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

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

Corresponding Author: Dr. Peter Bischoff, M.D.

Corresponding Author's Institution: Charité - University Medicine Berlin

First Author: Peter Bischoff, M.D.

Order of Authors: Peter Bischoff, M.D.; Nejla Z Kubilay, M.D.; Benedetta Allegranzi, M.D.; Matthias Egger, M.D.; Petra Gastmeier, M.D.

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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; I²=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; I²=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; I²=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.

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

Peter Bischoff, MD 1*, N Zeynep Kubilay, MD 2, Benedetta Allegranzi, MD 2, Matthias Egger, MD 3
(Professor), Petra Gastmeier, MD 1 (Professor)

1 Institute of Hygiene and Environmental Health, Charité - University Medicine Berlin,
Hindenburgdamm 27, 12203 Berlin, Germany

2 World Health Organization Patient Safety Program, World Health Organization 20, Av Appia CH-1211 Geneva 27, Switzerland

3 Institute of Social and Preventive Medicine (ISPM), University of Bern, Finkenhubelweg 11, 3012 Bern, Switzerland

*Correspondence to: Dr. Peter Bischoff, Institute of Hygiene and Environmental Health, Charité - University Medicine Berlin, Hindenburgdamm 27, 12203 Berlin, Germany; Phone: 0049-03-450-570161, Email: peter.bischoff@charite.de

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.

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**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. The role of the operating room’s (OR) ventilation system in preventing SSI has been discussed for many decades.

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. However, there is recent evidence that air contamination might not be associated with wound contamination. 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. In other countries their use is recommended for conventional ventilation systems as well based on national regulations or technical standards.

The keystone study investigating the impact of OR ventilation systems on SSI was conducted from 1974 to 1979 in the United Kingdom and Sweden. 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. 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. 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. 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. 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. 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.\textsuperscript{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?

   - **Population:** inpatients and outpatients of any age undergoing surgical operations (any type of procedure)
   - **Intervention:** LAF ventilation system in the OR
   - **Comparator:** normal/conventional ventilation system
   - **Outcomes:** 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 turbulent 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\textsuperscript{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 (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. 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 (appendix, pages 19-24). Sensitivity analyses were completed to test the robustness of our findings. Heterogeneity among studies was tested using the inconsistency index ($I^2$). Funnel plots were created to assess whether publication bias occurred (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.

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 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, while others reported the use of “conventional turbulent ventilation with HEPA-filtered air” in four studies, investigating THA and TKA performed in the USA between 2000 and 2009 and gastric surgery 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. Single studies were identified for abdominal and open vascular surgery (table 2). All studies on THA and TKA investigated deep SSI. Two studies assessed the overall (superficial and deep) SSI rate as well. We considered deep SSI as the critical outcome for further analysis. Brandt and colleagues reported on overall and deep SSI for abdominal surgery. Two studies on gastric and vascular surgery assessed the overall SSI rate. 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 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 and revision due to infection, whereas one small single centre study found LAF to be associated with a decreased risk of revision due to infection. The four other studies showed no difference in the risk of deep SSI or revision due to infection (table 1).

We identified six observational studies 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. Five studies found no difference in the risk of deep SSI (table 1). One study comparing the association of large LAF ceilings with at least 3.2 m² in size and conventional ventilation on the deep SSI rate after THA and TKA found no difference in the risk of deep SSI.

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; P = 83%; table 3; appendix, page 19) or TKA (OR 1.08, 95% CI 0.77–1.52, p=0.65; P = 71%; table 4; appendix page 21). The quality of the evidence for these comparisons was very low due to inconsistency shown by high P 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 for THA, the OR was 1.33 (95% CI 0.97–1.82, p=0.08; P = 85%; appendix, page 20) and 1.11 for TKA when excluding the studies by Namba and colleagues and Miner and colleagues (95% CI 0.68–1.83, p=0.68; P = 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 (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. The same study found no difference in overall risk of SSI in colon surgery, cholecystectomy, and herniorrhaphy in multivariable analysis. In gastric and open vascular surgery 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; P = 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.\textsuperscript{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 $0.72$–$1.68$, $p=0.66$; $P = 91\%$; 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,\textsuperscript{42} closed OR doors (vs. open doors in the control group),\textsuperscript{43} and wearing of body exhaust gowns\textsuperscript{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.\textsuperscript{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.\textsuperscript{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,\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{36,37} Overall, these factors led to considerable heterogeneity found in the statistical testing indicated by an $P$ of 83\% for comparison 1a, an $P$ of 71\% for comparison 1b, and an $P$ 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),\textsuperscript{33} or the study size was small (N=435 and N=170)\textsuperscript{30,40} and the case mix was heterogeneous.\textsuperscript{30} We excluded studies that were published before 1990. After discussion we excluded a study because its entire study period was before 1990.\textsuperscript{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,\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.  

Prior cost-effectiveness analyses found LAF to be more expensive than conventional ventilation systems. An Italian study found that building costs increased 24% and annual operating costs increased 36%. 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. 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. 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. 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. The threshold limit of ultra-clean air was arbitrarily defined by Lidwell and colleagues as <10 cfu/m³ and used as standard ever since.

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. 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.

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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

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Authors (year)</th>
<th>No. of procedures - total (intervention / control)</th>
<th>Country</th>
<th>Study period</th>
<th>Adjusted RR / HR / OR (95% CI) for LAF</th>
</tr>
</thead>
<tbody>
<tr>
<td>THA</td>
<td>Dale et al (2009)\textsuperscript{32}</td>
<td>97344 (45620 / 48338)</td>
<td>Norway</td>
<td>1987 – 2008</td>
<td>1·3 (1·1–1·5)</td>
</tr>
<tr>
<td></td>
<td>Pedersen et al (2010)\textsuperscript{36}</td>
<td>80756 (72423 / 8333)</td>
<td>Denmark</td>
<td>1995 – 2008</td>
<td>0·9 (0·7–1·14)</td>
</tr>
<tr>
<td></td>
<td>Song et al (2012)\textsuperscript{37}</td>
<td>3186 (2037 / 1149)</td>
<td>Republic of Korea</td>
<td>2006 – 2009</td>
<td>1·2 (0·6–2·16)*</td>
</tr>
<tr>
<td></td>
<td>Namba et al (2012)\textsuperscript{34}</td>
<td>30491 (8478 / 22013)</td>
<td>United States of America</td>
<td>2001 – 2009</td>
<td>1·08 (0·77–1·53)</td>
</tr>
<tr>
<td></td>
<td>Kakwani et al (2007)\textsuperscript{40}</td>
<td>435 (212 / 223)</td>
<td>United Kingdom</td>
<td>2000 – 2004</td>
<td>0·06 (0·00–0·95)*</td>
</tr>
<tr>
<td></td>
<td>Brandt et al (2008)\textsuperscript{31}</td>
<td>28623 (17657 / 10966)</td>
<td>Germany</td>
<td>2000 – 2004</td>
<td>1·63 (1·06–2·52)</td>
</tr>
<tr>
<td></td>
<td>Breier et al (2011)\textsuperscript{38}</td>
<td>42212 (29530 / 11682)</td>
<td>Germany</td>
<td>2004 – 2009</td>
<td>1·10 (0·56–2·17) (arthrosis)† 1·28 (0·67–2·43) (fracture)†</td>
</tr>
<tr>
<td></td>
<td>Hooper et al (2011)\textsuperscript{39}</td>
<td>51485 (16990 / 34495)</td>
<td>New Zealand</td>
<td>1999 – 2008</td>
<td>2·42 (1·35–4·32)*</td>
</tr>
<tr>
<td>TKA</td>
<td>Song et al (2012)\textsuperscript{37}</td>
<td>3088 (2151 / 937)</td>
<td>Republic of Korea</td>
<td>2006 – 2009</td>
<td>0·51 (0·29–0·89)†</td>
</tr>
<tr>
<td></td>
<td>Namba et al (2013)\textsuperscript{35}</td>
<td>56216 (16693 / 39523)</td>
<td>United States of America</td>
<td>2001 – 2009</td>
<td>0·91 (0·71–1·16)</td>
</tr>
<tr>
<td></td>
<td>Miner et al (2007)\textsuperscript{41}</td>
<td>8288 (3513 / 4775)</td>
<td>United States of America</td>
<td>2000</td>
<td>1·57 (0·75–3·31)</td>
</tr>
<tr>
<td></td>
<td>Brandt et al (2008)\textsuperscript{31}</td>
<td>9396 (5993 / 3403)</td>
<td>Germany</td>
<td>2000 – 2004</td>
<td>1·76 (0·80–3·85)</td>
</tr>
<tr>
<td></td>
<td>Breier et al (2011)\textsuperscript{38}</td>
<td>20554 (14456 / 6098)</td>
<td>Germany</td>
<td>2004 – 2009</td>
<td>0·95 (0·37–2·41)</td>
</tr>
<tr>
<td></td>
<td>Hooper et al (2011)\textsuperscript{39}</td>
<td>36826 (13994 / 22832)</td>
<td>New Zealand</td>
<td>1999 – 2008</td>
<td>1·92 (1·10–3·34)*</td>
</tr>
</tbody>
</table>
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; ‡not 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

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Authors (year)</th>
<th>No. of procedures - total (intervention / control)</th>
<th>Country</th>
<th>Study period</th>
<th>Adjusted OR (95% CI) for LAF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendectomy</td>
<td>Brandt et al (2008)³¹</td>
<td>10969 (7193 / 3776)</td>
<td>Germany</td>
<td>2000 – 2004</td>
<td>2·09 (1·08 – 4·02)</td>
</tr>
<tr>
<td>Colon surgery</td>
<td></td>
<td>8696 (6201 / 2495)</td>
<td>Germany</td>
<td>2000 – 2004</td>
<td>1·17 (0·65 – 2·11)</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td></td>
<td>20676 (12419 / 8257)</td>
<td>Germany</td>
<td>2000 – 2004</td>
<td>1·53 (0·9 – 2·45)</td>
</tr>
<tr>
<td>Herniorrhaphy</td>
<td></td>
<td>20870 (12667 / 8203)</td>
<td>Germany</td>
<td>2000 – 2004</td>
<td>1·67 (0·9 – 2·91)</td>
</tr>
<tr>
<td>Gastric surgery</td>
<td>Jeong et al (2013)³³</td>
<td>2091 (1919 / 172)</td>
<td>Republic of Korea</td>
<td>2010 – 2011</td>
<td>0·13 (0·08 – 0·22)*</td>
</tr>
<tr>
<td>Open vascular surgery</td>
<td>Bosanquet et al (2013)³⁰</td>
<td>170 (56 / 114)</td>
<td>Wales, United Kingdom</td>
<td>not reported</td>
<td>0·38 (0·12 – 1·19)*</td>
</tr>
</tbody>
</table>

*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)

<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>Laminar airflow</th>
<th>Conventional ventilation</th>
<th>Weight</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of SSI</td>
<td>Total</td>
<td>No. of SSI</td>
<td>Total</td>
</tr>
<tr>
<td>Brand et al (2008)</td>
<td>242</td>
<td>17657</td>
<td>99</td>
<td>10966</td>
</tr>
<tr>
<td>Breier et al (2011)</td>
<td>356</td>
<td>29530</td>
<td>77</td>
<td>11682</td>
</tr>
<tr>
<td>Dale et al (2009)</td>
<td>324</td>
<td>45620</td>
<td>260</td>
<td>48338</td>
</tr>
<tr>
<td>Hooper et al (2011)</td>
<td>25</td>
<td>16990</td>
<td>21</td>
<td>34495</td>
</tr>
<tr>
<td>Kakwani et al (2007)</td>
<td>0</td>
<td>212</td>
<td>9</td>
<td>223</td>
</tr>
<tr>
<td>Namba et al (2012)</td>
<td>46</td>
<td>8478</td>
<td>109</td>
<td>22013</td>
</tr>
<tr>
<td>Pederson et al (2010)</td>
<td>517</td>
<td>72423</td>
<td>80</td>
<td>8333</td>
</tr>
<tr>
<td>Song et al (2012)</td>
<td>34</td>
<td>2037</td>
<td>16</td>
<td>1149</td>
</tr>
<tr>
<td>Total</td>
<td>1544</td>
<td>192947</td>
<td>671</td>
<td>137199</td>
</tr>
</tbody>
</table>

Heterogeneity: P = 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)

<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>Laminar airflow</th>
<th>Conventional ventilation</th>
<th>Weight</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of SSI</td>
<td>Total</td>
<td>No. of SSI</td>
<td>Total</td>
</tr>
<tr>
<td>Brand et al (2008)</td>
<td>55</td>
<td>5993</td>
<td>22</td>
<td>3403</td>
</tr>
<tr>
<td>Breier et al (2011)</td>
<td>93</td>
<td>14456</td>
<td>36</td>
<td>6098</td>
</tr>
<tr>
<td>Hooper et al (2011)</td>
<td>27</td>
<td>13994</td>
<td>23</td>
<td>22832</td>
</tr>
<tr>
<td>Miner et al (2007)</td>
<td>15</td>
<td>3513</td>
<td>13</td>
<td>4775</td>
</tr>
<tr>
<td>Namba et al (2013)</td>
<td>105</td>
<td>16693</td>
<td>299</td>
<td>39523</td>
</tr>
<tr>
<td>Song et al (2012)</td>
<td>27</td>
<td>2151</td>
<td>23</td>
<td>937</td>
</tr>
<tr>
<td>Total</td>
<td>322</td>
<td>56800</td>
<td>416</td>
<td>77568</td>
</tr>
</tbody>
</table>

Heterogeneity: P = 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)

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Laminar airflow</th>
<th>Conventional ventilation</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of SSI</td>
<td>Total</td>
<td>No. of SSI</td>
<td>Total</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>194</td>
<td>7193</td>
<td>70</td>
<td>3776</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>191</td>
<td>12419</td>
<td>109</td>
<td>8257</td>
</tr>
<tr>
<td>Colon surgery</td>
<td>316</td>
<td>6201</td>
<td>176</td>
<td>2495</td>
</tr>
<tr>
<td>Gastric surgery</td>
<td>45</td>
<td>1919</td>
<td>26</td>
<td>172</td>
</tr>
<tr>
<td>Herniorrhaphy</td>
<td>198</td>
<td>12667</td>
<td>69</td>
<td>8203</td>
</tr>
<tr>
<td>Open vascular surgery</td>
<td>4</td>
<td>56</td>
<td>19</td>
<td>114</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>948</strong></td>
<td><strong>40455</strong></td>
<td><strong>469</strong></td>
<td><strong>23017</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: \( P = 95\% \)

Appendectomy, colon surgery, cholecystectomy and herniorrhaphy were investigated by Brand and colleagues\(^3\), gastric surgery by Jeong and colleagues\(^3\), and open vascular surgery by Bosanquet and colleagues\(^3\); SSI: surgical site infection; THA: total hip arthroplasty; M-H: Mantel-Haenszel; CI: confidence interval
References

