Elsevier Editorial System(tm) for The Lancet Infectious Diseases
Manuscript Draft

Manuscript Number: THELANCETID-D-16-00789R1

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

Article Type: Articles (Meta-analysis)

Keywords: Key words: surgical wound infection, operating room, laminar flow, endoprosthetic surgery, infection control

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Manuscript Region of Origin: GERMANY

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

Methods: Medline, EMBASE, Cochrane Central Register of Controlled Trials and WHO regional medical databases were searched from 1990 to 31 January 2014. The search was updated for Medline for the time period between 1 February 2014 and 27 May 2016. GRADE methodology was used to assess the quality of the retrieved evidence. Meta-analyses of available comparisons were performed using RevMan 5.3.
Findings: The search identified 1947 records of which 12 observational studies were identified comparing LAF ventilation with conventional turbulent ventilation in orthopedic, abdominal, and vascular surgery. The meta-analysis of eight cohort studies showed no difference in risk for deep SSIs following total hip arthroplasty (THA, 330 146 procedures; odds ratio (OR) 1·29, 95% CI 0·98-1·71, p=0·07; I^2=83%). For total knee arthroplasty (TKA, 134 368 procedures) the meta-analysis of six cohort studies showed no difference in risk for deep SSIs (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 SSI (OR 0·75, 95% CI 0·43-1·33, p=0·33; I^2=95%)
Interpretation: The available evidence shows no benefit for LAF compared with conventional turbulent OR ventilation in reducing the risk of SSI in THA, TKA and abdominal surgery. Decision makers, medical and administrative, should not choose to install and use LAF equipped ORs as a preventive measure to reduce the risk of SSI.
Funding: None.

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

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The manuscript is being submitted as an original article. Part of this work was presented at the 25th ECCMID Conference, Copenhagen, Denmark, April 25-28, 2015 and at the 26th ECCMID Conference, Amsterdam, Netherlands, April 9-12, 2016. This review has been performed within the framework of developing the WHO Global Guidelines for the Prevention of Surgical Site Infections issued 2016.

Abstract

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

Methods: Medline, EMBASE, Cochrane Central Register of Controlled Trials and WHO regional medical databases were searched from 1990 to 31 January 2014. The search was updated for Medline for the time period between 1 February 2014 and 27 May 2016. GRADE methodology was used to assess the quality of the retrieved evidence. Meta-analyses of available comparisons were performed using RevMan 5.3.

Findings: The search identified 1947 records of which 12 observational studies were identified comparing LAF ventilation with conventional turbulent ventilation in orthopedic, abdominal, and vascular surgery. The meta-analysis of eight cohort studies showed no difference in risk for deep SSIs following total hip arthroplasty (THA, 330 146 procedures; odds ratio (OR) 1·29, 95% CI 0·98–1·71, p=0·07; I^2=83%). For total knee arthroplasty (TKA, 134 368 procedures) the meta-analysis of six cohort studies showed no difference in risk for deep SSIs (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 SSI (OR 0·75, 95% CI 0·43–1·33, p=0·33; I^2=95%)

Interpretation: The available evidence shows no benefit for LAF compared with conventional turbulent OR ventilation in reducing the risk of SSI in THA, TKA and abdominal surgery. Decision makers, medical and administrative, should not choose to install and use LAF equipped ORs as a preventive measure to reduce the risk of SSI.

Funding: None.

Key words: surgical wound infection, operating room, laminar flow, endoprosthetic surgery, infection control

Introduction

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

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

The keystone study investigating the impact of OR ventilation systems on SSI was conducted from 1974 to 1979 in the United Kingdom and Sweden.[15] The investigators found a significant reduction of deep SSI rates in total hip (THA) and total knee arthroplasties (TKA) associated with the use of UCV in the OR in comparison with procedures performed in conventionally ventilated ORs. The use of body-exhaust suits was left to the discretion of the surgical team. Is not clear, if the "modern positive-pressure air supply" of the ORs in the control group of the study compares with conventional turbulent ventilation systems used in ORs today. Furthermore, there was no uniform method for random allocation and the study did not control for the administration of surgical antibiotic prophylaxis (SAP) which was given in about 60% of cases. From 1974 to 1985, a non-randomized single centre study comparing the association of LAF in a tent-like enclosure within the OR and HEPA-filtered conventional ventilation on the deep SSI rate after various arthroplasties, mainly THA, found no difference in risk.[16] SAP, which was introduced in this hospital in 1979, resulted in a significant decrease in SSI rate in both settings. The first published study in which patients were randomized to ORs equipped with horizontal LAF or to conventional airflow and in which all patients received appropriate SAP was conducted from 1981 to 1990.[17] The investigators found no difference in risk of deep SSI following THA and TKA.

A systematic review published in 2012 on the influence of LAF on prosthetic joint infections found LAF ventilation to be a risk factor for the development of a severe SSI.[18] There are only a few current guidelines that have provided recommendations regarding ventilation systems in the OR. The United States Centers for Disease Control and Prevention (CDC) guidelines for environmental infection control in healthcare facilities issued in 2003 offer no recommendation for performing orthopedic implant operations in ORs supplied with LAF due to lack of evidence.[19] The SSI prevention guidelines published by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) in 2014 recommend to follow the American Institute of Architects' recommendations for proper air handling in the OR.[20] The Royal College of Anaesthetists guidelines for the provision of anaesthesia services issued in 2016 recommend to perform major joint replacements in an OR with multiple air changes per hour, not necessarily equipped with laminar flow, to reduce the risks of wound infection.[21]

The purpose of this systematic review is to assess the effectiveness of ventilation systems in the OR on the prevention of SSI. In this context, LAF ventilation was compared with conventional ventilation in any type of surgery. This review has been performed within the framework of developing the WHO Global Guidelines for the Prevention of Surgical Site Infections issued 2016.

Methods

Search strategy and selection criteria
To evaluate the evidence on this topic, literature was examined according to a predefined PICO question.

1. Is the use of laminar airflow in the OR associated with the reduction of overall or deep SSI?

- **P**opulation: inpatients and outpatients of any age undergoing surgical operations (any type of procedure)
- **I**ntervention: LAF ventilation system in the OR
- **C**omparator: normal/conventional ventilation system
- **O**utcomes: SSI, SSI-attributable mortality

OR ventilation systems without LAF technology were considered as comparator. In most of the cases these would be classified as conventional, ordinary, mixed or tubulent ventilation systems with or without HEPA-filtered air. Superficial, deep and overall SSI were considered as outcomes. SSI referred to in primary studies as severe SSI, periprosthetic infection, (deep) infection requiring revision were considered as deep SSI. The following databases were searched: Medline (PubMed), Excerpta Medica Database (EMBASE), Cochrane Central Register of Controlled Trials (CENTRAL), and WHO regional medical databases. A comprehensive list of search terms, i.e. “ventilation”, “surgical wound infection”, “operating rooms” was used, including Medical Subject Headings (MeSH) (appendix, page 1). The time limit for the review was between 1 January 1990 and 31 January 2014. The search was updated for Medline (PubMed) for the time period between 1 February 2014 and 25 May 2016. Language was restricted to English, French, German, and Spanish. Two independent reviewers 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 for eligibility. Exclusion criteria were studies not relevant to the PICO question, studies not in the selected languages, studies published before 1 January 1990 or after 25 May 2016, meeting or conference abstracts and studies of which the full text was not available for review. Reference lists of all reviewed studies as well as of literature reviews were systematically screened 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 was missing. Duplicate studies were excluded. We report this systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement. The PRISMA flow diagram was used to demonstrate the study selection process[22] (figure 1).

Data analysis

The two authors extracted data in a predefined evidence table including the following information: year of publication, study design, setting, scope, location, population, type of surgery, SSI definitions, statistical methodology and limitations (appendix, page 3) and critically appraised the retrieved studies. Quality was assessed using the Newcastle-Ottawa Quality Assessment Scale for cohort studies[23] (appendix, page 18). Any disagreements were resolved through discussion or after consultation with the senior author, when necessary. Meta-analyses of available comparisons were performed using Review Manager version 5.3 as appropriate.[24] Crude estimates were pooled as odds ratios (OR) with 95% confidence intervals (CI) by use of a DerSimonian and Laird random effect model for each comparison[25] (appendix, pages 19-24). Sensitivity analyses were completed to test the robustness of our findings. Heterogeneity among studies was tested using the inconsistency index (I^2).[26] Funnel plots were created to assess whether publication bias occurred[27] (appendix, pages 19,21,23). The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (GRADE Pro software) was used to assess the quality of the body of retrieved evidence as appropriate[28,29].

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 initial search identified 1947 records. After removal of duplicates and screening, 109 articles were assessed for eligibility. Finally, 12 observational cohort studies[30-41] comparing LAF with conventional ventilation in the OR were identified. Most investigators described the ventilation system used in the control group as "conventional (plenum)" or "ordinary" ventilation system,[30,32,36,39,40] while others reported the use of "conventional turbulent ventilation with HEPA-filtered air".[31,37,38] In four studies, investigating THA[34] and TKA[35,41] performed in the USA between 2000 and 2009 and gastric surgery[33] performed in the Republic of Korea between 2010 and 2011, the authors did not provide additional information about the ventilation system of the ORs without LAF. These studies were included after discussion. No randomized clinical trials (RCTs) were included. The populations studied were mostly adult patients. Most studies focused on THA (330146 procedures) or TKA (134368 procedures; table 1). One small study on hemiarthroplasty of the hip was included with studies on THA because the procedures are similar.[40] Single studies were identified for abdominal and open vascular surgery[30,31,33] (table 2). All studies on THA and TKA investigated deep SSI. Two studies assessed the overall (superficial and deep) SSI rate as well.[31,37] We considered deep SSI as the critical outcome for further analysis. Brandt and colleagues reported on overall and deep SSI for abdominal surgery.[31] Two studies on gastric and vascular surgery assessed the overall SSI rate.[30,33] We considered overall SSI as the critical outcome in abdominal and open vascular surgery.

The following comparisons were evaluated:

1. LAF ventilation *vs*. conventional ventilation
    a. in THA

b. in TKA
c. in abdominal and open vascular surgery

Some of the 12 studies provided data for more than one comparison. We identified eight observational studies [31,32,34,36-40] comparing the association of LAF ventilation and conventional ventilation on the deep SSI rate after THA. Three large multicentre studies based on data obtained from national joint registries and surveillance systems found that LAF was associated with a higher risk of deep SSI[31] and revision due to infection,[32,39] whereas one small single centre study found LAF to be associated with a decreased risk of revision due to infection.[40] The four other studies showed no difference in the risk of deep SSI [34,37,38] or revision due to infection [36] (table 1).

We identified six observational studies [31,35,37-39,41] comparing the effect of LAF ventilation *vs*. conventional ventilation on the rate of SSI after TKA. One multicentre joint registry study found LAF to be associated with an increased risk of revision due to infection.[39] Five studies found no difference in the risk of deep SSI[31,35,37,38,41] (table 1). One study comparing the association of large LAF ceilings with at least 3.2 m^2 in size and conventional ventilation on the deep SSI rate after THA and TKA found no difference in the risk of deep SSI.[38]

The meta-analyses found that LAF ventilation did not reduce the SSI rate when compared with conventional ventilation in THA (OR 1·29, 95% CI 0·98–1·71, p=0·07; I^2 = 83%; table 3; appendix, page 19) or TKA (OR 1·08, 95% CI 0·77–1·52, p=0·65; I^2 = 71%; table 4; appendix page 21). The quality of the evidence for these comparisons was very low due to inconsistency shown by high I^2 values (appendix, page 25). Publication bias was not detected. Kakwani and colleagues seem to have reported a small study with a large effect (appendix, pages 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 ORs without LAF. There was no difference in the results, if the studies were included or not. When excluding the study by Namba and colleagues[34] for THA, the OR was 1·33 (95% CI 0·97–1·82, p=0·08; I^2 = 85%; appendix, page 20) and 1·11 for TKA when excluding the studies by Namba and colleagues[35] and Miner and colleagues[41] (95% CI 0·68–1·83, p=0·68; I^2 = 75%; appendix, page 22)

Concerning other types of surgery, only three single observational studies on abdominal and open vascular surgery were identified with a SSI outcome[30,31,33] (table 2). With regard to this very limited evidence per type of procedure and outcome, the reviewers agreed not to separately assess the quality of evidence using the GRADE approach. LAF was found to be associated with an overall increased SSI risk following appendectomy in one observational study.[31] The same study found no difference in overall risk of SSI in colon surgery,[31] cholecystectomy,[31] and herniorrhaphy in multivariable analysis.[31] In gastric [33] and open vascular surgery [33] the absence of laminar flow was found to increase the overall risk of SSI. The meta-analysis found that LAF ventilation did not reduce the SSI rate when compared with conventional ventilation after abdominal and open vascular surgery (OR 0·75, 95% CI 0·43–1·33, p=0·33; I^2 = 95%; table 5; appendix, page 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 ORs without LAF.[33] There was no difference in the results, if 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, page 24). Publication bias was not detected. With only few studies included, the interpretation of the funnel plot is very limited but there seems to be a lack of small to medium-sized studies showing no effect or an effect in favour of conventional ventilation (appendix, page 23).

Finally, four additional single centre studies were identified with combined interventions. LAF in combination with behavioral changes in the OR discipline code,[42] closed OR doors (*vs*. open doors in the control group),[43] and wearing of body exhaust gowns [44,45] in THA/TKA, cardiac surgery with sternotomy, and spine surgery, respectively. As these studies had additional interventions and were compared with conventional ventilation without the same additional measures, they were excluded from further assessment. One randomized trial comparing the association of horizontal LAF ventilation and conventional ventilation on the deep SSI rate after THA and TKA was excluded after discussion as the entire study period was before 1990.[17] This trial found no statistically significant difference in the deep SSI rate after THA and TKA. One large multicentre joint registry study reporting on the comparison of LAF with "ordinary" ventilation in THA was excluded as missing primary data could not be retrieved from the authors upon request.[46] 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. The updated search covering the time period between 1 February 2014 and 25 May 2016 did not identify any further eligible studies for this PICO question.

The individual cohort studies included in the systematic review had Newcastle-Ottawa Quality Assessment Scale (NOS) scores ranging from 5 to 8 out of 9 possible items (appendix, page 18).

Discussion

The main finding of this systematic review and meta-analysis is that LAF ventilation does not reduce the risk of deep SSI after THA and TKA compared with conventional OR ventilation. The odds for developing a deep SSI following THA are even higher under LAF condition, although this effect was not significant. The evidence is more limited for other procedures, but it seems that LAF does not reduce the risk of overall SSI after abdominal and open vascular surgery as well. The findings of our meta-analysis are consistent with the results of previous literature reviews,[18,47,48] adding many more 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 LAF systems decrease the risk of SSI. Surveillance databases and registries may not include data on 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 on the ventilation systems used in the ORs without LAF.[33-35,41] We decided to include them after discussion. In a Korean study, 26% of the ORs in the control group were equipped with HEPA filters. Furthermore, we believe that, in the USA, THA and TKA were performed in conventional ORs if not in ORs equipped with LAF. Corresponding recommendations on OR ventilation had been issued before the study periods.[13] In sensitivity analysis, there was no difference in the results, if the studies were included or not. Second, because data from a surveillance database and a registry are submitted by numerous hospitals. Differences in hospital or surgeon volume, patient characteristics or implementation of other SSI prevention measures may confound the results. Third, the definitions for severe SSI differed across the individual studies. Fourth, the meta-analysis evaluated crude data from the primary studies. For example, crude data from two multicentre studies (N=80756 and N=3088) indicated that LAF was associated with decreased risk of deep SSI. In contrast, the published adjusted and multivariable analyses did not find a difference in risk.[36,37] Overall, these factors led to considerable heterogeneity found in the statistical testing indicted by an I^2 of 83% for comparison 1a, an I^2 of 71% for comparison 1b, and an I^2 of 95% for comparison 1c (appendix, pages 19,21,23). Results from the studies that reported a benefit from LAF ventilation may have been biased because the SSI rate in the control group was quite high and almost all operations were performed in ORs with LAF ventilation (N=1919, control: N=172),[33] or the study size was small (N=435 and N=170)[30,40] and the case mix was heterogeneous.[30] 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 the ventilation systems used before 1990 might not technically compare with the ventilation systems used in hospitals today for orthopedic implant surgery. Furthermore, not only OR ventilation technology has improved over the last 20 to 30 years but the use of SAP has become a standard practice. After the study published by Lidwell and colleagues in July 1982,[15] there are only two further studies published, covering the time period from 1974 to 1990, and investigating the association of LAF ventilation and conventional ventilation with the deep SSI rate after THA and TKA.[16,17] They found no difference in risk. 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 limiting 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 OR personnel create thermal convection currents, and ventilation exhausts from medical equipment such as saws or drills, all disrupt the laminar airflow. In addition OR personnel and medical devices disburse airborne microorganisms and particles. Consequently the OR air around the open surgical field is not particle-free.[49-53] Furthermore, the fresh air from a LAF system cools the surgical wound and the patient, which can lower tissue temperatures in the surgical wound or cause systemic hypothermia, if the patient's temperature is not monitored and maintained intraoperatively. A recent study found that the odds of becoming hypothermic were 1·53 (95% CI 1·19–1·96) for patients whose procedures were done in LAF rooms compared with patients whose procedures were done in traditional ORs.[54]

Prior cost-effectiveness analyses found LAF to be more expensive than conventional ventilation systems. An Italian study [55] found that building costs increased 24% and annual operating costs increased 36%. [55] In Australia, Merollini and colleagues evaluated the costs of performing THA and found that doing the procedures in ORs with LAF would add 4·59 million Australian dollars per 30000 THA performed. [56] In Germany, Kramer and colleagues calculated additional costs of 3·24 Euros/procedure, if a 1000 procedures were done in ORs with LAF per year for 15 years.[57] Graves and colleagues evaluated strategies to reduce the risk of deep SSI following THA and concluded that the combination of administering systemic antibiotics, using antibiotic-impregnated cement and performing THA in ORs with conventional ventilation led to the largest annual cost savings and the greatest gains in quality adjusted life years. When including LAF instead of conventional ventilation higher costs and worse health outcomes were found.[58] In addition, validation of LAF ventilation systems is more expensive compared with 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 SSI.[59] The threshold limit of ultra-clean air was arbitrarily defined by Lidwell and colleagues as <10 cfu/m³ and used as standard ever since.[15,60]

The prior studies assessing whether LAF ventilation decreases the risk of SSI had numerous weaknesses and the evidence provided by those studies is of very low quality. The last randomized trials addressing this question were conducted in the 1970s and 1980s.[15,17] Thus, we need further research, particularly well-designed clinical trials of endoprosthetic surgery, to determine whether OR ventilation reduces SSI rates. However, believe that such trials will most likely not be conducted. RCTs may not be reasonable as they would require very high sample size to have enough power to detect a significant difference and would be very expensive. For example, if the deep SSI rate in the control group was about 0·5% after THA and TKA (appendix, page 25), approximately 10000 patients would be needed in each group to detect a 50% reduction to an SSI rate of 0·25% (1-alpha: 95%, 1-beta: 80%). Even more patients would be needed to detect a difference of 40% or 30%. Cluster randomized trials could be problematic as it would be almost impossible to control for confounding factors in between the sites, such as different surgeons operating in the same OR. Therefore, nationwide databases may provide the best affordable information. However, to avoid the weakness of prior studies and meta-analyses thereof, national surveillance systems and registries would need to provide consistent and internationally standardized information about risk factors and confounders such as the OR ventilation system. Furthermore, surveillance of healthcare-associated infections should be based upon internationally standardized definitions.

Very low quality of evidence suggests that compared with conventional ventilation, LAF ventilation does not reduce the risk of deep SSI after THA and TKA. Even more limited evidence suggests that LAF does not reduce the overall SSI rate when compared with conventional ventilation after abdominal and open vascular surgery. Conventional OR ventilation systems appear to provide air that is clean enough for procedures involving orthopaedic implants. Given the available evidence demonstrated by this systematic review and the prior cost-effectiveness analyses, which found LAF systems to be more expensive than conventional ventilation systems, the surgical team, infection prevention and control professionals, hospital administrators, and policy makers should not choose to install and use LAF equipped ORs as a preventive measure to reduce the risk of SSI.

Contributors
BA and ZK designed the study. PB and PG conducted the study. PB, PG, ZK, ME and BA analyzed and interpreted the data. PB drafted the manuscript. PB, ZK and BA contributed to the writing of the manuscript. All authors helped revise the manuscript.

Declaration of interests
We declare no competing interests.

Acknowledgments
We are grateful to all authors who kindly provided data for our meta-analyses. We especially thank Rosemary Sudan for her editing assistance and Bassim Zayed for critically revising the manuscript.

Research in context

Evidence before this study

Surgical site infections (SSI) range between the leading and the second most frequently reported health care-associated infections worldwide. The role of the laminar airflow (LAF) ventilation system in preventing SSI has been discussed for many decades, especially for orthopedic implant surgery. Apart from a randomized trail conducted in the 1970s, which did not control for the administration of prophylactic antibiotics, demonstrating a reduction of deep SSI rates in total hip (THA) and total knee arthroplasties (TKA) associated with the use of LAF in the operating room (OR) in comparison with procedures performed in conventionally ventilated ORs, these findings could not be reproduced in large studies published thereafter. We searched Medline, EMBASE, Cochrane Central and WHO Global Health from Jan 1, 1990 to Jan 31, 2014 using a combination of search terms of "ventilation", "surgical wound infection", and "operating rooms". The search was updated for Medline for the time period between Feb 1, 2014 and May 27, 2016.

Added value of this study

Our study makes an important contribution to understanding the effects of LAF ventilation on clinical outcomes and shows there is consistent evidence reporting that LAF does not reduce the risk of SSI. We show that after THA, TKA, and abdominal surgery there is no difference in SSI rate whether the operations are performed in ORs equipped with LAF or with conventional ventilation systems.

Implications of all the available evidence

Given the available evidence demonstrated by this systematic review and prior cost-effectiveness analyses, which found LAF systems to be more expensive than conventional ventilation systems, LAF equipped ORs should not be used as a preventive measure to reduce the risk of SSI. As randomized trials are not likely to be conducted, national surveillance systems and registries would need to provide internationally standardized information on risk factors and confounders, and should use internationally standardized SSI definitions in order to increase our confidence in the results of further cohort studies.

Figure legend

Figure 1: Flow diagram of study selection
PICO=population, intervention, comparator, outcome

Table 1: Characteristics of primary studies included in the meta-analysis of LAF vs. conventional ventilation for patients undergoing THA and TKA; outcome: deep SSI

Type of surgery	Authors (year)	No. of procedures - total (intervention / control)	Country	Study period	Adjusted RR / HR / OR (95% CI) for LAF
THA	Dale et al (2009)[32]	97344 (45620 / 48338)	Norway	1987 – 2008	1·3 (1·1–1·5)
	Pedersen et al (2010)[36]	80756 (72423 / 8333)	Denmark	1995 – 2008	0·9 (0·7–1·14)
	Song et al (2012)[37]	3186 (2037 / 1149)	Republic of Korea	2006 – 2009	1·2 (0·6 –2·16)*
	Namba et al (2012)[34]	30491 (8478 / 22013)	United States of America	2001 – 2009	1·08 (0·77–1·53)
	Kakwani et al (2007)[40]	435 (212 / 223)	United Kingdom	2000 – 2004	0·06 (0·00–0·95)*
	Brandt et al (2008)[31]	28623 (17657 / 10966)	Germany	2000 – 2004	1·63 (1·06–2·52)
	Breier et al (2011)[38]	42212 (29530 / 11682)	Germany	2004 – 2009	1·10 (0·56–2·17) (arthrosis)† 1·28 (0·67–2·43) (fracture)†
	Hooper et al (2011)[39]	51485 (16990 / 34495)	New Zealand	1999 – 2008	2·42 (1·35–4·32)*
TKA	Song et al (2012)[37]	3088 (2151 / 937)	Republic of Korea	2006 – 2009	0·51 (0·29–0·89)ǂ
	Namba et al (2013)[35]	56216 (16693 / 39523)	United States of America	2001 – 2009	0·91 (0·71–1·16)
	Miner et al (2007)[41]	8288 (3513 / 4775)	United States of America	2000	1·57 (0·75–3·31)
	Brandt et al (2008)[31]	9396 (5993 / 3403)	Germany	2000 – 2004	1·76 (0·80–3·85)
	Breier et al (2011)[38]	20554 (14456 / 6098)	Germany	2004 – 2009	0·95 (0·37–2·41)
	Hooper et al (2011)[39]	36826 (13994 / 22832)	New Zealand	1999 – 2008	1·92 (1·10–3·34)*

*not adjusted (calculated with crude data, no multivariable analysis); †adjusted odds ratios were provided separately for elective procedures due to arthrosis and for urgent procedures due to fracture; ǂnot adjusted (calculated with crude data, not significant in multivariable analysis); LAF: laminar airflow ventilation; THA: total hip arthroplasty; TKA: total knee arthroplasty; SSI: surgical site infection; RR: risk ratio; HR: Hazard ratio; OR: odds ratio; CI: confidence interval

Table 2: Characteristics of primary studies included in the meta-analysis of LAF vs. conventional ventilation for patients undergoing abdominal and open vascular surgery; outcome: overall SSI

Type of surgery	Authors (year)	No. of procedures - total (intervention / control)	Country	Study period	Adjusted OR (95% CI) for LAF
Appendectomy	Brandt et al (2008)[31]	10969 (7193 / 3776)	Germany	2000 – 2004	2·09 (1·08 – 4·02)
Colon surgery		8696 (6201 / 2495)	Germany	2000 – 2004	1·17 (0.65 – 2·11)
Cholecystectomy		20676 (12419 / 8257)	Germany	2000 – 2004	1·53 (0·9 – 2·45
Herniorrhaphy		20870 (12667 / 8203)	Germany	2000 – 2004	1·67 (0·9 – 2·91)
Gastric surgery	Jeong et al (2013)[33]	2091 (1919 / 172)	Republic of Korea	2010 – 2011	0·13 (0·08 – 0·22)*
Open vascular surgery	Bosanquet et al (2013)[30]	170 (56 / 114)	Wales, United Kingdom	not reported	0·38 (0·12 – 1·19)*

*not adjusted (calculated with crude data, the authors only provide adjusted odds ratios for the *absence* of laminar airflow: 2·45 (1·13–5·31) after gastric surgery and 4·02 (1·18–13·69) after open vascular surgery); LAF: laminar airflow ventilation; SSI: surgical site infection; OR: odds ratio; CI: confidence interval

Table 3: Meta-analysis comparing the risk of deep SSI after THA: laminar airflow *vs.* conventional ventilation (comparison 1a)

Authors (year)	**Laminar airflow**		**Conventional ventilation**		**Weight**	**Odds Ratio**
	No. of SSI	Total	No. of SSI	Total		M-H, Random, 95% CI
Brand et al (2008)[31]	242	17657	99	10966	16·1%	1·53 (1·21, 1·93)
Breier et al (2011)[38]	356	29530	77	11682	15·9%	1·84 (1·44, 2·36)
Dale et al (2009)[32]	324	45620	260	48338	17·1%	1·32 (1·12, 1·56)
Hooper et al (2011)[39]	25	16990	21	34495	10·1%	2·42 (1·35, 4·32)
Kakwani et al (2007)[40]	0	212	9	223	0·9%	0·05 (0·00, 0·92)
Namba et al (2012)[34]	46	8478	109	22013	14·2%	1·10 (0·78, 1·55)
Pederson et al (2010)[36]	517	72423	80	8333	16·0%	0·74 (0·59, 0·94)
Song et al (2012)[37]	34	2037	16	1149	9·8%	1·20 (0·66, 2·19)
Total	**1544**	**192947**	**671**	**137199**	**100·0%**	**1·29 (0·98, 1·71)**
Heterogeneity: $I^2 = 83\%$						

SSI: surgical site infection; THA: total hip arthroplasty; M-H: Mantel-Haenszel; CI: confidence interval

Table 4: Meta-analysis comparing the risk of deep SSI after TKA: laminar airflow *vs.* conventional ventilation (comparison 1b)

Authors (year)	**Laminar airflow**		**Conventional ventilation**		**Weight**	**Odds Ratio**
	No. of SSI	Total	No. of SSI	Total		M-H, Random, 95% CI
Brand et al (2008)[31]	55	5993	22	3403	16·5%	1·42 (0·87, 2·34)
Breier et al (2011)[38]	93	14456	36	6098	19·1%	1·09 (0·74, 1·60)
Hooper et al (2011)[39]	27	13994	23	22832	15·1%	1·92 (1·10, 3·34)
Miner et al (2007)[41]	15	3513	13	4775	11·4%	1·57 (0·75, 3·31)
Namba et al (2013)[35]	105	16693	299	39523	22·9%	0·83 (0·66, 1·04)
Song et al (2012)[37]	27	2151	23	937	15·0%	0·51 (0·29, 0·89)
Total	**322**	**56800**	**416**	**77568**	**100·0%**	**1·08 (0·77, 1·52)**
Heterogeneity: $I^2 = 71\%$						

SSI: surgical site infection; TKA: total knee arthroplasty; M-H: Mantel-Haenszel; CI: confidence interval

Table 5: Meta-analysis comparing the risk of overall SSI after abdominal and open vascular surgery: laminar airflow *vs.* conventional ventilation (comparison 1c)

Type of surgery	**Laminar airflow**		**Conventional ventilation**		**Weight**	**Odds Ratio**
	No. of SSI	Total	No. of SSI	Total		M-H, Random, 95% CI
Appendectomy	194	7193	70	3776	18·0%	1·47 (1·11, 1·93)
Cholecystectomy	191	12419	109	8257	18·3%	1·17 (0·92, 1·48)
Colon surgery	316	6201	176	2495	18·5%	0·71 (0·58, 0·86)
Gastric surgery	45	1919	26	172	16·4%	0·13 (0·08, 0·22)
Herniorrhaphy	198	12667	69	8203	18·1%	1·87 (1·42, 2·47)
Open vascular surgery	4	56	19	114	10·8%	0·38 (0·12, 1·19)
Total	**948**	**40455**	**469**	**23017**	**100·0%**	**0·75 (0·43, 1·33)**
Heterogeneity: $I^2 = 95\%$						

Appendectomy, colon surgery, cholecystectomy and herniorrhaphy were investigated by Brand and colleagues[31], gastric surgery by Jeong and colleagues[33], and open vascular surgery by Bosanquet and colleagues[30]; SSI: surgical site infection; THA: total hip arthroplasty; M-H: Mantel-Haenszel; CI: confidence interval

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**(9761): 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**(13): 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. Stockholm: ECDC, 2013. Available from: http://www.ecdc.europa.eu/en/publications/Publications/Forms/ECDC_DispForm.aspx?ID=1155 (Accessed 24 May 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**(5): 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**(3): 193-201.
6. Charnley J. Operating-theatre ventilation. *Lancet* 1970; **1**(7655): 1053-4.
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**(5): 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**(7): e25-9.
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**(6): 665-9.
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**(6): 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**(7): e228-32.
12. UK Dept. of Health. Heating and ventilation systems Health Technical Memorandum 03-01: Specialised ventilation for healthcare premises. Leeds: UK Dept. of Health, 2007. Available from: https://www.gov.uk/government/publications/guidance-on-specialised-ventilation-for-healthcare-premises-parts-a-and-b (Accessed 24 May 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**(2): 97-132; quiz 3-4; discussion 96.
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. *Br Med J (Clin Res Ed)* 1982; **285**(6334): 10-4.
16. Marotte JH, Lord GA, Blanchard JP, et al. Infection rate in total hip arthroplasty as a function of air cleanliness and antibiotic prophylaxis. *The Journal of Arthroplasty* 1987; **2**(1): 77-82.
17. Fitzgerald RH, Jr. Total hip arthroplasty sepsis. Prevention and diagnosis. *Orthop Clin North Am* 1992; **23**(2): 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**(2): 73-8.

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**(Rr-10): 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**(6): 605-27.
21. The Royal College of Anaesthetists. Guidelines for the Provision of Anaesthetic Services (GPAS) 2016. London: RCoA, 2016. Available from: http://www.rcoa.ac.uk/gpas2016 and http://www.rcoa.ac.uk/system/files/GPAS-2016-16-TRAUMA.pdf (Accessed 04 November 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**(7): 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. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (Accessed 8 February 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**(3): 177-88.
26. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002; **21**(11): 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**(7304): 101-5.
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**(4): 383-94.
29. GRADEpro Guideline Development Tool [website]. Summary of findings tables, health technology assessment and guidelines. GRADE Working Group, Ontario: McMaster University and Evidence Prime Inc.; 2015 (http://www.gradepro.org, accessed 5 May 2016).
30. 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**(1): 15-9.
31. 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**(5): 695-700.
32. 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**(6): 639-45.
33. 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**(4): 422-30.
34. 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**(10): 1330-8.
35. 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**(9): 775-82.
36. 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 80,756 primary procedures in the Danish Hip Arthroplasty Registry. *Acta Orthop* 2010; **81**(5): 542-7.
37. 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**(11): 1086-93.
38. 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**(11): 1097-102.
39. 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**(1): 85-90.

40. Kakwani RG, Yohannan D, Wahab KH. The effect of laminar air-flow on the results of Austin-Moore hemiarthroplasty. *Injury* 2007; **38**(7): 820-3.
41. 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**(2): 222-6.
42. 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**(2): 174-80.
43. 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**(9): 958-63.
44. 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 (Phila Pa 1976)* 2004; **29**(20): 2330-4.
45. 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**(2): 99-106.
46. 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**(6): 644-51.
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**: 495-8.
48. McHugh SM, Hill AD, Humphreys H. Laminar airflow and the prevention of surgical site infection. More harm than good? *Surgeon* 2015; **13**(1): 52-8.
49. 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**(11): 1537-44.
50. 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**(6): 1008-13.
51. 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**(3): 132-40.
52. Legg AJ, Hamer AJ. Forced-air patient warming blankets disrupt unidirectional airflow. *Bone Joint J* 2013; **95-b**(3): 407-10.
53. Young SW, Chisholm C, Zhu M. Intraoperative contamination and space suits: a potential mechanism. *Eur J Orthop Surg Traumatol* 2014; **24**(3): 409-13.
54. 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**: 14-7.
55. 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**(6): 803-9.
56. 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**(9): 803-9.
57. 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**(1): 11-7.

58. 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**(54): 1-144.
59. Dharan S, Pittet D. Environmental controls in operating theatres. *J Hosp Infect* 2002; **51**(2): 79-84.
60. Whyte W, Lidwell OM, Lowbury EJL, Blowers R. Suggested bacteriological standards for air in ultraclean operating rooms. *Journal of Hospital Infection* 1983; **4**(2): 133-9.