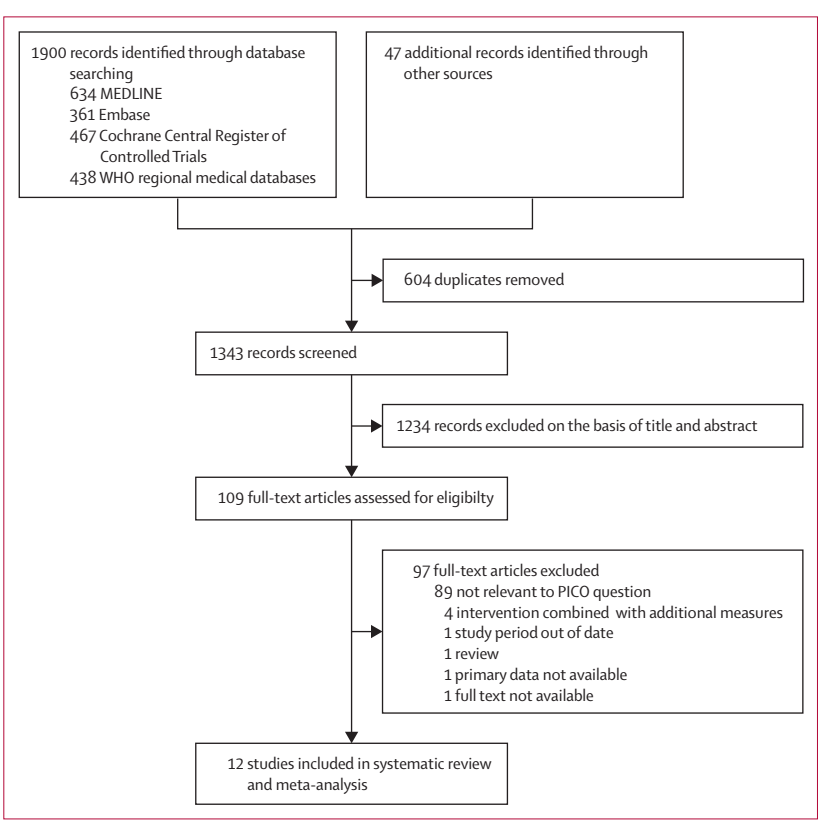

Figure: **Flow diagram of study selection**
PICO=population, intervention, comparator, and outcome.

	Procedures (intervention/control)	Country	Study period	Point estimate (95% CI) for laminar airflow
Total hip arthroplasty				
Kakwani et al (2007)[39]	435 (212/223)	UK	2000–04	RR 0·06 (0·00–0·95)*
Brandt et al (2008)[30]	28 623 (17 657/10 966)	Germany	2000–04	OR 1·63 (1·06–2·52)
Dale et al (2009)[31]	93 958 (45 620/48 338)	Norway	1987–2008	RR 1·3 (1·1–1·5)
Pedersen et al (2010)[35]	80 756 (72 23/8333)	Denmark	1995–2008	HR 0·9 (0·7–1·14)
Breier et al (2011)[37]	41 212 (29 530/11 682)	Germany	2004–09	Arthrosis OR 1·10 (0·56–2·17); fracture OR 1·28 (0·67–2·43)†
Hooper et al (2011)[38]	51 485 (16 990/34 495)	New Zealand	1999–2008	RR 2·42 (1·35–4·32)*
Namba et al (2012)[33]	30 491 (8478/22 013)	USA	2001–09	HR 1·08 (0·77–1·53)
Song et al (2012)[36]	3186 (2037/1149)	South Korea	2006–09	RR 1·2 (0·6–2·16)*
Total knee arthroplasty				
Miner et al (2007)[40]	8288 (3513/4775)	USA	2000	RR 1·57 (0·75–3·31)
Brandt et al (2008)[30]	9396 (5993/3403)	Germany	2000–04	OR 1·76 (0·80–3·85)
Breier et al (2011)[37]	20 554 (14 456/6098)	Germany	2004–09	OR 0·95 (0·37–2·41)
Hooper et al (2011)[38]	36 826 (13 994/22 832)	New Zealand	1999–2008	RR 1·92 (1·10–3·34)*
Song et al (2012)[36]	3088 (2151/937)	South Korea	2006–09	RR 0·51 (0·29–0·89)‡
Namba et al (2013)[34]	56 216 (16 693/39 523)	USA	2001–09	HR 0·91 (0·71–1·16)

RR=risk ratio. HR=hazard ratio. OR=odds ratio. *Not adjusted (relative risk [RR] calculated with crude data, no multivariable analysis). †Adjusted ORs were provided separately for elective procedures due to arthrosis and for urgent procedures due to fracture. ‡Not adjusted (relative risk [RR] calculated with crude data, not significant in multivariable analysis).

Table 1: **Characteristics of primary studies included in the meta-analysis of laminar airflow *vs* conventional ventilation for deep surgical site infection in patients undergoing total hip and knee arthroplasties**

	Procedures (intervention/control)	Country	Study period	Adjusted odds ratio (95% CI) for laminar airflow
Brandt et al (2008)[30]				
Appendectomy	10 969 (7193/3776)	Germany	2000–04	2·09 (1·08–4·02)
Colon surgery	8696 (6201/2495)	Germany	2000–04	1·17 (0·65–2·11)
Cholecystectomy	20 676 (12 419/8257)	Germany	2000–04	1·53 (0·9–2·45)
Herniorrhaphy	20 870 (12 667/8203)	Germany	2000–04	1·67 (0·9–2·91)
Bosanquet et al (2013)[29]				
Open vascular surgery	170 (56/114)	Wales	Not reported	0·38 (0·12–1·19)*
Jeong et al (2013)[32]				
Gastric surgery	2091 (1919/172)	South Korea	2010–11	0·13 (0·08–0·22)*

*Not adjusted (calculated with crude data, the authors provide only adjusted odds ratios for the absence, rather than presence, of laminar airflow: 2·45 [95% CI 1·13–5·31] after gastric surgery and 4·02 [1·18–13·69] after open vascular surgery).

Table 2: **Characteristics of primary studies included in the meta-analysis of laminar airflow *vs* conventional ventilation for overall surgical site infection in patients undergoing abdominal and open vascular surgery**

four studies—investigating total hip[33] and knee[34,40] arthroplasties done in the USA between 2000 and 2009, and gastric surgery[32] done in South Korea between 2010 and 2011—the investigators did not provide additional information about the ventilation system of the operating rooms without laminar airflow. These studies were included after discussion. No randomised clinical trials were included. The populations studied were mostly adult patients. Ten studies focused on total hip arthroplasty (330 146 procedures) or total knee arthroplasty (134 368 procedures; table 1). One small study on hemiarthroplasty of the hip was included with studies on total hip arthroplasty because the procedures are similar.[39] Three single studies were identified for abdominal and open vascular surgery (table 2).[29,30,32] All studies on total hip and knee arthroplasties investigated deep SSIs. Two studies assessed overall (superficial and deep) SSIs.[30,36] We considered deep SSIs the primary outcome for further analysis. Brandt and colleagues[30] reported on overall and deep SSI for abdominal surgery. Two studies on gastric and vascular surgery assessed overall SSIs.[29,32] We considered overall SSI as the primary outcome in abdominal and open vascular surgery. The following comparisons were assessed: laminar airflow ventilation versus conventional ventilation in total hip arthroplasty, total knee arthroplasty, and abdominal and open vascular surgery.

Four of the 12 studies provided data for more than one comparison. We identified eight observational studies[30,31,33,35–39] comparing the association of laminar airflow ventilation and conventional ventilation on deep SSIs after total hip arthroplasty. Three large multicentre studies based on data obtained from national joint registries and surveillance systems showed that laminar airflow was associated with a higher risk of deep SSIs[30] and revision due to infection than was conventional ventilation,[31,38] whereas one small single centre study showed laminar airflow to be associated with a decreased risk of revision due to infection compared with conventional ventilation.[39] The four other studies showed no difference in the risk of deep SSI[33,36,37] or revision due to infection[35] (table 1).

We identified six observational studies[30,34,36–38,40] comparing the effect of laminar airflow ventilation versus conventional ventilation on SSI after total knee arthroplasty. One multicentre joint registry study found laminar airflow to be associated with an increased risk of revision due to infection compared with conventional ventilation.[38] Five studies found no difference in the risk of deep SSI (table 1).[30,34,36,37,40] One study comparing the association of large laminar airflow ceilings with at least 3·2 m² in size and conventional ventilation on deep SSI after total hip and knee arthroplasties found no difference in the risk of deep SSI.[37]

Our meta-analyses found that laminar airflow ventilation did not reduce deep SSIs when compared with conventional ventilation in total hip arthroplasty (p=0·07; table 3 and appendix p 19) or total knee arthroplasty (p=0·65; table 4 and appendix p 21). The quality of the evidence for these comparisons was very low because of inconsistency shown by high I^2 values (appendix p 25). Publication bias was not detected. Kakwani and colleagues[39] reported a small study with a large effect (appendix pp 19, 21).

In a sensitivity analysis, we compared the overall effect of the included studies with or without the studies that did not provide additional information about the ventilation system of the operating rooms without laminar airflow. Results did not differ irrespective of whether the studies were included or not. When excluding the study by Namba and colleagues[33] for total hip arthroplasty, the OR was 1·33 (95% CI 0·97–1·82, p=0·08, I^2=85%; appendix p 20), and 1·11 (0·68–1·83, p=0·68, I^2=75%; appendix p 22) for total knee arthroplasty when excluding the studies by Namba and colleagues[34] and Miner and colleagues.[40]

Concerning other types of surgery, only three single observational studies on abdominal and open vascular surgery were identified with an SSI outcome (table 2).[29,30,32] With regard to this inadequacy of evidence per type of procedure and outcome, the reviewers agreed not to separately assess the quality of evidence with the GRADE method. Laminar airflow was found to be associated with an overall increased SSI risk following appendectomy in one observational study.[30] The same study found no difference in overall risk of SSI in colon surgery, cholecystectomy, and herniorrhaphy in multivariable analysis.[30] In gastric[32] and open vascular surgery,[29] the absence of laminar airflow was found to increase the overall risk of SSI. Our meta-analysis found that laminar airflow ventilation did not reduce overall SSI when compared with conventional ventilation after abdominal and open vascular surgery (p=0·33; table 5 and appendix p 23). In a sensitivity analysis, we compared the overall effect of the included studies with or without the study that did not provide additional information about the ventilation system of the operating rooms without laminar airflow.[32] There was no difference in the results irrespective of whether the study was included or not. However, the effect estimate shifted in the favour of conventional ventilation (OR 1·10, 95% CI 0·72–1·68, p=0·66, I^2=91%; appendix p 24). Publication bias was not detected. With only a few studies included, the interpretation of the funnel plot is limited but there might be an inadequacy of small-to-medium-sized studies showing no effect or an effect in favour of conventional ventilation (appendix p 23).

Four additional single centre studies were identified with combined interventions; laminar airflow in combination with behavioural changes in the operating room such as discipline code in total hip and knee arthroplasties,[41] closed operating room doors versus open doors in the control group in cardiac surgery with sternotomy,[42] and wearing of body exhaust gowns in spinal surgery and total hip and knee arthroplasties.[43,44] Because these studies had additional interventions and were compared with conventional ventilation without the same additional measures, they were excluded from further assessment. One randomised trial comparing the association of horizontal laminar airflow ventilation and conventional ventilation on deep SSI after total hip

	Laminar airflow		Conventional ventilation		Weight	Odds ratio (95% CI)
	Events	Total	Events	Total		
Kakwani et al (2007)[39]	0	212	9	223	0·9%	0·05 (0·00–0·92)
Brandt et al (2008)[30]	242	17 657	99	10 966	16·1%	1·53 (1·21–1·93)
Dale et al (2009)[31]	324	45 620	260	48 338	17·1%	1·32 (1·12–1·56)
Pedersen et al (2010)[35]	517	72 423	80	8333	16·0%	0·74 (0·59–0·94)
Breier et al (2011)[37]	356	29 530	77	11 682	15·9%	1·84 (1·44–2·36)
Hooper et al (2011)[38]	25	16 990	21	34 495	10·1%	2·42 (1·35–4·32)
Namba et al (2012)[33]	46	8478	109	22 013	14·2%	1·10 (0·78–1·55)
Song et al (2012)[36]	34	2037	16	1149	9·8%	1·20 (0·66–2·19)
Total	1544	192 947	671	137 199	100·0%	1·29 (0·98–1·71)

Events are number of surgical site infections. Test for heterogeneity showed very high inconsistency between the studies (I^2=83%).

Table 3: **Meta-analysis comparing the risk of deep surgical site infection after total hip arthroplasty for laminar airflow *vs* conventional ventilation**

	Laminar airflow		Conventional ventilation		Weight	Odds ratio (95% CI)
	Events	Total	Events	Total		
Miner et al (2007)[40]	15	3513	13	4775	11·4%	1·57 (0·75–3·31)
Brandt et al (2008)[30]	55	5993	22	3403	16·5%	1·42 (0·87–2·34)
Breier et al (2011)[37]	93	14 456	36	6098	19·1%	1·09 (0·74–1·60)
Hooper et al (2011)[38]	27	13 994	23	22 832	15·1%	1·92 (1·10–3·34)
Song et al (2012)[36]	27	2151	23	937	15·0%	0·51 (0·29–0·89)
Namba et al (2013)[34]	105	16 693	299	39 523	22·9%	0·83 (0·66–1·04)
Total	322	56 800	416	77 568	100·0%	1·08 (0·77–1·52)

Events are number of surgical site infections. Test for heterogeneity showed high inconsistency between the studies (I^2=71%).

Table 4: **Meta-analysis comparing the risk of deep surgical site infection after total knee arthroplasty for laminar airflow *vs* conventional ventilation**

	Laminar airflow		Conventional ventilation		Weight	Odds ratio (95% CI)
	Events	Total	Events	Total		
Brandt et al (2008)[30]						
Appendectomy	194	7193	70	3776	18·0%	1·47 (1·11–1·93)
Cholecystectomy	191	12 419	109	8257	18·3%	1·17 (0·92–1·48)
Colon surgery	316	6201	176	2495	18·5%	0·71 (0·58–0·86)
Herniorrhaphy	198	12 667	69	8203	18·1%	1·87 (1·42–2·47)
Bosanquet et al (2013)[29]						
Open vascular surgery	4	56	19	114	10·8%	0·38 (0·12–1·19)
Jeong et al (2013)[32]						
Gastric surgery	45	1919	26	172	16·4%	0·13 (0·08–0·22)
Total	948	40 455	469	23 017	100·0%	0·75 (0·43–1·33)

Events are number of surgical site infections. Test for heterogeneity showed very high inconsistency between the studies (I^2=95%).

Table 5: **Meta-analysis comparing the risk of overall surgical site infection after abdominal and open vascular surgery for laminar airflow *vs* conventional ventilation**

and knee arthroplasties was excluded after discussion because the entire study period was before 1990.[17] This trial found no significant difference in deep SSIs after total hip and knee arthroplasties. One large, multicentre, joint registry study reporting on the comparison of laminar airflow with ordinary ventilation in total hip arthroplasty was excluded because missing primary data could not be retrieved from the authors upon request.[45] The investigators described that they did not detect any difference in relative risk of revision due to infection.

The literature search did not identify any studies that reported on SSI-attributable mortality. At the time of our updated search, covering Feb 1, 2014, to May 25, 2016, we did not identify any further eligible studies for this study question. However, a study published in March, 2016, on total knee arthroplasty, which would have been eligible for inclusion, was later identified. Inclusion of this study[46] into the meta-analysis would not have changed our results (162 108 procedures, OR 1·05, 95% CI 0·78–1·42; p=0·74, I^2=71%).

The individual cohort studies included in the systematic review had NOS scores ranging from five to eight of nine possible items (appendix p 18).

Discussion

Our systematic review and meta-analysis showed that laminar airflow ventilation does not reduce the risk of deep SSIs after total hip and knee arthroplasties compared with conventional operating room ventilation. The probability of developing a deep SSI following total hip arthroplasty is higher in the laminar airflow condition than in conventional ventilation, although this effect was not significant. The evidence is more inadequate for other procedures, but it seems that laminar airflow does not reduce the risk of overall SSIs after abdominal and open vascular surgery. The findings of our meta-analysis are consistent with the results of previous literature reviews,[18,47,48] adding several studies to the body of evidence.

This meta-analysis had some limitations. First, most data were obtained from national surveillance systems and registries. Although surveillance databases and registries often provided large sample sizes, these databases were not designed specifically to address whether laminar airflow systems decrease the risk of SSIs. Surveillance databases and registries might not include data for possible confounders related to risk factors and the infection rate, such as smoking, obesity, intraoperative temperature, glycaemia, or cautery. More important, some studies did not provide information about the ventilation systems used in the operating rooms without laminar airflow.[32–34,40] However, we decided to include them after discussion. In a South Korean study,[32] 26% of the operating rooms in the control group were equipped with HEPA filters. Furthermore, we believe that, in the USA, total hip and knee arthroplasties were done in conventional operating rooms if not in operating rooms equipped with laminar airflow. Corresponding recommendations on operating room ventilation had been issued before the study periods.[13] In our sensitivity analysis, there was no difference in the results whether the studies were included or not. Second, because data from a surveillance database and registry are submitted by numerous hospitals, differences in hospital or surgeon volume, patient characteristics, or implementation of other SSI prevention measures might confound the results. Third, the definitions for severe SSIs differed across the individual studies. Fourth, the meta-analysis measured crude data from the primary studies. For example, crude data from two multicentre studies (n=80 756 and n=3088) indicated that laminar airflow was associated with decreased risk of deep SSIs. By contrast, the adjusted and multivariable analyses of these studies did not find a difference in risk.[35,36] Overall, these factors led to considerable heterogeneity found in the statistical tests indicted by an I^2 of 83% for deep SSIs of laminar airflow versus conventional ventilation in total hip arthroplasty, 71% for deep SSI of laminar airflow versus conventional ventilation in total knee arthroplasty, and 95% for overall SSI of laminar airflow versus conventional ventilation in abdominal and open vascular surgery (appendix pp 19, 21, 23). Results from the studies that reported a benefit from laminar airflow ventilation might have been biased because the SSI in the control group was high and almost all operations were done in operating rooms with laminar airflow ventilation (n=1919 and control n=172),[32] or the study size was small (n=435 and n=170)[29,39] and the casemix was heterogeneous.[29]

We excluded studies that were published before 1990. After discussion we excluded a study because its entire study period was before 1990.[17] This time limit is arbitrarily set and debatable. We considered that the

ventilation systems used before 1990 might not technically compare with the ventilation systems used in hospitals today for orthopaedic implant surgery. Furthermore, not only has operating room ventilation technology improved in the past 20–30 years but the use of surgical antibiotic prophylaxis has become a standard practice. Apart from the study published by Lidwell and colleagues,[15] there are four more studies published between 1981 and 1992, covering the period from 1972 to 1990, and investigating the association of laminar airflow and conventional ventilation with deep SSIs after total hip and knee arthroplasties.[16,17,49,50] One observational study[16] and one randomised trial[17] found no difference in risk. One observational study[49] found no difference in risk in total hip arthroplasty and an increased risk associated with laminar airflow in total knee arthroplasty. A randomised trial focusing on administration of prophylactic antibiotics in total hip arthroplasty found that with antibiotic prophylaxis there is no difference in risk.[50] Inclusion of the studies would not have changed the findings and conclusion of this review. Unfortunately, the current version of the NOS does not provide a threshold score, which substantially limits its ability to differentiate between studies with good quality and those with poor quality.

The concept of creating a clean, particle-free zone by ultra-clean low-turbulence displacement flow originated from a need for a clean environment for industrial manufacturing. However, during surgical procedures, several forces and obstacles disrupt the airflow, reducing the effectiveness of this intervention. For example, obstacles such as lights, personnel, and instruments create a turbulent reverse flow on their lee sides; heat-emitting operating lights, heating devices, and the body heat from the operating room personnel create thermal convection currents; and ventilation exhausts from medical equipment such as saws or drills all disrupt the laminar airflow. Additionally, operating room personnel and medical devices disburse airborne microorganisms and particles. Consequently, the operating room air around the open surgical field is not particle-free.[51–55] Furthermore, the fresh air from a laminar airflow system cools the surgical wound and the patient, which can reduce tissue temperatures in the surgical wound or cause systemic hypothermia, if the patient's temperature is not monitored and maintained intraoperatively. Yang and colleagues' recent study[56] found that the odds ratio of becoming hypothermic were 1·53 (95% CI 1·19–1·96) for patients whose procedures were done in laminar airflow rooms compared with patients whose procedures were done in traditional operating rooms.

Previous cost-effectiveness analyses found laminar airflow to be more expensive than conventional ventilation systems. An Italian study[57] found that building costs increased 24% and annual operating costs increased 36%. In Australia, Merollini and colleagues[58] assessed the costs of doing total hip arthroplasty and found that doing the procedures in operating rooms with laminar airflow would add AUS$4·59 million per 30 000 procedures done.[58] In Germany, Kramer and colleagues[59] calculated additional costs of €3·24 per procedure if 1000 procedures were done in operating rooms with laminar airflow per year for 15 years. Graves and colleagues[60] evaluated strategies to reduce the risk of deep SSIs following total hip arthroplasty and concluded that the combination of administering systemic antibiotics, with antibiotic-impregnated cement, and doing this procedure in operating rooms with conventional ventilation led to the largest annual cost savings and the greatest gains in quality-adjusted life-years. Inclusion of laminar airflow instead of conventional ventilation showed higher costs and worse health outcomes.[60] Additionally, validation of laminar airflow ventilation systems is more expensive than conventional ventilation systems, without having any method and target limits based on scientific evidence of the relation between contamination of the air and risk of SSIs.[61] The threshold limit of ultra-clean air was arbitrarily defined by Lidwell and colleagues as less than ten colony-forming units per m^3 and has been used as the standard ever since.[15,62]

The previous studies assessing whether laminar airflow ventilation decreases the risk of SSI had numerous weaknesses, and the evidence provided by those is of low quality. The last randomised trials addressing this question were done in the 1970s and 1980s.[15,17] Thus, we need further research, particularly well designed clinical trials of endoprosthetic surgery, to determine whether operating room ventilation reduces SSIs. However, we believe that such trials will probably not be done. Randomised clinical trials might not be reasonable because they would require very large sample size to have enough power to detect a significant difference and would be very expensive. For example, if deep SSIs in the control group was about 0·5% after total hip and knee arthroplasties (appendix p 25), approximately 10 000 patients would be needed in each group to detect a 50% reduction to an SSI of 0·25% ($1-\alpha$ 95%, $1-\beta$ 80%). Even more patients would be needed to detect a difference of 40% or 30%. Cluster randomised trials could be problematic because it would be almost impossible to control for confounding factors in between the sites, such as different surgeons operating in the same operating room. Therefore, nationwide databases might provide the best affordable information. However, to avoid the weakness of previous studies and meta-analyses thereof, national surveillance systems and registries would need to provide consistent and internationally standardised information about risk factors and confounders, such as the operating room ventilation system. Furthermore, surveillance of health-care-associated infections should be based on internationally standardised definitions.

Very low-quality evidence suggests that compared with conventional ventilation, laminar airflow ventilation does not reduce the risk of deep SSI after total hip and

knee arthroplasties. Inadequate evidence suggests that laminar airflow does not reduce the overall SSI when compared with conventional ventilation after abdominal and open vascular surgery. Conventional operating room ventilation systems appear to provide air that is clean enough for procedures involving orthopaedic implants. Given the available evidence shown by this systematic review and the previous cost-effectiveness analyses—which found laminar airflow systems to be more expensive than conventional ventilation systems—the surgical team, infection prevention and control professionals, hospital administrators, and policy makers should not install laminar airflow equipment in new operating rooms. Although, there seems to be no need to discontinue surgery in existing operating rooms equipped with laminar airflow, it should not be regarded as a preventive measure to reduce the risk of SSIs.

Contributors

BA and NZK designed the study. PB and PG did the study. PB, PG, NZK, ME, and BA analysed and interpreted the data. PB drafted the manuscript. PB, NZK, and BA contributed to the writing of the manuscript. All authors helped to revise the manuscript.

Declaration of interests

We declare no competing interests.

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References

1 Allegranzi B, Bagheri Nejad S, Combescure C, et al. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. *Lancet* 2011; **377:** 228–41.

2 Magill SS, Edwards JR, Bamberg W, et al. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med* 2014; **370:** 1198–208.

3 European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011–2012. 2013. http://www.ecdc.europa.eu/en/publications/Publications/Forms/ECDC_DispForm.aspx?ID=1155 (accessed May 24, 2016).

4 de Lissovoy G, Fraeman K, Hutchins V, Murphy D, Song D, Vaughn BB. Surgical site infection: incidence and impact on hospital utilization and treatment costs. *Am J Infect Control* 2009; **37:** 387–97.

5 Broex EC, van Asselt AD, Bruggeman CA, van Tiel FH. Surgical site infections: how high are the costs? *J Hosp Infect* 2009; **72:** 193–201.

6 Charnley J. Operating-theatre ventilation. *Lancet* 1970; **1:** 1053–54.

7 Birgand G, Toupet G, Rukly S, et al. Air contamination for predicting wound contamination in clean surgery: a large multicenter study. *Am J Infect Control* 2015; **43:** 516–21.

8 Diab-Elschahawi M, Berger J, Blacky A, et al. Impact of different-sized laminar air flow versus no laminar air flow on bacterial counts in the operating room during orthopedic surgery. *Am J Infect Control* 2011; **39:** e25–29.

9 Erichsen Andersson A, Petzold M, Bergh I, Karlsson J, Eriksson BI, Nilsson K. Comparison between mixed and laminar airflow systems in operating rooms and the influence of human factors: experiences from a Swedish orthopedic center. *Am J Infect Control* 2014; **42:** 665–69.

10 Hansen D, Krabs C, Benner D, Brauksiepe A, Popp W. Laminar air flow provides high air quality in the operating field even during real operating conditions, but personal protection seems to be necessary in operations with tissue combustion. *Int J Hyg Environ Health* 2005; **208:** 455–60.

11 Hirsch T, Hubert H, Fischer S, et al. Bacterial burden in the operating room: impact of airflow systems. *Am J Infect Control* 2012; **40:** e228–32.

12 UK Department of Health. Heating and ventilation of health sector buildings (HTM 03-01): specialised ventilation for healthcare premises. 2007. http://www.gov.uk/government/publications/guidance-on-specialised-ventilation-for-healthcare-premises-parts-a-and-b (accessed May 24, 2016).

13 Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999; **27:** 97–132.

14 Nastase I, Croitoru C, Vartires A, Tataranu L. Indoor environmental quality in operating rooms: an European standards review with regard to Romanian guidelines. *Energy Procedia* 2016; **85:** 375–82.

15 Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomised study. *BMJ* 1982; **285:** 10–14.

16 Marotte JH, Lord GA, Blanchard JP, et al. Infection rate in total hip arthroplasty as a function of air cleanliness and antibiotic prophylaxis. *J Arthroplasty* 1987; **2:** 77–82.

17 Fitzgerald RH Jr. Total hip arthroplasty sepsis. Prevention and diagnosis. *Orthop Clin North Am* 1992; **23:** 259–64.

18 Gastmeier P, Breier AC, Brandt C. Influence of laminar airflow on prosthetic joint infections: a systematic review. *J Hosp Infect* 2012; **81:** 73–78.

19 Sehulster L, Chinn RY. Guidelines for environmental infection control in health-care facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR Recomm Rep* 2003; **52:** 1–42.

20 Anderson DJ, Podgorny K, Berrios-Torres SI, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014; **35:** 605–27.

21 The Royal College of Anaesthetists. Guidelines for the Provision of Anaesthetic Services (GPAS) 2016. 2016. http://www.rcoa.ac.uk/gpas2016 (accessed Nov 4, 2016).

22 Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6:** e1000097.

23 Wells GA, Shea B, O'Connell D, et al. The Newcastle–Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed Feb 8, 2014).

24 The Nordic Cochrane Centre TCC. Review Manager (RevMan). Version 5.3. Copenhagen: the Cochrane Collaboration. 2014.

25 DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7:** 177–88.

26 Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002; **21:** 1539–58.

27 Sterne JA, Egger M, Smith GD. Systematic reviews in health care: investigating and dealing with publication and other biases in meta-analysis. *BMJ* 2001; **323:** 101–05.

28 Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011; **64:** 383–94.

29 Bosanquet DC, Jones CN, Gill N, Jarvis P, Lewis MH. Laminar flow reduces cases of surgical site infections in vascular patients. *Ann R Coll Surg Engl* 2013; **95:** 15–19.

30 Brandt C, Hott U, Sohr D, Daschner F, Gastmeier P, Ruden H. Operating room ventilation with laminar airflow shows no protective effect on the surgical site infection rate in orthopedic and abdominal surgery. *Ann Surg* 2008; **248:** 695–700.

31 Dale H, Hallan G, Hallan G, Espehaug B, Havelin LI, Engesaeter LB. Increasing risk of revision due to deep infection after hip arthroplasty. *Acta Orthop* 2009; **80:** 639–45.

32 Jeong SJ, Ann HW, Kim JK, et al. Incidence and risk factors for surgical site infection after gastric surgery: a multicenter prospective cohort study. *Infect Chemother* 2013; **45:** 422–30.

33 Namba RS, Inacio MC, Paxton EW. Risk factors associated with surgical site infection in 30,491 primary total hip replacements. *J Bone Joint Surg Br* 2012; **94:** 1330–38.

34 Namba RS, Inacio MC, Paxton EW. Risk factors associated with deep surgical site infections after primary total knee arthroplasty: an analysis of 56 216 knees. *J Bone Joint Surg Am* 2013; **95:** 775–82.

35 Pedersen AB, Svendsson JE, Johnsen SP, Riis A, Overgaard S. Risk factors for revision due to infection after primary total hip arthroplasty. A population-based study of 80756 primary procedures in the Danish Hip Arthroplasty Registry. *Acta Orthop* 2010; **81:** 542–47.

36 Song KH, Kim ES, Kim YK, et al. Differences in the risk factors for surgical site infection between total hip arthroplasty and total knee arthroplasty in the Korean Nosocomial Infections Surveillance System (KONIS). *Infect Control Hosp Epidemiol* 2012; **33:** 1086–93.

37 Breier AC, Brandt C, Sohr D, Geffers C, Gastmeier P. Laminar airflow ceiling size: no impact on infection rates following hip and knee prosthesis. *Infect Control Hosp Epidemiol* 2011; **32:** 1097–102.

38 Hooper GJ, Rothwell AG, Frampton C, Wyatt MC. Does the use of laminar flow and space suits reduce early deep infection after total hip and knee replacement? The ten-year results of the New Zealand Joint Registry. *J Bone Joint Surg Br* 2011; **93:** 85–90.

39 Kakwani RG, Yohannan D, Wahab KH. The effect of laminar air-flow on the results of Austin-Moore hemiarthroplasty. *Injury* 2007; **38:** 820–23.

40 Miner AL, Losina E, Katz JN, Fossel AH, Platt R. Deep infection after total knee replacement: impact of laminar airflow systems and body exhaust suits in the modern operating room. *Infect Control Hosp Epidemiol* 2007; **28:** 222–26.

41 Knobben BA, van Horn JR, van der Mei HC, Busscher HJ. Evaluation of measures to decrease intra-operative bacterial contamination in orthopaedic implant surgery. *J Hosp Infect* 2006; **62:** 174–80.

42 Simsek Yavuz S, Bicer Y, Yapici N, et al. Analysis of risk factors for sternal surgical site infection: emphasizing the appropriate ventilation of the operating theaters. *Infect Control Hosp Epidemiol* 2006; **27:** 958–63.

43 Gruenberg MF, Campaner GL, Sola CA, Ortolan EG. Ultraclean air for prevention of postoperative infection after posterior spinal fusion with instrumentation: a comparison between surgeries performed with and without a vertical exponential filtered air-flow system. *Spine* 2004; **29:** 2330–34.

44 van Griethuysen AJ, Spies-van Rooijen NH, Hoogenboom-Verdegaal AM. Surveillance of wound infections and a new theatre: unexpected lack of improvement. *J Hosp Infect* 1996; **34:** 99–106.

45 Engesaeter LB, Lie SA, Espehaug B, Furnes O, Vollset SE, Havelin LI. Antibiotic prophylaxis in total hip arthroplasty: effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22 170 primary hip replacements followed 0–14 years in the Norwegian Arthroplasty Register. *Acta Orthop Scand* 2003; **74:** 644–51.

46 Tayton ER, Frampton C, Hooper GJ, Young SW. The impact of patient and surgical factors on the rate of infection after primary total knee arthroplasty: an analysis of 64,566 joints from the New Zealand Joint Registry. *Bone Joint J* 2016; **98:** 334–40.

47 James M, Khan WS, Nannaparaju MR, Bhamra JS, Morgan-Jones R. Current evidence for the use of laminar flow in reducing infection rates in total joint arthroplasty. *Open Orthop J* 2015; **9:** 495–98.

48 McHugh SM, Hill AD, Humphreys H. Laminar airflow and the prevention of surgical site infection. More harm than good? *Surgeon* 2015; **13:** 52–58.

49 Salvati EA, Robinson RP, Zeno SM, Koslin BL, Brause BD, Wilson PD Jr. Infection rates after 3175 total hip and total knee replacements performed with and without a horizontal unidirectional filtered air-flow system. *J Bone Joint Surg Am* 1982; **64:** 525–35.

50 Hill C, Flamant R, Mazas F, Evrard J. Prophylactic cefazolin versus placebo in total hip replacement. Report of a multicentre double-blind randomised trial. *Lancet* 1981; **1:** 795–96.

51 McGovern PD, Albrecht M, Belani KG, et al. Forced-air warming and ultra-clean ventilation do not mix: an investigation of theatre ventilation, patient warming and joint replacement infection in orthopaedics. *J Bone Joint Surg Br* 2011; **93:** 1537–44.

52 Sommerstein R, Ruegg C, Kohler P, Bloemberg G, Kuster SP, Sax H. Transmission of *Mycobacterium chimaera* from heater-cooler units during cardiac surgery despite an ultraclean air ventilation system. *Emerg Infect Dis* 2016; **22:** 1008–13.

53 Wood AM, Moss C, Keenan A, Reed MR, Leaper DJ. Infection control hazards associated with the use of forced-air warming in operating theatres. *J Hosp Infect* 2014; **88:** 132–40.

54 Legg AJ, Hamer AJ. Forced-air patient warming blankets disrupt unidirectional airflow. *Bone Joint J* 2013; **95:** 407–10.

55 Young SW, Chisholm C, Zhu M. Intraoperative contamination and space suits: a potential mechanism. *Eur J Orthop Surg Traumatol* 2014; **24:** 409–13.

56 Yang L, Huang CY, Zhou ZB, et al. Risk factors for hypothermia in patients under general anesthesia: is there a drawback of laminar airflow operating rooms? A prospective cohort study. *Int J Surg* 2015; **21:** 14–17.

57 Cacciari P, Giannoni R, Marcelli E, Cercenelli L. Cost evaluation of a ventilation system for operating theatre: an ultraclean design versus a conventional one. *Ann Ig* 2004; **16:** 803–09 (in Italian).

58 Merollini KM, Crawford RW, Whitehouse SL, Graves N. Surgical site infection prevention following total hip arthroplasty in Australia: a cost-effectiveness analysis. *Am J Infect Control* 2013; **41:** 803–09.

59 Kramer A, Kulpmann R, Wille F, et al. Importance of displacement ventilation for operations and small surgical procedures from the infection preventive point of view. *Zentralbl Chir* 2010; **135:** 11–17 (in German).

60 Graves N, Wloch C, Wilson J, et al. A cost-effectiveness modelling study of strategies to reduce risk of infection following primary hip replacement based on a systematic review. *Health Technol Assess* 2016; **20:** 1–144.

61 Dharan S, Pittet D. Environmental controls in operating theatres. *J Hosp Infect* 2002; **51:** 79–84.

62 Whyte W, Lidwell OM, Lowbury EJL, Blowers R. Suggested bacteriological standards for air in ultraclean operating rooms. *J Hosp Infect* 1983; **4:** 133–39.