Region Västra Götaland, HTA-centrum
Regional activity based HTA [Verksamhetsbaserad HTA]
Health Technology Assessment
HTA report 2019:109

Effectiveness of laminar versus turbulent airflow in operating theaters, with regard to risk for postoperative surgical infections

Houltz E., Björkander E, Grant P, Gustén J, Malchau H, Jivegård L, Liljegren A, Moonen J, Petzold M, Svanberg T, Svensson M, Sjövall H.

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Effectiveness of laminar versus turbulent airflow in operating theaters, with regard to risk for postoperative surgical infections [Effekten av laminär jämfört med turbulent ventilation i operationssalar, avseende risk för postoperativa infektioner]

Houltz E[*1], Björkander E[2], Grant P[3], Gustén J[4], Malchau H[3] Jivegård L[5], Liljegren A[2], Moonen J[1] Petzold M[5], Svanberg T[2], Svensson M[5], Sjövall H[5]

[*]Coordinator and corresponding author
[1]Department of Anaesthesiology and Intensive Care, Sahlgrenska University Hospital, Gothenburg, Sweden
[2] Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden
[3] Department of Orthopedics, Sahlgrenska University Hospital, Mölndal, Sweden
[4] Chalmers University of Technology, Gothenburg, Sweden
[5] HTA-centrum of Region Västra Götaland, Gothenburg, Sweden

Published July 2019
2019:109
Suggested citation: Houltz E., Björkander, E., Grant P, Gustén J, Malchau H, Jivegård L, Liljegren A, Moonen J, Petzold M, Svanberg T, Svensson M, Sjövall H.
Effectiveness of laminar versus turbulent airflow in operating theaters, with regard to risk for postoperative surgical infections [Effekten av laminär jämfört med turbulent ventilation i operationssalar, avseende risk för postoperativa infektioner]. Göteborg: Västra Götalandsregionen, Sahlgrenska Universitetssjukhuset, HTA-centrum; 2019.
Regional activity based HTA 2019:109

Table of contents

1. Abstract

Background: Postoperative infections, particularly in implant surgery, are a major clinical problem. Possible mechanisms behind infections are multifaceted, one of them being contamination from bacteria present in operating room air. The role of this factor is controversial and probably varies with type of surgery. To minimize this risk, super-clean ventilation systems have been designed, a recent example being vertical laminar airflow (LAF). The introduction of this technique has been based on studies of the surrogate marker concentration of colony forming units (CFUs) in operating room air. However, several recent systematic reviews of registry based studies have been unable to demonstrate the expected risk reduction for postoperative infections when using LAF systems.

Objective: Is the use of a laminar airflow systems, compared with any other type of ventilation system in operating rooms, associated with a reduction of the risk for mortality, serious surgical site infections (sSSI), other surgical site infections (SSI) and concentration of CFUs in air sampled from the operation area?

Methods: Systematic literature searches were conducted in PubMed, Medline, Embase, CINAHL, Cochrane Library and a number of HTA databases. RCTs, controlled cohort studies and systematic reviews/HTA reports were considered for inclusion. The included controlled studies were critically appraised, and data was extracted. Whenever possible, data was pooled in meta-analysis using RevMan 5.3 and presented as Forest plots.

Results: We identified 33 studies, 28 cohort studies and five systematic reviews/HTA reports, based on more than a million operations. 14 cohort studies were based on implant orthopaedic surgery and 14 on non-implant-orthopedics/GI/vascular/mixed surgery. For the outcome serious SSI, there was a significantly increased risk in LAF theaters in the subgroup non-implant orthopaedic surgery (OR=1.13[1.08, 1.18], $p<0.001$). For the other outcomes and subgroups, no significant differences were seen. LAF was associated with a clearcut reduction in the concentration of CFUs in operating room air ($p<0.0001$).

Conclusions: Depending on type of surgery, vertical laminar airflow compared with any other type of ventilation system in operating rooms may be associated with an increase or little or no difference in the risk for serious surgical site infections (GRADE ⊕⊕◯◯). It is uncertain whether vertical laminar airflow compared with any other type of ventilation system in operating rooms is associated with changes in mortality or surgical site infections (GRADE ⊕◯◯◯). Vertical laminar airflow, compared with any other type of ventilation system in operating rooms, is probably associated with a further reduction of CFU concentration in air sampled near the operation table (GRADE ⊕⊕⊕◯).

*OR values larger than 1 indicate higher risk for mortality or higher rates of infection with LAF. Values within brackets ([ ]) are 95% confidence intervals.

2. Svensk sammanfattning – Swedish summary

Bakgrund: Postoperativa infektioner, och då i synnerhet inom protesortopedin, utgör ett stort kliniskt problem. Orsakerna är mångfacetterade, en av dessa är nedsmutsning med bakterier från oren luft i operationssalen. Den relativa betydelsen av denna faktor är kontroversiell och varierar troligen med typen av kirurgi. För att minimera denna risk har man byggt super-rena ventilationssystem, där det numera vanligast förekommande är vertikalt laminärt luftflöde (förkortat LAF). Införandet av denna teknik har i huvudsak baserats på reduktion av surrogatmarkören koncentration av bakteriekolonibildande enheter (CFUs) i operationsluft. Flera relativt färska systematiska översikter av studier baserade på registerdata rapporterar dock avsaknad av förväntad riskreduktion vad gäller postoperativa infektioner i salar försedda med LAF.

Syfte: Är användning av laminärt luftflöde på operationssalar, jämfört med andra ventilationssystem, associerat med minskad risk för mortalitet, allvarliga postoperativa infektioner, andra postoperativa infektioner eller med reducerad koncentration av CFUs samlade från luft i operationsområdet?

Sökmetoder och identifiering av studier: Systematiska litteratursökningar genomfördes i PubMed, Medline, Embase, CINAHL, Cochrane Library and ett antal HTA-databaser. RCTer, kontrollerade kohortstudies och systematiska översikter/HTA rapporter bedömdes för eventuell inklusion. De inkluderade studierna utvärderades kritiskt, och data extraherades. Om möjligt poolades data i metaanalyser med användning av Revman 5.3. och presenterades som Forest plottar.

Resultat: Vi fann 33 studier baserade på mer än en million operationer varav 28 kohortstudier och fem systematiska översikter/HTA rapporter. 14 kohorter berörde ortopedisk proteskirurgi och 14 studier icke-implantat-ortopedi/magtarmkirurgi/kärlkirurgi/blandad kirurgi. För utfallet allvarliga postoperativa sårinfektioner sågs i subgruppen traumaortopedi en signifikant ökad risk i LAF-försedda operationssalar (OR=1.13[1.08, 1.18], p<0.001). För övriga utfall och subgrupper sågs inga signifikanta skillnader. LAF var däremot associerad med en tydlig reduktion av koncentrationen av bakteriekolonibildande partiklar (CFUs) i operationssalsluft (-33[-37, -30] CFUs/m^3, p<0.0001).

Slutsats: Beroende på typ av kirurgi kan vertikalt laminärflöde, jämfört med annan typ av ventilationssystem i operationssalar, antingen vara associerat med en ökad risk eller med en liten eller oförändrad riskförändring för allvarliga postoperativa infektioner (GRADE ⊕⊕). Det är osäkert huruvida vertikalt laminärflöde, jämfört med annan typ av ventilationssystem i operationssalar, är associerat med en förändrad risk för mortalitet eller icke-allvarliga postoperativa infektioner (GRADE ⊕). Vertikalt laminärflöde, jämfört med annan typ av ventilationssystem i operationssalar, är troligen associerat med ytterligare reduktion av CFU- koncentrationen i operationssalsluft (GRADE ⊕⊕⊕).

* OR värden större än 1 indikerar högre risk för mortalitet eller högre infektionsrisk med LAF. Värden inom hakparenteser. ([ ]) indikerar 95% konfidensintervall.

The above summaries were written by representatives from the HTA-centrum. The HTA report was approved by the Regional board for quality assurance of activity-based HTA. The abstract is a concise summary of the results of the systematic review. The Swedish summary is a brief summary of the systematic review intended for decision makers, and is ended with a concluding summary.

Christina Bergh, Professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden, March 20 2019 and May 29 2019.

Quality control group	
Bergenheim, Anna	PT, PhD
Bergh, Christina	MD, Professor
Bernhardsson, Susanne	PT, PhD
Hakeberg, Magnus	OD, Professor
Hansson-Olofsson, Elisabeth	PhD, Senior lecturer
Jivegård, Lennart	MD, Senior university lecturer
Larsson, Anders	MD, PhD
Nelzén, Olle	MD, Associate professor
Petzold, Max	Statistician, professor
Rylander, Christian	MD, Associate professor
Sjögren, Petteri	DDS, PhD
Sjövall, Henrik	MD, Professor
Skogby, Maria	RN, PhD
Strandell, Annika	MD, Associate professor
Svanberg, Therese	HTA librarian
Svensson, Mikael	Health economist, Professor
Wallerstedt, Susanna	MD, Professor
Wartenberg, Constanze	Psychologist, PhD

DDS Doctor of dental surgery
MD Medical doctor
PhD Doctor of Philosophy
OD Odontology doctor
PT Physiotherapist
RN Registered Nurse

3. Summary of findings.

Outcomes	Study design, number of cohorts	Relative effect OR[95%CI] *(OR> 1 denotes increased risk with LAF)*	Absolute effect (events/total number of operations, %)	Certainty of evidence GRADE + reason for up/down-grading
Mortality	1 cohort	1.09 [0.28, 4.23], p=0.90	LAF: 5/85 = 5.9% No LAF: 4/74 = 5.4%	⊕◯◯◯ 1
Serious surgical site infection or need for revision	Implant orthopaedic surgery (hip or knee), n=16	1.20[0.97, 1.49], p=0.09	LAF: 1834/260023= 0.71% No LAF: 1068/198207= 0.54%	⊕⊕◯◯ 2
	Other orthopaedic (e.g. trauma), n=3	1.13[1.08, 1.18], p < 0.0001	LAF: 13708/507024= 2.70% No LAF: 1956/81509 = 2.40%	
	GI/vascular/mixed, n=4	1.23[0.97, 1.56], p=0.09	LAF: 477/40973= 1.16% No LAF: 240/25199= 0.95%	
Surgical site infection	Implant orthopaedic surgery (hip or knee), n=4	1.18[0.78, 1.80], p=0.43	LAF: 493/27838= 1.77% No LAF: 221/16455= 1.34%	⊕◯◯◯ 3
	Other orthopaedic (e.g. trauma), n=2	1.36[0.75, 2.48], p=0.31	LAF: 60/1674= 3.58% No LAF:16/1016 = 1.57%	
	GI/vascular/mixed, n=5	0.44[0.19, 1.01], p=0.058	LAF: 610/43936 = 1.39% No LAF: 391/26337 = 1.48%	
Bacterial contamination in room air (CFU/m3, active air sampling)	5 cohorts (pooled)		Mean delta CFU/m^3= - 33.4[-37.2, -29.6]; p<0.0001	⊕⊕⊕◯ 4
	Orthopedic implants, n=3		MD=-41.8[-52.0, -31.5], p<0.0001	
	Other types of surgery, n=2		MD = -32.1[-36.2, -28.0], p<0.0001	

Reasons for up/downgrading:

1. Downgraded for only one study, imprecision
2. Downgraded for study limitations (sicker patients in newer theaters?), upgraded for consistent results based on very large patient populations.
3. Downgraded for study limitations, heterogeneity and in the case of GI/vascular/mixed surgery, imprecision
4. Upgraded for consistent and large effect.

Certainty of evidence

High certainty ⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty ⊕⊕⊕◯	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty ⊕⊕◯◯	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty ⊕◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

4. Abbreviations/Acronyms

CFU: colony forming units

DAIR: debridement, antibiotics and implant retention

HEPA: High efficiency particulate air

HVAC: Heating, ventilation and air conditioning

LAF: Laminar air flow

OR: Odds ratio

SSI: Surgical site infection

sSSI: Serious surgical site infection

THR: Total hip replacement

UDF: Unidirectional airflow

5. Background

Disease/disorder of interest, its degree of severity and the studied intervention

Postoperative surgical site infection (SSI) is one of the most common and also most dreaded complications after surgery. It can be a disaster for the patient and also consumes large economic resources, i.e. preventing this chain of events is worth a lot of effort. Theoretically, bacteria can reach and remain in the wound via three routes: from the patient (skin or haematogenous), via contaminated instruments/implants, or via contaminated air. The risk for the patient to develop an SSI differs depending on patient- and operation specific factors. Patient factors are e.g. the presence of immuno-suppression, disturbed metabolic state, smoking, hypothermia or other severe illnesses. Surgical risk factors also play a large role, e.g. duration of surgery, implantation of foreign material and occurrence of bleeding.

The relative importance of air contamination has been a subject for debate since the early day when Lister first tried to kill airborne bacteria by carbolic acid spray (Lister, 1867). The evolution of prosthetic implant surgery, especially orthopedic implant surgery, increased the focus on airborne infection during the 1950s. Charnley and coworkers (Charnley & Eftekhar, 1969). developed a concept with a totally closed space containing the patient and the surgical team (Charnley´s box) in which the operating team wore covering suits and got their air supply from outside the box. Using this system, Charnley reported a lowering of infection rates from 8.5% to 0.7%.

Charnley´s box is no longer being used and has been replaced by **vertical laminar air flow ventilation (LAF)**. The underlying physical principle is to try to generate unbroken lamina of air flow from ceiling to floor, to minimize admixture with undesired particles from other parts of the room. However, since the patient and the operating team are also surrounded by these jetstreams, a more correct description would be distorted LAF or distorted unidirectional ventilation. The actual setup is that you have a large area in the ceiling above the operating field where you deliver a very high outflow of air. Near the outflow area, this air will have a laminar flow-pattern but it will inevitably get distorted on the pathway downward, due to obstacles such as the operating table with the patient, the staff and the equipment, and by physical factors like heat generated from the lighting systems.

The LAF concept gained popularity after studies by Lidwell and coworkers in the early 1980s in which these authors were able to demonstrate a substantial reduction in the incidence of SSIs that was attributed to an effect of ultraclean air (Lidwell et al., 1982). This work has had an enormous impact on the evolution of ultraclean surgery, in particular orthopedic implant surgery, but the causal role of air bacteria has also been questioned due to possible presence of important confounders like different modes of antibiotic prophylaxis in the studied groups.

Nowadays, SSIs are fortunately relatively rare, usually in the order of magnitude 1-3%, depending on definitions and type of surgery. This means that to measure a clinically relevant effect (-30%) of an intervention to further reduce this low risk, a power calculation shows that one needs to collect quite large materials. For example, if demanding a power of 80% and with an expected SSI incidence of 2%, 10000 patients would be required to show a clinically relevant effect (30% reduction) of a hypothetical independent variable like change of ventilation system (Evans, 2011). To perform an RCT at this scale is not considered feasible and therefore one has taken recourse to the “second best” type of data, i.e. real world outcomes obtained from large quality registers.

This data will of course be observational only and subject to variations related to other factors in addition to ventilation, the most important one being the risk for varying thresholds and time windows for reporting of complications like SSI. There is also a risk for allocation bias related to a tendency to operate more vulnerable patients in "newer" (= often LAF-supplied) operating rooms. On the other hand, the data in the large registries are "real world data" rather than idealized (sometimes even unrealistically so) data from the desired rigorously controlled RCT studies.

Collecting clinical data is complicated and time consuming, and therefore researchers have been looking for easier-to-measure surrogate variables. The method of choice has in this case been to sample and count the number of bacterial colony forming units (CFUs) in operating room air. A CFU is a small particle that contains bacteria forming a colony of growth when applied to a culturing medium, typically an agar plate. The use of this surrogate variable is based on the assumption that contamination with airborne bacteria is indeed the major cause of SSIs, an assumption that can be questioned.

Measuring relevant CFUs in room air is however not as easy as it seems since concentrations vary markedly depending on site and mode of sampling and traffic in and out of the room. Ideally, one needs to keep track of disturbing factors like number of door-openings, number of people present in the room and their movements, the choice of clothing regimen, the overall surface cleanliness and the type of surgery. Without this information, moderate changes in CFU data become very hard to interpret. It is also important to sample from a clinically relevant location. For air sampling, it is recommended to use an active air sampling method, a slit-sampler (impaction) or a filtering based device. For measurements in the surgical area and on the instrument tables, one can used a sterilized silicone hose with the filter holder attached to the end. There is also the alternative approach to the active sampling, passive sampling by agar plates put in various positions in the operating room. If done appropriately, active and passive sampling methods usually give similar results (Shaw et al., 2018).

Ever since the early studies of Lidwell and coworkers (Lidwell et al., 1982) indicating a protective effect of ultra-clean air ventilation on the risk for SSI, a large number of LAF equipped operating rooms have been and are being built all over the world. Recently, however, a number of retrospective register studies have failed to demonstrate the expected positive effect of LAF on SSIs occurrence, studies based on large patient data sets from Germany (Brandt et al., 2008; Breier et al., 2011), New Zealand (Hooper et al., 2011; Taynton et al., 2016) and Great Britain (Pinder et al., 2016). In fact, some of these studies even indicate that the use of LAF may be a risk factor for SSIs. Late in 2016, WHO published international guidelines (WHO, 2016) for prevention of surgical site infections. The commission concluded that "Therefore, the GDG unanimously agreed that laminar airflow ventilation systems should not be used as a preventive measure to reduce the risk of SSI for total arthroplasty surgery" (WHO, 2016, p,158). As a part of the preparation of this document, Bischoff and coworkers undertook a survey of published data regarding the effect of LAF on SSI (Bischoff et al., 2017). They concluded that there was no convincing support for a patient benefit and even expressed the opinion that new operating rooms should perhaps not be equipped with LAF. Despite this caveat, LAF systems have now largely taken over the entire market for operating room ventilation.

The aim of the current HTA-analysis was to reassess the scientific literature regarding patient value of LAF systems, with strong emphasis on key clinical outcomes like mortality and different types of surgical site infections.

Prevalence and incidence

In VGR, based on point prevalence measures, about 350 postoperative wound infections occur each year, about half of which emanate from orthopedic surgery (data from 2018: surgical specialites: 169; orthopedics: 170, urology: 48). (SKL, 2018, Andel med vårdrelaterad infection).

According to Västfastigheter (personal communication Eva Lindblad, data from 2019-02-21), the Sahlgrenska University Hospital has 93 operating theaters, 18 of which are supplied with LAF roofs. The other hospitals in the VGR region together have another 98 theaters, 18 of which have LAF roofs. Approximately 80% of the operating theaters in VGR are accordingly still supplied with conventional turbulent ventilation.

Present treatment of the main adverse outcome, periprosthetic joint infections

One very important adverse outcome is periprosthetic joint infection. The treatment options for manifest implant infections are DAIR (debridement, antibiotics and implant retention), revision of THR (total hip replacement), excision of the implant, antibiotic suppression or ultimately amputation. The choice of treatment follows algorithms based on the classification of the infection into early and chronic, which are handled differently. Early infections can frequently be treated with DAIR but late infections may, despite antibiotics and repeated revisions, require failure excision (= removal of implant) or ultimately amputation (Guren et al., 2017).

Present recommendations from medical societies or health authorities

There are currently no recommendations from medical societies or health societies regarding the use of laminar flow ventilation in operating theaters. However, SIS, the Swedish Institute for Standards, has advocated the current directive SIS-TS 39:2015.

It should be emphasized that the Swedish Institute for Standards is an international organisation specialised in national and international standards. SIS publishes and sells standards and manuals, as well as offering training and consulting services. It is consequently not an official authority.

According to the mentioned SIS directive, all new theaters where “extracorporeal material” (including e.g. nets used in hernia surgery and indwelling catheters) may become inserted, should be supplied with a system that reduces the concentration of colony forming units to < 10 CFU/m3. These levels can in actual practice only be attained with a LAF system. There are also plans to further reduce this level to < 5 CFU/m^3.

Health Technology at issue: Vertical laminar airflow-based operating room ventilation

The design of heating, ventilation and air conditioning (HVAC) systems for an operating theater is aimed to prevent the risk for infections while maintaining adequate comfort conditions for the patient and the work environment climate for the surgical staff. LAF ventilation is a special case of ‘unidirectional airflow’, UDF ventilation. This technique and design is based on the principle that the supplied air is pressed through High Efficiency Particulate Air (HEPA) filters in the ceiling above the operating table at a high airflow rate. The air velocity should be high enough to preserve a stable, controlled flow over the surgery table even when it is impeded by staff activity and equipment, but still low enough not to induce auto-turbulence.

Compared with other ultraclean room technology, the size of the air supply device area and the air velocities are somewhat lower in hospital applications. Nevertheless, a number of studies confirm low contaminant levels for the UDF principle.

The definition of unidirectional airflow can be found in SS-EN ISO 14644-1:2016 and is expressed as controlled airflow through the entire cross-section of a cleanroom or a clean zone, with a steady velocity and airstreams that are considered to be parallel. The flow pattern can be described as displacement air flow, in which the air flow is unidirectional, spreading contaminants as little as possible.

The alternative air distribution technique is named mixing air flow or turbulent air flow, in which temperature and concentration of contaminants are evenly distributed in the room (non-unidirectional airflow**)** and where the supply air entering the cleanroom or clean zone mixes with the internal air by means of induction.

The design of a LAF roof thus enables supply of the room with a large air volume flow at comparatively low air velocities. Supply air is filtered with HEPA air filters and the supplied air flow is concentrated to the critical surgical zone. The air, in a unidirectional downward flow, is supplied at a lower temperature level compared to the room temperature, in order to stabilize the air flow at low air velocities, less than 0,3 m/s. The air flow should also create protection against penetration of particles from the surgical team.

6. Objective

Is the use of a laminar airflow system in operating rooms associated with a reduced risk for mortality, serious surgical site infection, surgical site infection or a reduced concentration of colony forming units in operating room air, as compared with any other type of ventilation system?

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

P1 **P2**	Orthopedic implant surgery Other types of surgery
I	I1: Permanently installed unidirectional vertical laminar airflow system (not UV light) I2: I1+ with defined and described number of air exchanges per unit time
C	Other ventilation solutions (not UV light)
O	Critical for decision making • Mortality • Serious Surgical Site Infection (sSSI), implant infection, sepsis, need for revision Important but not critical for decision making • Surgical site infection (SSI) • Bacterial exposure, measured as Colony Forming Units, CFU, measured per unit time and volume, either passively (precipitation) or actively (air sampling) during ongoing operation • Complications

Eligibility criteria
Study design:
Systematic reviews (the majority of included articles should be published after 1990)
Randomized controlled trials
Non- Randomized controlled trials

Language:
English, Swedish, Danish, Norwegian

Publication date:
1990-

7. Methods

Systematic literature search (Appendix 1)

During October 2017, with an update in May 2018 two authors (EB, AL respective AL, TS**)** performed systematic searches in Medline, PubMed, Embase, the Cochrane Library, Cinahl and a number of HTA-databases. Reference lists of relevant articles were also scrutinised for additional references. Search strategies, eligibility criteria and a graphic presentation of the selection process are presented in Appendix 1. These authors conducted the literature searches, selected studies, and independently of one another assessed the obtained abstracts and made a first selection of full-text articles for inclusion or exclusion. Any disagreements were resolved in consensus. The remaining articles were sent to all the participants of the project group.

All authors read the articles independently of one another and it was finally decided in a consensus meeting which articles should be included in the assessment

Critical appraisal and certainty of evidence

The included studies and their design and patient characteristics are presented in Appendix 2. The excluded studies and the reasons for exclusion are presented in Appendix 3. The included studies have been critically appraised using checklists from the SBU for assessment of cohort studies and a checklist for assessment of randomised controlled trials, both checklists are modified by HTA-centrum. The results and the assessed quality of each article have been summarised per outcome in Appendix 4. A summary result per outcome and the associated certainty of evidence are presented in a Summary-of-findings table (page 7). The certainty of evidence was defined according to the GRADE system (Atkins et al., 2004; GRADE Working group, 2017).

Ongoing research

A search in Clinicaltrials.gov (2019-02-26 using the search terms (laminar OR laminated OR ultraclean OR ultra-clean OR unidirectional) identified 148 trials. None of the trials was considered relevant for our question.

8. Results

Description of included studies and patient data base

The identified literature consisted of 33 studies, five of which were systematic reviews/HTA reports. We found one RCT (outcome passive sampling of CFUs) that was handled as a cohort since the relevant comparison, type of ventilation, was not randomized. There were 27 other cohort studies containing data from more than 1 million operations (mainly retrospective registry data). For the critical outcome serious surgical site infections, there were more than 19000 events (Table 1).

Cohorts	Implant orthopedics (P1)	Other surgery (P2)	Total
Number of studies	14	13	27
Outcome mortality	0	1	1
Number of operations	0	159	159
Number of events	0	9	9
Outcome serious SSI or need for revision	10	7	17
Number of operations	458230	650738	1108968
Number of events	2902	16500	19402
Outcome SSI	2	8	10
Number of operations	44293	71484	115777
Number of events	714	1060	1774
Outcome CFU/m^3 in room air	3	2	5
Number of measurements	370	197	567

Table 1: Summary of identified database in terms of number of studies, number of events and number of operations.

The structure of the results section is as follows: In the first section (1.1-1.4), we present the effects of LAF as unadjusted odds ratios calculated directly from number of events and total number of operations in theaters with or without LAF ventilation. This approach makes it possible to calculate absolute risk (number of events/number of operations). This straightforward approach does not compensate for possible confounders, most notably in this case differences regarding type of operation and allocation bias (= a possible tendency to operate more "vulnerable" patients in newer theaters). Therefore, in the second section (2.1-2.4) we also performed subgroup analyses in the implant surgery material and for the critical outcome serious SSI. The aim of the subgroup analysis was to assess some of the following potential confounding factors:

1. Differences between hip and knee implant surgery (type of implant surgery).
2. Differences between registry studies and before-and-after studies (the latter will be expected to have a lower risk for allocation bias);
3. Differences between studies describing or not describing air volume flow (the former may have a lower risk for inappropriate intervention);
4. Comparison of unadjusted and adjusted Odds ratios, in the latter case with adjustment for age, sex, risk index/ diagnosis and length of operation, by multivariate analysis (attempt to reduce allocation bias).

1. **Analysis of the entire unadjusted data, with ORs calculated from number of events and number of operations.**

    1.1. For the outcome mortality, we only found one small study of low quality involving orthopedic trauma surgery patients (P2 group). OR [95% CI] for mortality was 1.09[0.28, 4.23], p=0.90

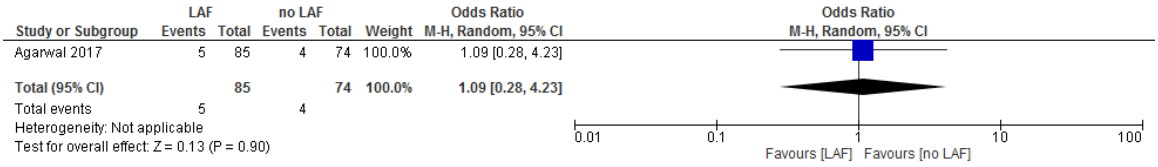


Fig 1: OR for mortality with or without LAF ventilation in operating theater.

Conclusion: It is uncertain whether laminar airflow compared with any other ventilation in operating theaters is associated with changes in postoperative mortality. Very low certainty of evidence, GRADE⊕◯◯◯

1.2.Serious surgical site infection or need for revision (sSSI).

This key outcome was studied in both patient groups (P1 and P2), with a total material consisting of more than 1.1 million patients and almost 20000 events. Due to the heterogeneity of the material, the data was separately analysed in the three subpopulations (implant surgery, other orthopedic surgery, and GI, vascular, mixed surgery) and was not pooled. There was no significant effect of LAF in in orthopedic implant surgery (OR=1.20[0.97, 1.49], p=0.09) or GI/vascular/mixed surgery (OR=1.23[0.97, 1.56], p=0.09. However, in non-implant orthopedic surgery (mainly trauma surgery), there was a significantly increased risk for sSSI in LAF theaters (OR= 1.13[1.08, 1.18], p<0.0001). This finding was based on a large UK study of high quality with 507024+81509 operations and 13690+1956 events.

Please note that an OR value greater than 1 implies an increased risk in LAF theaters.

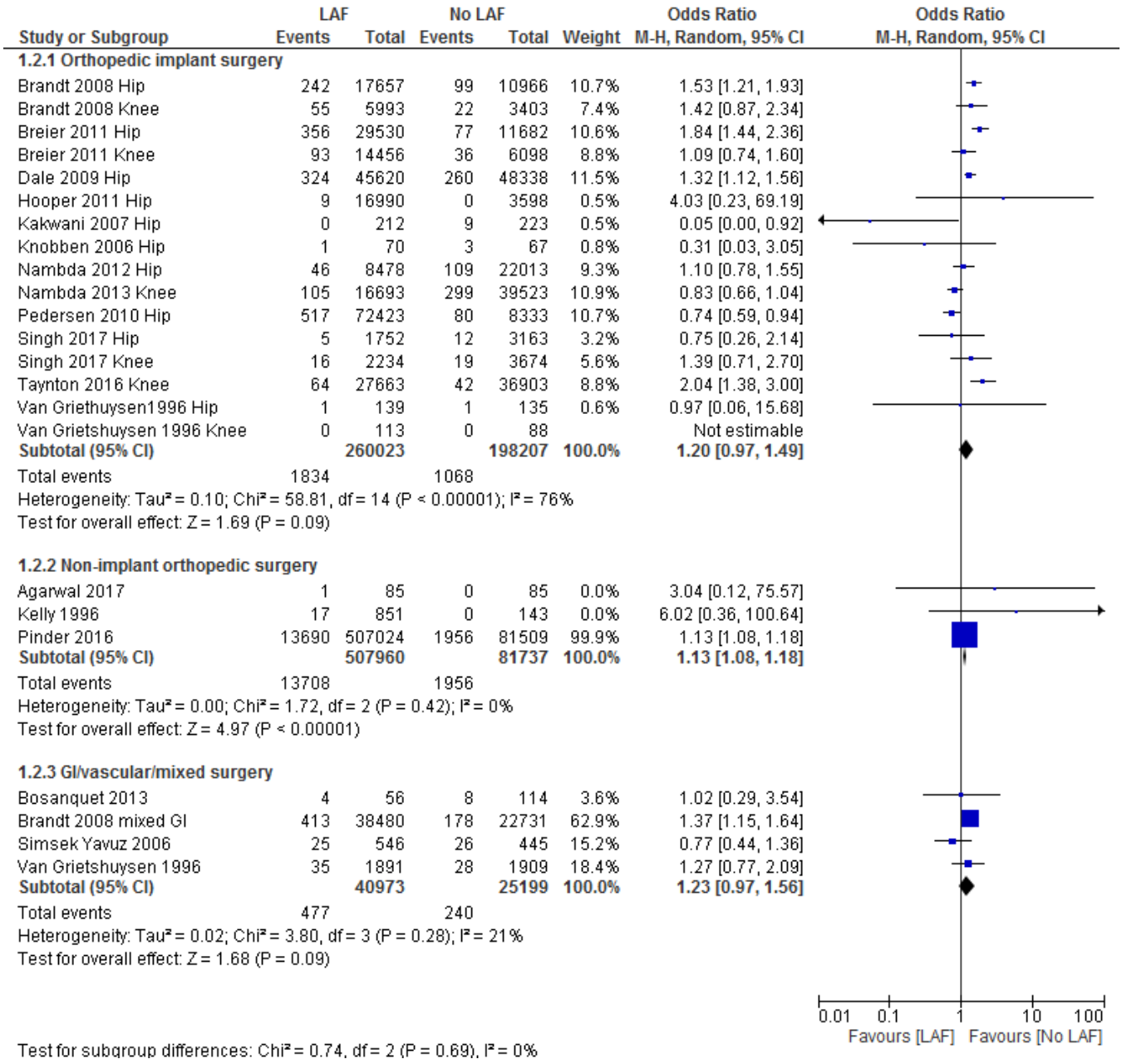


Fig 2: Unadjusted OR for serious surgical site infection (sSSI) calculated from number of events and number of operations, in theaters with or without LAF ventilation.

The funnel plot (relating OR to its confidence interval/study size, where asymmetry may reflect possible publication bias in smaller studies) showed a tendency to a more favourable effect of LAF in small studies in orthopedic implant surgery (4/5 estimations were to the left of the mean OR line).

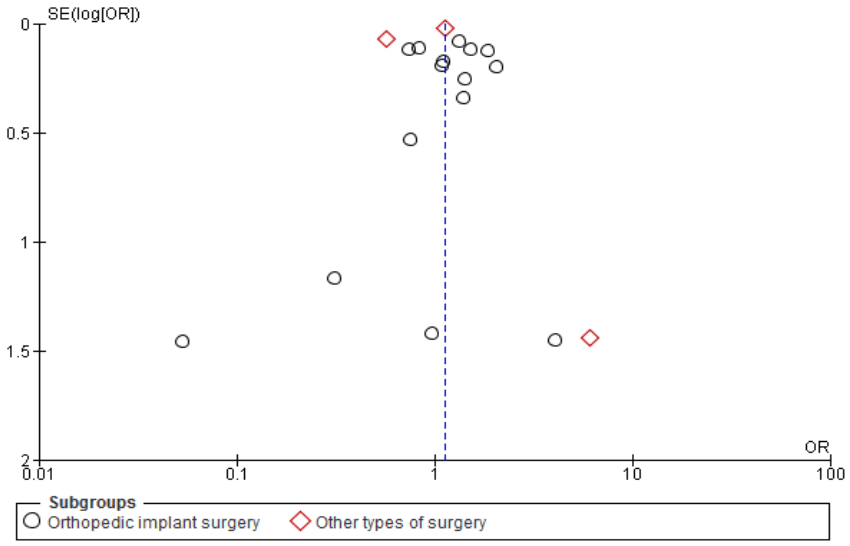


Fig 3: Funnel plot of confidence interval of unadjusted OR related to unadjusted OR in the individual studies. Studies with a large confidence interval (high SE(log OR)) are expected to vary more, but symmetrically around the same OR as in the studies with narrower confidence interval.

Conclusion: Depending on type of surgery, laminar airflow compared with any other ventilation in operating theaters may be associated with increased risk or little or no difference in risk for serious surgical site infection. Low certainty of evidence, GRADE ⊕⊕◯◯.

1.3.Surgical site infection (SSI)

There was no significant effect on SSI in the orthopedic groups (OR in implant group: 1.18[0.78, 1.80], p=0.43; OR in non-implant group = 1.36[0.75, 2.48], p=0.31) or in the GI/vascular/mixed group (OR= 0.44[0.19, 1.01], p=0.058 (p-value 0.05 in figure is a two-digit number rounding error in Revman). Like for serious SSI, we refrained from pooling data due to clinical heterogeneity.

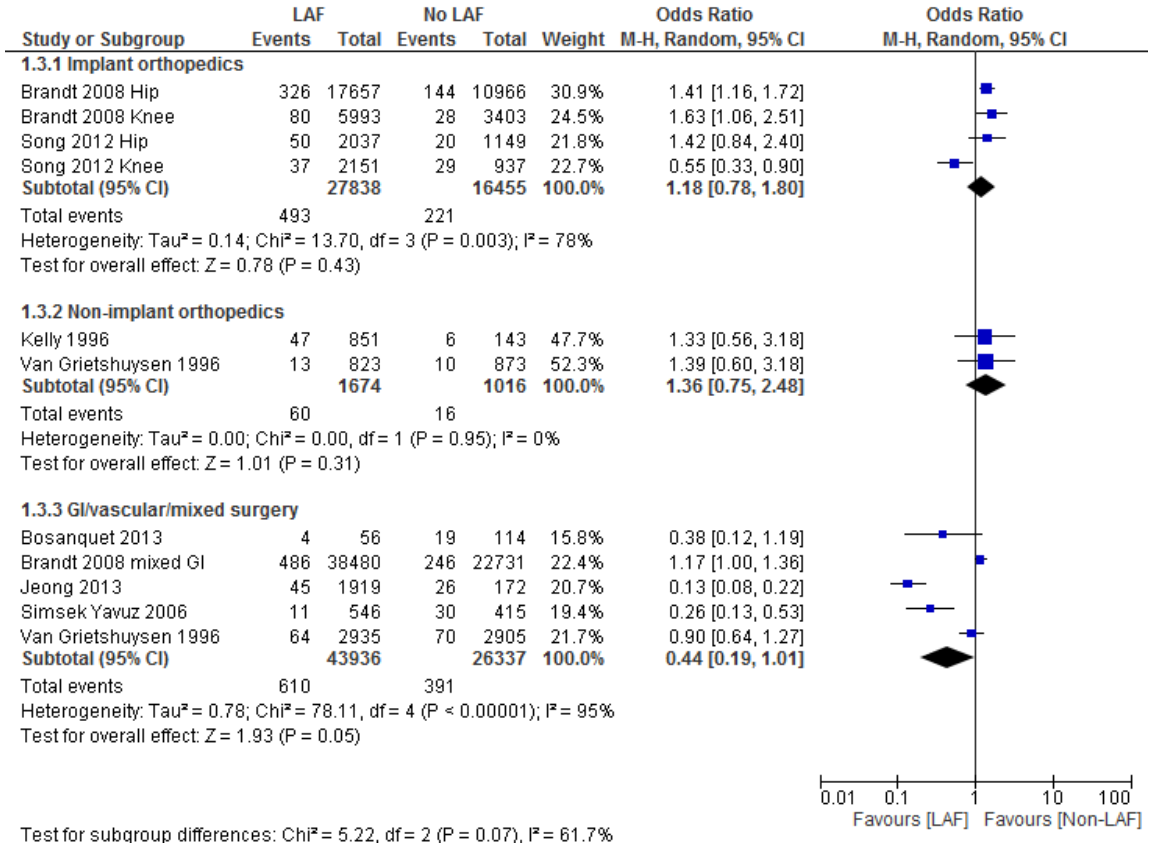


Fig 4: Unadjusted OR for surgical site infection, calculated from number of events and number of operations in theaters with or without LAF.

Conclusion: It is uncertain whether laminar airflow ventilation in operating theaters is associated with changes in the risk for surgical site infections, in mixed materials of implant- and other types of surgery. Very low certainty of evidence, GRADE ⊕◯◯◯.

1.4.Colony forming unit (CFU) concentration in air sampled adjacent to operating table

The mean CFU reduction with LAF in the whole material was based on 366+201= 567 air samplings. In elective orthopedic surgery, mean difference (MD) with LAF was a reduction of -42[-52, -32] CFU/m^3 and in other types of surgery (trauma orthopedics and cardiothoracic/urological respectively) -32[-36,-28] CFU/m^3, in both cases $p<0.0001$.The basal CFU count (mean (SD)) in non-LAF theaters was 51(18) CFU/m^3, i.e. there was a substantial reduction with LAF. There was no significant subgroup difference, making it reasonable to calculate a pooled estimate (MD = -33[-37, -30] CFU/m^3, $p<0.0001$.

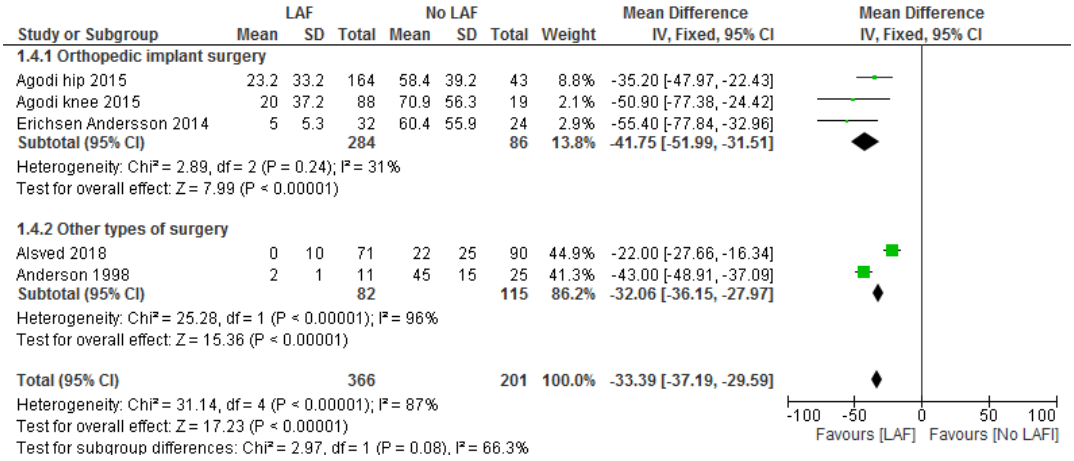


Fig 5: Mean difference and 95% confidence intervals of number of CFUs/m^3 in room air, in theaters supplied or not supplied with LAF.

1.5. Passive bacterial sampling

This outcome was assessed in seven cohort studies (see appendix 4.1.5). Different sampling sites and different methods of sampling were used, making metaanalysis of the entire dataset impossible. LAF ventilation did however consistently lead to a substantial reduction in the numbers of bacteria recovered by passive sampling, with some variations depending on where in the operating room the culture media had been placed.

Conclusion: LAF is probably associated with a substantial reduction in the concentration of CFUs in air sampled in the vicinity of the operating table. Moderate certainty of evidence, GRADE⊕⊕⊕◯.

2. Subgroup analyses in group P1 (implant surgery), regarding the outcome serious SSI

Since there was substantial heterogeneity among studies measuring this critical outcome, further subgroup analyses were performed to try to identify subgroups with a different risk profile. Four subgroups were studied: hip and knee implant surgery, register-based cohort studies and before-and-after studies, studies with or without numeric data regarding air volume flow, and studies using multivariate regression to adjust for some important potential confounders.

2.1. Subgroups hip and knee implant surgery

OR was 1.18[0.91, 1.52], p=0.20 in the hip implant group and 1.26[0.87, 1.83], p=0.21 in the knee implant group. The absolute risk for serious SSI in the hip group was 1546/201279 = 0.78% for LAF systems and 756/130464 = 0.58% for No LAF systems. The corresponding numbers in the knee group were 333/67152= 0.50% for LAF and 418/89689 = 0.46% for non-LAF systems (p=0.21). There was significant heterogeneity but no significant subgroup difference (p=0.77). Location of joint implant surgery accordingly did not significantly influence the effects of LAF on the risk for serious SSI.

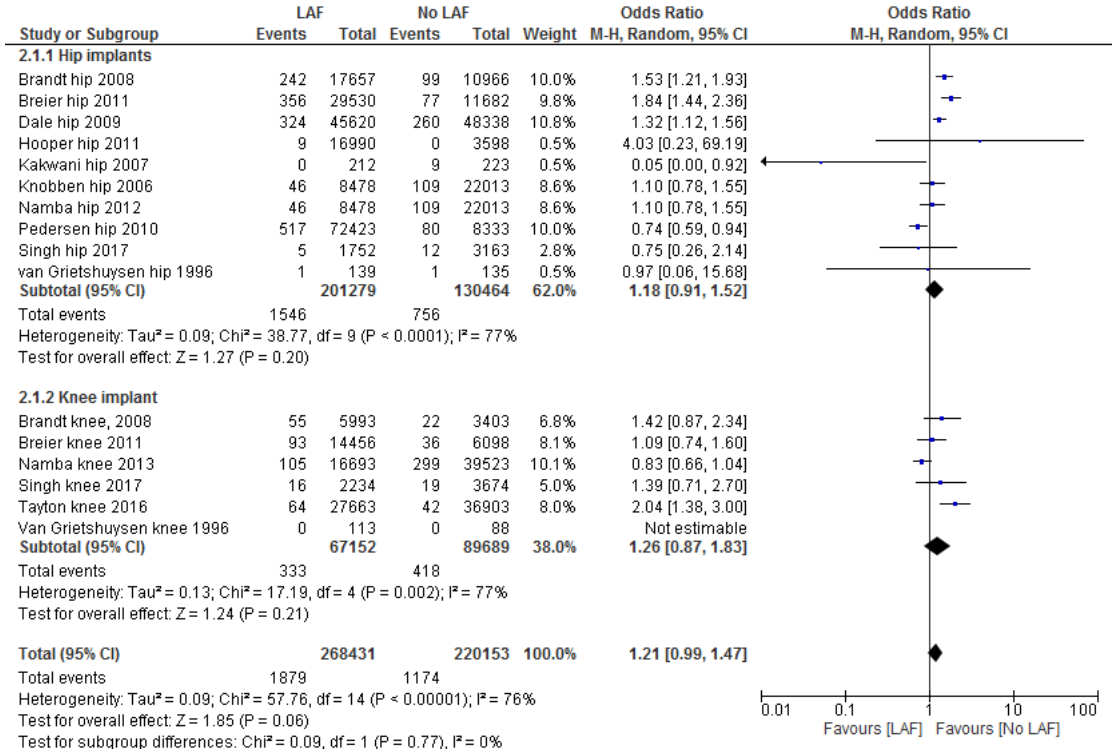


Fig 6: Unadjusted OR for serious surgical site infection separated calculated in hip and knee implant surgery on the basis of events and number of operations. Mean and 95% confidence intervals.

2.2.Subgrouping based on study type

Since the main source of analysis was registry data with an inherent but unknown risk for allocation bias due to a possible tendency to operate more severe cases in newer theaters, we separately evaluated studies in which LAF ventilation had been introduced at a certain time point in the same setting, thus enabling before-and-after analysis. Data was only available for the hip implant group.

Odds ratio for serious SSI in the cohorts (registry studies) was 1.22[0.91, 1.62], p=0.18 and in the three small before-and-after studies of low quality 0.26[0.05, 1.33], p=0.11. While there were 2127 events in the registry studies, there were only 15 events in the before-and-after studies. The subgroup difference in OR was not statistically significant (p=0.07).

We also identified one larger study based on trauma orthopedic surgery (Pinder et al., 2016) that contained data for SSI before and after installation of a LAF system. SSI risk in theaters never supplied with LAF (14018 operations) was set as 1. Before installation (n=739), relative OR was 1.22[1.00, 1.51](p=0.055) and after installation (1406 operations), relative OR was 1.26[1.04, 1.54], p=0.021 as compared to never LAF group.

Before-and-after design did not significantly change the effect of LAF on the risk for sSSI.

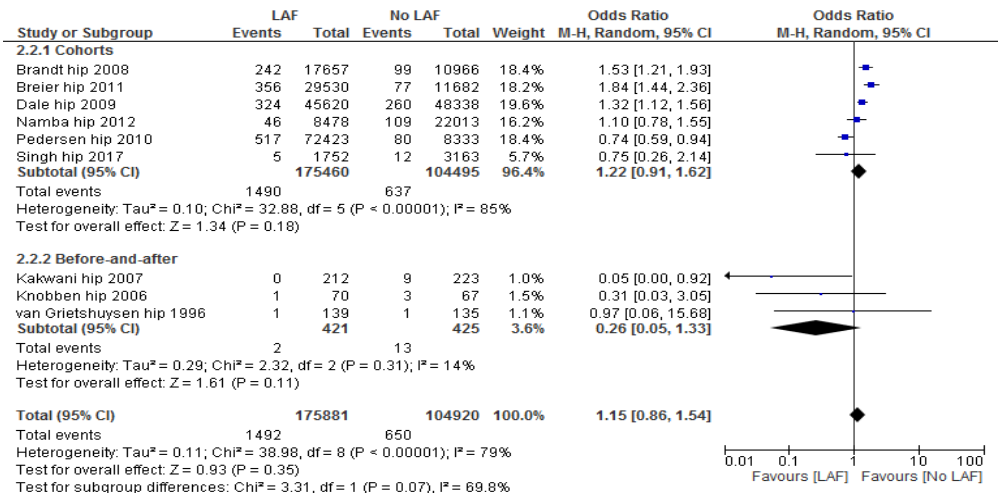


Fig 7: Subgrouping of unadjusted ORs, as calculated from number of events and number of operations, in cross-sectional/cohort studies and in studies containing before-and-after data, i.e. data before and after installation of a LAF system. OR denotes risk for serious SSI in theaters with or without LAF and a value higher than 1 indicates an increased risk with LAF.

2.3.Subgrouping based on statement or not of air volume flow (assessment of intervention I2)

The rationale for this analysis was that studies not stating volume flow might be based on the wrong intervention, e.g. technically suboptimal conditions. OR for serious SSI in studies without statement of air volume flow was 1.09[0.81, 1.45], p=0.58 and for those stating air volume flow 0.91[0.11, 7.34], p=0.93. The difference was not statistically significant (p=0.87). OR in studies containing statements regarding of air volume flow was not significantly different from that reported in those lacking air volume flow data.

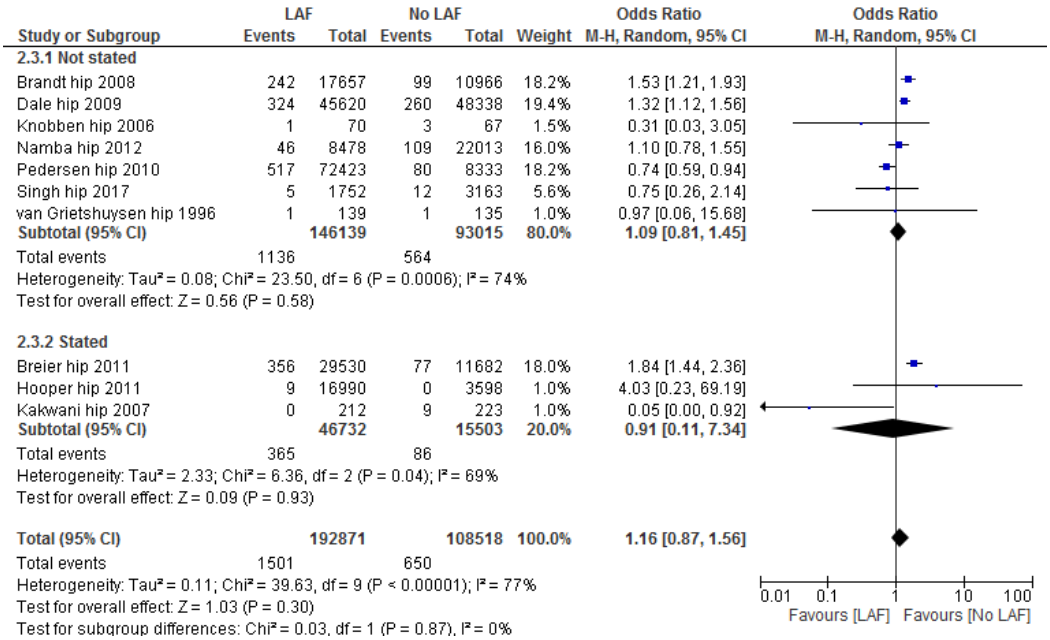
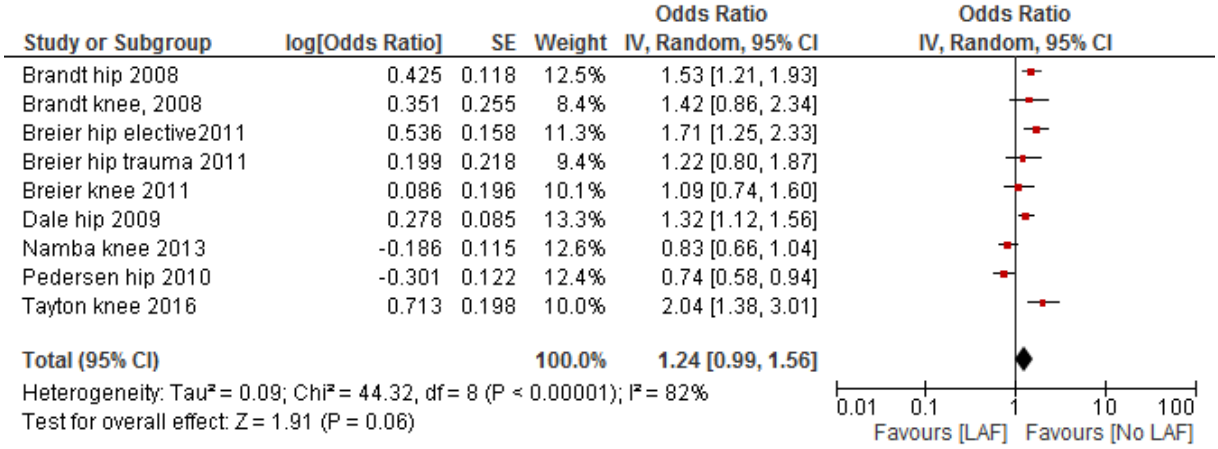


Fig 8: Unadjusted OR for serious SSI, calculated from number of events and number of operations in theaters with or without LAF. Data from studies stating or not stating air volume flow are placed in two different subgroups.

2.4. Results with or without multivariate analysis with adjustment for some possible covariates: A subgroup of studies (6 studies with 9 separate data sets) contained both unadjusted and adjusted data. To increase the power of the analysis, we here included both hip- and knee implant as well as trauma surgeries (n=9 patient data sets). The main adjustment factors assessed were age, gender, risk index/diagnosis and operation time. Before multivariable analysis, OR for serious SSI was 1.24[0.99, 1.56] and after correction 1.17[0.96, 1.43]. OR increased after adjustment in five data sets, decreased in three data sets and remained unchanged in one data set. The difference in OR calculated without or with adjustment for these covariates was not statistically significant (p=0.54). Adjustment for the covariates age, gender, risk index/diagnosis or operation time accordingly did not significantly influence OR for the effect of LAF on serious SSI.

Before correction:



After correction:

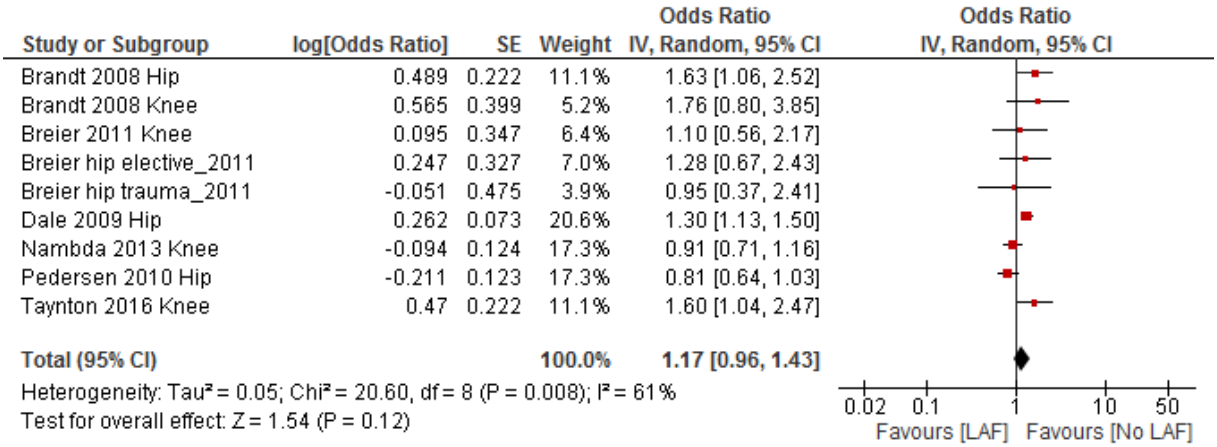


Fig 9: Unadjusted and adjusted ORs for serious surgical site infection, in studies giving both kinds of data. Adjustments were made for age, sex, diagnosis and duration of surgery. The comparison was operation in a theater supplied or not supplied with LAF and an OR value higher than 1 implies an increased risk with LAF.

9. Ethical aspects

The analysis does not support the hypothesis that laminar airflow ventilation is associated with any reduction of important adverse outcomes like serious or less serious surgical site infections. In one subgroup (orthopaedic trauma surgery), a significantly increased risk for serious SSI was actually seen. LAF systems have, based on effects of surrogate variables like colony forming units in operating theatre room air, nevertheless become the modern standard for operation theatre ventilation. Recommending this type of ventilation in the absence of scientific evidence for any patient benefit or even with a possible detrimental effect in some patient groups, does not follow the ethical principles benefit versus harm or, in situations where there is no effect, the cost-efficiency principle.

10. Organisational aspects

Time frame for the putative introduction of the new health technology

As stated above, approximately 20% of operating theaters in VGR are today supplied with LAF ventilation (see introductory section). Sooner or later, these theaters will have to be rebuilt and then supplying them with LAF or not will be an important strategic decision.

Consequences of the new health technology for personnel

LAF ventilation offers a method to distribute a large amount of ultra clean air into the operation theatre with maintained acceptable working conditions. Mixed ventilation results in multiple smaller outlets of ultraclean air resulting in high velocity flow creating noise and “jet streams” that may have a negative effect on the working environment for staff present in the operating theatre.

Consequences for other clinics or supporting functions at the hospital or in the Region Västra Götaland

Region Västra Götaland currently has a large number of building projects where the type of ventilation in operating theaters is under consideration. Rebuilding these theaters just for the sake of conversion to LAF systems would involve very substantial costs (see economic section).

11. Economic aspects

Present costs of studied adverse outcomes

The differences in running costs among current systems (LAF or non-LAF) are relatively small, given that it relates to the energy use and frequency of filter changes. The main cost-differences apply to investment costs for new ventilation systems. On the other hand, handling of postoperative infection is extremely costly (see below) and if ventilation systems did indeed substantially reduce postoperative wound infections, this would rapidly balance these investment costs. With around 350 annual postoperative wound infections in VGR and an average cost per infection (serious SSI) at around 107,000 SEK (increases length of stay on the average by more than 10 days), this gives a total cost for postoperative wound infections of around 37.5 million SEK per year.

Expected costs of the new health technology
There are around 200 operating theaters in VGR, about 20% of which are supplied with LAF roofs. Cost consequences with LAF can be viewed in two main scenarios with different comparators: (1) a scenario comparing costs to conventional ventilation when e.g. renovating existing rooms, (2) a scenario comparing costs between LAF and other "modern" ventilation techniques marketed by suppliers.

Costs compared to conventional ventilation
Investment costs include the LAF-roof, circulation unit, air handling unit, and filters. Based on recent tenders, the average investment costs per room can be approximated to 800,000 – 900,000 SEK (excluding costs related to building alterations). Adding building alterations will of course dramatically increase this cost.

Assuming a life-length of 15 years and a discount rate of 3% and 500 operations per room and year this gives an added cost per each operation of about 130 – 140 SEK.

Costs compared to other modern ventilation techniques
LAF ventilation systems are not more expensive compared to other modern ventilation systems supplied by the major producers (including TAF solutions). If anything, based on recent tenders, LAF has slightly lower investment costs. Due to higher airflow and energy use, running costs are slightly higher with LAF. The difference in cost per operation, when comparing different modern ventilation systems offered by producers in a recent tender, are relatively minor.

Total change in costs
Investment cost to introduce LAF in existing operation rooms with conventional ventilation adds up to at least 800,000 – 900,000 SEK per room (see above). Since there are about 160 non-LAF operating theaters in VGR, conversion of all these theaters into LAF rooms – as it seems on the basis of an arbitrarily set CFU threshold - will generate a cost of at least 128 million SEK, without any scientifically proven patient value.

Possibility to adopt and use the new technology within the present budget
There are no available funds in the present budget to fund LAF investments. Thus, other currently offered health services will be displaced if investments in LAF are carried out.

Available economic evaluations
A few studies regarding cost consequences and/or cost-effectiveness of laminar airflow ventilation were identified in the searches, but none from a Swedish health care setting. Since there is no documented patient benefit, these calculations are only relevant in terms of cost calculations.

Graves et al. (2016) evaluated the cost-effectiveness of nine different combination treatment strategies to reduce the (postulated) i.e. risk of infection following primary hip replacement. They reported a mean added cost per case (operation) between £6.33 and £9.50 with LAF compared to conventional ventilation, which is slightly lower compared to our estimate above, but no improvement in terms of quality adjusted life years (QALYs). LAF was dominated (= more costly and worse health outcomes) by e.g. the combination of the use of systemic antibiotics, antibiotic-impregnated cement and conventional ventilation.

A similar study was published by Merollini et al. (2013), in which they evaluated the cost-effectiveness of LAF using a decision-analytic model that was created based on data retrieved from a systematic review. They compared the costs with the change in QALYs and the results indicated that costs increased by approx. 153 Australian dollars per each total hip arthroplasty without any added health benefits.

Hooper et al. (2011) evaluated LAF together with space suits based on observational register data from New Zealand. They found that LAF (admittedly combined with space suits) increased costs and was furthermore associated with a higher rate of early deep infections.

12. Discussion

Summary of main results

Our literature search identified five previous systematic reviews on this topic since 2001 (Segadal et al., 2001; Ventilation pa operationsstuer 2011; Lowson et al., 2011 (mainly economics), Gastmeier, Breier & Brandt, 2012; Bischoff et al., 2017). All these systematic reviews conclude that there is no evidence for a beneficial effect of LAF ventilation on the risk for the key patient outcome serious surgical site infection. This lack of effect is seen despite clearcut reductions in the concentration of number of colony forming units (CFUs) in operating room air. The consistent results are not surprising, since the majority of these reviews are based on the same underlying patient data. The current report can therefore be regarded as an update, but we also added a number of subgroup analyses to identify potential confounders that might mask a hypothetical beneficial effect. The confounders tested were type of orthopedic implant surgery (hip or knee), comparison of register data and before-and-after studies (to minimize allocation bias), comparison of studies stating air volume flow or not, and finally studies correcting (or not) for important allocation factors like age, sex, diagnosis or duration of operation. However, none of these confounding factor focused analyses revealed any evidence for a significant beneficial effect of LAF ventilation on the studied patient outcomes.

Overall completeness and applicability of evidence

When interpreting data from registry studies there are some important possible sources of error in the form of confounders that can be roughly grouped into risks for allocation and detection bias.

Allocation bias might in this case be generated by a tendency to operate more severe cases with a presumed larger risk in the (generally newer) LAF theaters. Since we found no randomised or even interventional trials regarding the sSSI outcome, this possibility cannot be excluded. However, if that were the case, one would have expected unmasking of a beneficial effect in the subgroups before-and-after studies (same setting, different ventilation) and those with adjustment for main putative confounders, but this was not the case. Such a trend was indeed seen in the before-and-after group, but these studies were small with very few events and of low quality, and the tendency for a beneficial effect was not statistically significant. Moreover, since the conversion was always from conventional ventilation to LAF theaters, the tendency to improved results may simply be a time phenomenon. Moreover, in a larger study by Pinder et al. (2016) on trauma surgery patients, Odds ratio for sSSI was compared before, during and after supplying operating theaters with LAF. OR in a larger database of patients not operated in LAF theaters was used as reference (= 1). After installation of LAF, relative OR for sSSI was 1.26[1.04, 1.54], p=0.021.

Another potential source of error is detection bias, e.g. the occurrence of adverse events not identified in the register studies**.** As described in the introduction, late SSIs can be missed in the registries, a phenomenon that might cause substantial errors. The magnitude of the combined incidence of SSIs (serious and less serious) in the current data set was 1-2%, lower in implant surgery and higher in other types of surgery. For hip implants, serious SSI incidence was 0.58% in non LAF and 0.77% in LAF. This is a somewhat lower frequency than in the Swedish Hip Arthroplasty Registry (SHAR): 1.3%, a figure that may also be an underestimation due to incomplete reporting. However, why underreporting should occur more frequently in patients operated in non LAF theaters is difficult to envisage.

This error would have to be quite large to mask a hypothetical beneficial effect of LAF, in view of the actual tendency to a harmful effect in the large underlying data set with more than a million operations.

The evidence that LAF systems are associated with a reduction in the number of bacteria-containing particles in room air, so called colony forming units, is convincing. The meta-analysis was admittedly based on air sampling data only but the studies using passive sampling gave essentially the same results.
A good correlation between results from technically appropriately performed active and passive sampling is well supported in the literature (Shaw et al., 2018).

This is not the place to discuss mechanisms behind the discrepancy between CFU counting and clinical data, but our findings (confirming previous systematic reviews and a WHO report, see next section), imply that in the low concentration range that is relevant here, the CFU surrogate variable cannot be used as a straightforward basis for decisions to rebuild operating theaters.

Agreements and disagreements with other studies and reviews

Our conclusions are in accordance with those of four previous systematic reviews and one HTA-report based on parts of the datasets underlying the current report.

Implications for research

The lack of congruence between data from bacterial sampling and clinical outcomes needs to be better understood, e.g. by collecting both types of data from the same patients.

13. Future perspectives

Scientific knowledge gaps

The conclusion of a lack of a beneficial effect of LAF on patient outcomes is based on “real-world” registry studies and a few before-and-after observational studies. There is strong need for a proper prospective, randomized intervention trials, with direct comparison of LAF- and non LAF theaters and with thorough standardization of as many confounding factors as possible. There is also a need to get a better understanding of the lack of congruence between low-range CFU concentrations in operating room air with patient outcomes, including threshold phenomena.

Ongoing research

At a search conducted 2019-02-26, we identified 148 planned trials indirectly related to operation room ventilation. However, none of these protocols fitted exactly with our PICO.

14. Participants in the project

The question was nominated by

Erik Houltz, M.D., Ph.D., senior consultant, Department of Anaesthesiology and Intensive Care, Sahlgrenska University Hospital, Gothenburg, and clinical lecturer at the Institution of Clinical Sciences, Sahlgrenska

Participating evaluation team members

Erik Houltz, M.D., Ph.D., senior consultant, Department of Anaesthesiology and Intensive Care, Sahlgrenska University Hospital, Gothenburg, Sweden and clinical lecturer at the Institution of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
Henrik Malchau, MD, professor. Department of Orthopaedics, Sahlgrenska University Hospital, Mölndal, Sweden
Jan Gustén, Professor in Building Services Engineering, Chalmers University of Technology, Gothenburg, Sweden
Jonathan Moonen, MD, Department of Anaesthesiology and Intensive Care, Sahlgrenska University Hospital, Gothenburg, Sweden
Peter Grant, M.D. PhD, consultant, Department of Orthopaedics, Sahlgrenska University Hospital, Mölndal, Sweden

Participants from the HTA-centrum

Ann Liljegren, medical librarian, Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden
Emil Björkander, medical librarian, Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden
Henrik Sjövall, MD. professor, HTA-centrum, Region Västra Götaland, Gothenburg, Sweden
Lennart Jivegård, MD, Senior university lecturer, HTA-centrum, Region Västra Götaland, Gothenburg, Sweden
Max Petzold, professor, HTA-centrum, Region Västra Götaland, Gothenburg, Sweden
Mikael Svensson, professor, HTA-centrum, Region Västra Götaland, Gothenburg, Sweden
Pernilla Brown, project coordinator, Region Västra Götaland, Gothenburg, Sweden
Therese Svanberg, medical librarian, Medical Library, Sahlgrenska University Hospital, Gothenburg, Sweden

External reviewers

Christian Rylander, MD, Associate Professor, Intensive Care Unit 96/CIVA, Department of Anaesthesia and Intensive Care Sahlgrenska University Hospital, Göteborg, Sweden
Peter Ulleryd, Regional Medical Officer, Dept. of Communicable Disease Control and Prevention Region Västra Götaland, Borås, Sweden

Declarations of interests

Erik Houltz: None declared
Henrik Malchau: None declared
Jan Gustén: None declared
Jonathan Moonen: None declared
Peter Grant: Research on operating theater ventilation, checks performance of operating theater ventilation through own company (PeterGrantOrtopediAB)

Participants from the HTA-centrum

Ann Liljegren: None declared
Henrik Sjövall: None declared
Lennart Jivegård: None declared
Max Petzold None declared
Mikael Svensson: None declared
Pernilla Brown: None declared
Therese Svanberg: None declared

Project time

The HTA was accomplished during the period of 2017-10-02 – 2019-06-11.
Literature searches were made in 2017-10-16 and updated 2018-05-31.

Appendix 1: Search strategy, study selection and references

Objective

Is the use of a laminar airflow system in operating rooms associated with a reduced risk for mortality, serious surgical site infection, surgical site infection or a reduced concentration of colony forming units in operating room air, as compared with any other type of ventilation system?

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

P1 **P2**	Orthopedic implant surgery Other types of surgery
I	I1: Permanently installed unidirectional vertical laminar airflow system (not UV light) I2: I1+ with defined and described number of air exchanges per unit time
C	Other ventilation solutions (not UV light)
O	<u>Critical for decision making</u> • Mortality • Serious Surgical Site Infection (sSSI), implant infection, sepsis, need for revision <u>Important but not critical for decision making</u> • Surgical site infection (SSI) • Bacterial exposure, measured as Colony Forming Units, CFU, measured per unit time and volume, either passively (precipitation) or actively (air sampling) during ongoing operation • Complications

Study design:

- Systematic reviews (the majority of included articles will be published after 1990)
- Randomised controlled trials
- Non- Randomised controlled trials

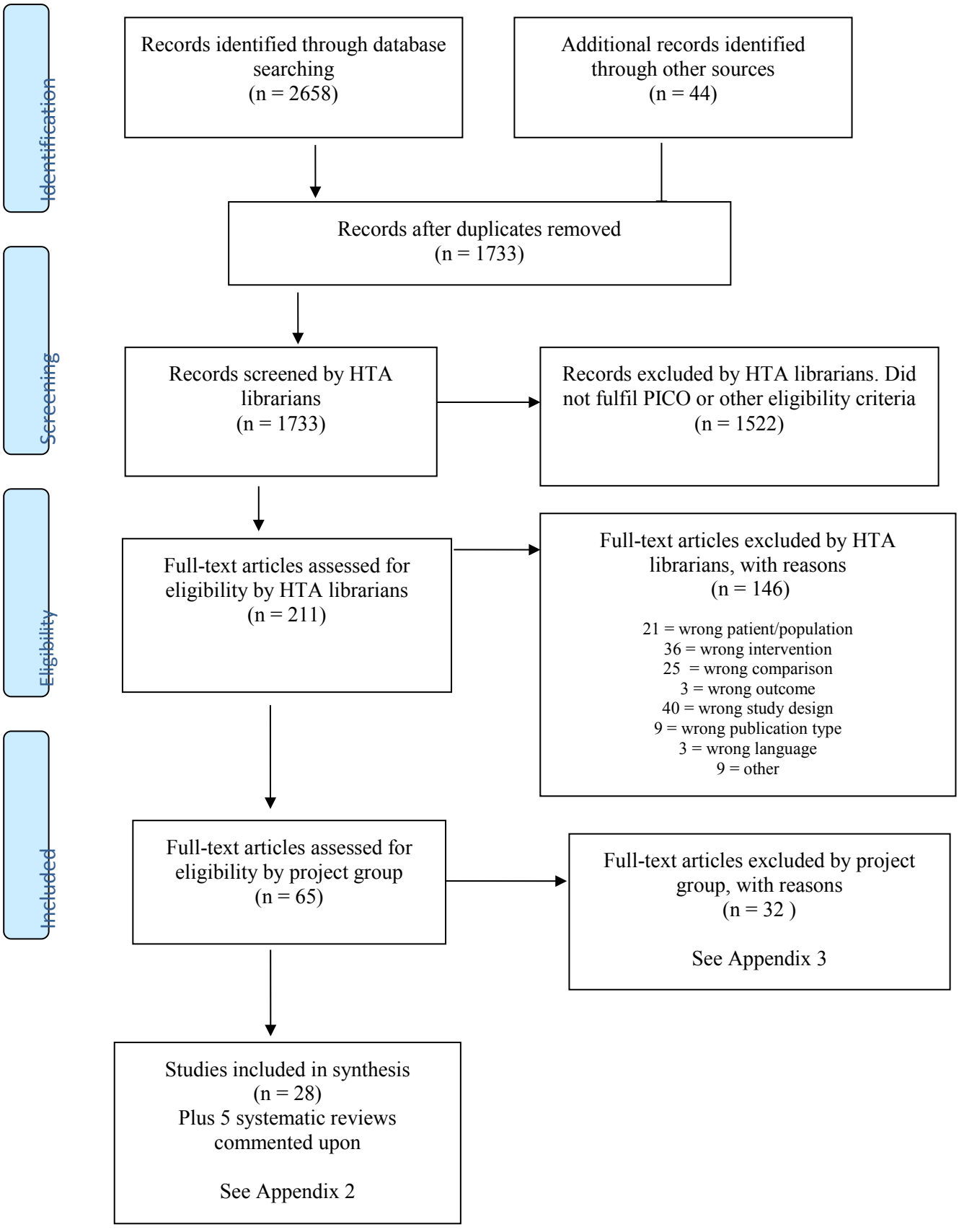
Language:

English, Swedish, Danish, Norwegian

Publication date:

1990-

Selection process – flow diagram



Search strategies

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Date: 2017-10-12
No of results: 774
Search updated: 2018-05-31, 45 results

#	Searches	Results
1	exp infection/	748113
2	exp bacteria/	1305988
3	exp microbiological techniques/	294919
4	exp Air Microbiology/	7334
5	((surg* or deep or severe or wound* or postoperative* or post-operative*) adj4 infection*).ab,ti.	82597
6	(colony adj3 form*).ab,ti.	44645
7	(SSI or CFU or sepsis or septic disease*).ab,ti.	131004
8	(implant* and infection*).ab,ti.	23331
9	((air or airborne) adj4 (bacteria* or bacterium* or partic* or infection* or contamination*or count* or sampl*)).ab,ti.	21553
10	((Bacteri* or bacterium or microbi*) adj4 (contamination* or colon* or fallout* or infection* or control* or content* or count* or load*)).ab,ti.	123361
11	exp reoperation/	82597
12	exp risk factors/	751280
13	(infection* adj6 risk*).ab,ti.	78949
14	(risk factor* or reoperation* or re-operation* or revision*).ab,ti.	604908
15	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	3261136
16	exp Environment, Controlled/	308633
17	exp air pollution, indoor/	12005
18	(laminar* or laminated* or ultraclean* or ultra-clean* or unidirectional*).ab,ti.	32018
19	((Temperature* or direc*) adj4 (air* or airflow* or air-flow* or flow*)).ab,ti.	28060
20	(LAF or UVC or TAF or aircon* or air con* or ventilation* or UDF).ab,ti.	122776
21	16 or 17 or 18 or 19 or 20	485317
22	exp operating rooms/	12727
23	((Operat* or surg*) adj5 (department* or room* or ward* or area*)).ab,ti.	88387
24	(theater* or theatre*).ab,ti.	11357
25	22 or 23 or 24	104254
26	15 and 21 and 25	1362
27	limit 26 to ((danish or swedish or english or norwegian) and yr="1990 -Current")	822
28	(animals not (animals and humans)).sh.	4642364
29	27 not 28	807
30	(comment or editorial or letter).pt.	1670464
31	29 not 30	774

Database: PubMed
Date: 2017-10-13
No of results: 239
Search updated: 2018-05-31, 90 results

Search	Query	Results
#24	Search #22 AND #23 Filters: Danish; English; Norwegian; Swedish	239
#23	Search (pubmednotmedline[sb] OR inprocess[sb] OR publisher[sb]) Filters: Danish; English; Norwegian; Swedish	3274823
#22	Search #13 AND #17 AND #20 Filters: Danish; English; Norwegian; Swedish	1535
#21	Search #13 AND #17 AND #20	1794
#20	Search #18 OR #19	270246
#19	Search theater*[tiab] or theatre*[tiab]	10804
#18	Search (Operat*[tiab] or surg*[tiab]) AND (department*[tiab] or room*[tiab] or ward*[tiab] or area*[tiab])	261937
#17	Search #14 OR #15 OR #16	268210
#16	Search LAF[tiab] or UVC[tiab] or TAF[tiab] or aircon*[tiab] or air cond*[tiab] or ventilation*[tiab] or UDF[tiab]	110552
#15	Search (Temperature*[tiab] or direc*[tiab]) AND (air*[tiab] or airflow*[tiab] or air-flow*[tiab] or flow*[tiab])	132925
#14	Search laminar*[tiab] or laminated*[tiab] or ultraclean*[tiab] or ultra-clean*[tiab] or unidirectional*[tiab]	30137
#13	Search #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	1352089
#12	Search risk factor*[tiab] or reoperation*[tiab] or re-operation*[tiab] or revision*[tiab]	567293
#11	Search (infection*[tiab]) AND (risk*[tiab])	193645
#10	Search (Bacteri*[tiab] or bacterium[tiab] or microbi*[tiab]) AND (contamination*[tiab] or colon*[tiab] or fallout*[tiab] or infection*[tiab] or control*[tiab] or content*[tiab] or count*[tiab])	367254
#9	Search (air[tiab] or airborne[tiab]) AND (bacteria*[tiab] or bacterium*[tiab] or partic*[tiab] or infection*[tiab] or contamination*[tiab] or count*[tiab] or sampl*[tiab])	76824
#8	Search (implant*[tiab]) and (infection*[tiab])	21928
#7	Search SSI[tiab] or CFU[tiab] or sepsis[tiab] or septic disease*[tiab]	123986
#6	Search (colony[tiab]) AND (form*[tiab])	26045
#5	Search (surg*[tiab] or deep[tiab] or severe[tiab] or wound*[tiab] or postoperative*[tiab] or post-operative*[tiab]) AND (infection*[tiab])	226200

Database: Embase 1974 to 2017 October 11 (OVD)
Date: 2017-10-12
No of results: 790
Search updated: 2018-05-31, 56 results

#	Searches	Results
1	exp infection/	3035985
2	exp colony forming unit/	34301
3	exp Airborne particle/	6847
4	exp airborne bacterium/	465
5	exp bacterial count/	26943
6	exp microbial contamination/	23394
7	((surg* or deep or severe or wound* or postoperative* or post-operative*) adj4 infection*).ab,ti.	106049
8	(colony adj3 form*).ab,ti.	53054
9	(SSI or CFU or sepsis or septic disease*).ab,ti.	173982
10	(implant* and infection*).ab,ti.	30760
11	((air or airborne) adj4 (bacteria* or bacterium* or partic* or infection* or contamination*or count* or sampl*)).ab,ti.	28787
12	((Bacteri* or bacterium or microbi*) adj4 (contamination* or colon* or fallout* or infection* or control* or content* or count* or load*)).ab,ti.	149473
13	exp reoperation/	68459
14	exp risk factor/	840749
15	exp infection risk/	72939
16	(infection* adj6 risk*).ab,ti.	100084
17	(risk factor* or reoperation* or re-operation* or revision*).ab,ti.	807034
18	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	4299229
19	exp air conditioning/	22713
20	exp laminar airflow/	872
21	exp room ventilation/	1441
22	exp indoor air pollution/	12290
23	(laminar* or laminated* or ultraclean* or ultra-clean* or unidirectional*).ab,ti.	34384
24	((Temperature* or direc*) adj4 (air* or airflow* or air-flow* or flow*)).ab,ti.	32964
25	(LAF or UVC or TAF or aircon* or air con* or ventilation* or UDF).ab,ti.	164691
26	19 or 20 or 21 or 22 or 23 or 24 or 25	244335
27	exp operating room/	29978
28	((Operat* or surg*) adj5 (department* or room* or ward* or area*)).ab,ti.	115061
29	(theater* or theatre*).ab,ti.	16890
30	27 or 28 or 29	139561
31	18 and 26 and 30	1647
32	limit 31 to ((danish or english or norwegian or swedish) and yr="1990 -Current")	1162
33	(animal not (animal and human)).sh.	1382292
34	32 not 33	1162
35	limit 34 to (article or conference paper or note or "review")	790

Database: The Cochrane Library
Date: 2017-10-16
No of results: 300
Cochrane Reviews (30)
Other Reviews (0)
Trials (266)
Methods Studies (0)
Technology Assessments (4)
Economic Evaluations (0)
Cochrane Groups (0)
Search updated: 2018-05-31, 19 results

ID	Search	Hits
#1	MeSH descriptor: [Infection] explode all trees	20729
#2	MeSH descriptor: [Bacteria] explode all trees	12643
#3	MeSH descriptor: [Microbiological Techniques] explode all trees	5699
#4	MeSH descriptor: [Air Microbiology] explode all trees	69
#5	(surg* or deep or severe or wound* or postoperative* or post-operative*) and (infection*):ti,ab,kw (Word variations have been searched)	22376
#6	(colony and form*):ti,ab,kw (Word variations have been searched)	1927
#7	SSI or CFU or sepsis or septic disease*:ti,ab,kw (Word variations have been searched)	9639
#8	implant* and infection*:ti,ab,kw (Word variations have been searched)	1504
#9	(air or airborne) and (bacteria* or bacterium* or partic* or infection* or contamination*or count* or sampl*):ti,ab,kw (Word variations have been searched)	3012
#10	(Bacteri* or bacterium or microbi*) and (contamination* or colon* or fallout* or infection* or control* or content* or count*):ti,ab,kw (Word variations have been searched)	30524
#11	MeSH descriptor: [Reoperation] explode all trees	1960
#12	MeSH descriptor: [Risk Factors] explode all trees	25050
#13	infection* and risk*:ti,ab,kw (Word variations have been searched)	19068
#14	risk factor* or reoperation* or re-operation* or revision*:ti,ab,kw (Word variations have been searched)	74692
#15	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14	141914
#16	MeSH descriptor: [Environment, Controlled] explode all trees	2690
#17	MeSH descriptor: [Air Pollution, Indoor] explode all trees	173
#18	laminar* or laminated* or ultraclean* or ultra-clean* or unidirectional*:ti,ab,kw (Word variations have been searched)	459
#19	(Temperature* or direc*) and (air* or airflow* or air-flow* or flow*):ti,ab,kw (Word variations have been searched)	5609
#20	LAF or UVC or TAF or aircon* or air con* or ventilation* or UDF:ti,ab,kw (Word variations have been searched)	23542
#21	#16 or #17 or #18 or #19 or #20	29887
#22	MeSH descriptor: [Operating Rooms] explode all trees	250
#23	(Operat* or surg*) and (department* or room* or ward* or area*):ti,ab,kw (Word variations have been searched)	19444
#24	theater* or theatre*:ti,ab,kw (Word variations have been searched)	793
#25	#22 or #23 or #24	19911
#26	#15 and #21 and #25 Publication Year from 1990 to 2017	300

Database: CINAHL (EBSCO)
Date: 2017-10-13
No of results: 311
Search updated: 2018-05-31, 34 results

#	Query	Results
S30	S17 AND S23 AND S27 Publiceringsdatum: 19900101-20171231; Språk: Danish, English, Norwegian, Swedish	311
S30	S17 AND S23 AND S27	311
S29	S17 AND S23 AND S27	318
S28	S17 AND S23 AND S27	325
S27	S24 OR S25 OR S26	19,558
S26	TI (theater* or theatre*) OR AB (theater* or theatre*)	3,192
S25	TI ((Operat* or surg*) N5 (department* or room* or ward* or area*)) OR AB ((Operat* or surg*) N5 (department* or room* or ward* or area*))	12,430
S24	(MH "Operating Rooms")	5,909
S23	S18 OR S19 OR S20 OR S21 OR S22	33,557
S22	TI (LAF or UVC or TAF or aircon* or air con* or ventilation* or UDF) OR AB (LAF or UVC or TAF or aircon* or air con* or ventilation* or UDF)	25,214
S21	TI ((Temperature* or direc*) N4 (air* or airflow* or air-flow* or flow*)) OR AB ((Temperature* or direc*) N4 (air* or airflow* or air-flow* or flow*))	1,181
S20	TI (laminar* or laminated* or ultraclean* or ultra-clean* or unidirectional*) OR AB (laminar* or laminated* or ultraclean* or ultra-clean* or unidirectional*)	810
S19	(MH "Air Pollution, Indoor")	1,641
S18	(MH "Environment, Controlled+")	6,925
S17	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	304,080
S16	TI (risk factor* or reoperation* or re-operation* or revision*) OR AB (risk factor* or reoperation* or re-operation* or revision*)	120,103
S15	TI infection* N6 risk* OR AB infection* N6 risk*	12,690
S14	(MH "Infection Risk (Saba CCC)")	1
S13	(MH "Risk for Infection (NANDA)")	101
S12	(MH "Risk Factors+")	90,464
S11	(MH "Reoperation+")	6,899
S10	TI ((Bacteri* or bacterium or microbi*) N4 (contamination* or colon* or fallout* or infection* or control* or content* or count*)) OR AB ((Bacteri* or bacterium or microbi*) N4 (contamination* or colon* or fallout* or infection* or control* or content* or count*))	7,445
S9	TI ((air or airborne) N4 (bacteria* or bacterium* or partic* or infection* or contamination*or count* or sampl*)) OR AB ((air or airborne) N4 (bacteria* or bacterium* or partic* or infection* or contamination*or count* or sampl*))	1,604
S8	TI (implant* and infection*) OR AB (implant* and infection*)	2,151
S7	TI (SSI or CFU or sepsis or septic disease*) OR AB (SSI or CFU or sepsis or septic disease*)	12,108
S6	TI (colony N3 form*) OR AB (colony N3 form*)	1,422
S5	TI ((surg* or deep or severe or wound* or postoperative* or post-operative*) N4 (infection*)) OR AB ((surg* or deep or severe or wound* or postoperative* or post-operative*) N4 (infection*))	9,889
S4	(MH "Microbial Contamination+")	3,201
S3	(MH "Microbiological Techniques+")	15,029
S2	(MH "Bacteria+")	29,665
S1	(MH "Infection+")	92,077

The web-sites of **SBU** and **Kunnskapssenteret** were visited
2017-10-11
Nothing relevant to the question at issue was found

Reference lists
A comprehensive review of reference lists brought 44 new records

---

Reference lists

Included studies:

Agarwal SK, Khan AA, Solan M, Lemon M. Hip fracture surgery in mixed-use emergency theatres: is the infection risk increased? A retrospective matched cohort study. Ann R Coll Surg Engl. 2017;99(8):641-4.

Agodi A, Auxilia F, Barchitta M, Cristina ML, D'Alessandro D, Mura I, et al. Operating theatre ventilation systems and microbial air contamination in total joint replacement surgery: results of the GISIO-ISChIA study. J Hosp Infect. 2015;90(3):213-9.

Alsved M, Civilis A, Ekolind P, Tammelin A, Andersson AE, Jakobsson J, et al. Temperature-controlled airflow ventilation in operating rooms compared with laminar airflow and turbulent mixed airflow. J Hosp Infect. 2018;98(2):181-90.

Andersen BM, Roed RT, Solheim N, Levy F, Bratteberg A, Kristoffersen K, et al. [Air quality and microbiologic contamination in operating theatres]. Tidsskr Nor Laegeforen. 1998;118(20):3148-51.

Birgand G, Toupet G, Rukly S, Antoniotti G, Deschamps MN, Lepelletier D, et al. Air contamination for predicting wound contamination in clean surgery: A large multicenter study. Am J Infect Control. 2015;43(5):516-21.

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.

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.

Breier AC, Brandt C, Sohr D, Geffers C, Gastmeier P. Laminar airflow ceiling size: no impact on infection rates following hip and knee prosthesis.[Erratum appears in Infect Control Hosp Epidemiol. 2012 May;33(5):538]. Infect Control Hosp Epidemiol. 2011;32(11):1097-102.

Dale H, Hallan G, Espehaug B, Havelin LI, Engesaeter LB. Increasing risk of revision due to deep infection after hip arthroplasty: A study on 97,344 primary total hip replacements in the Norwegian Arthroplasty Register from 1987 to 2007. Acta Orthopaedica. 2009;80(6):639-45.

Diab-Elschahawi M, Berger J, Blacky A, Kimberger O, Oguz R, Kuelpmann R, 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.

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.

Fischer S, Thieves M, Hirsch T, Fischer KD, Hubert H, Beppler S, et al. Reduction of Airborne Bacterial Burden in the OR by Installation of Unidirectional Displacement Airflow (UDF) Systems. Med Sci Monit. 2015;21:2367-74.

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.

Jeong SJ, Ann HW, Kim JK, Choi H, Kim CO, Han SH, et al. Incidence and risk factors for surgical site infection after gastric surgery: a multicenter prospective cohort study. Infect. 2013;45(4):422-30.

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.

Kelly AJ, Bailey R, Davies EG, Pearcy R, Winson IG. An audit of early wound infection after elective orthopaedic surgery. J R Coll Surg Edinb. 1996;41(2):129-31.

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.

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.

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.

Oguz R, Diab-Elschahawi M, Berger J, Auer N, Chiari A, Assadian O, et al. Airborne bacterial contamination during orthopedic surgery: A randomized controlled pilot trial. J Clin Anesth. 2017;38:160-4.

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 orthopaedica. 2010;81(5):542-7.

Pinder EM, Bottle A, Aylin P, Loeffler MD. Does laminar flow ventilation reduce the rate of infection? an observational study of trauma in England. Bone Joint J. 2016;98-B(9):1262-9.

Simsek Yavuz S, Bicer Y, Yapici N, Kalaca S, Aydin OO, Camur G, 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.

Singh S, Reddy S, Shrivastava R. Does laminar airflow make a difference to the infection rates for lower limb arthroplasty: a study using the National Joint Registry and local surgical site infection data for two hospitals with and without laminar airflow.[Erratum appears in Eur J Orthop Surg Traumatol. 2016 Nov 7;:; PMID: 27822734]. Eur. 2017;27(2):261-5.

Song KH, Kim ES, Kim YK, Jin HY, Jeong SY, Kwak YG, 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.

Stather P, Salji M, Hassan SU, Abbas M, Ahmed A, Mills H, et al. A comparison of airborne bacterial fallout between orthopaedic and vascular surgery. Ann R Coll Surg Engl. 2017;99(4):295-8.

Tayton ER, Frampton C, Hooper GJ, Young SW. The impact of patient and surgical factors on the rate of infection after primary total knee arthroplasty: an analysis of 64,566 joints from the New Zealand Joint Registry. Bone Joint J. 2016;98-b(3):334-40.

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.

Systematic reviews, no appraisal done, only commented on:

Bischoff P, Kubilay NZ, Allegranzi B, Egger M, Gastmeier P. Effect of laminar airflow ventilation on surgical site infections: a systematic review and meta-analysis. Lancet Infect Dis. 2017;17(5):553-61.

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.

Lowson K, Kelly J, Bending M, Whitehead S, Wright D, Lowson P, et al. Cost-Effectiveness of Hospital Design: Options to Improve Patient Safety and Wellbeing: Final Report. York: York Health Economics Consortium; 2011. p. 1-219.

Segadal L, Andersen B M, Haugsbo A, Hotvedt R, Jacobsen T, Kristiansen I S, Nordsletten L, Sondenaa V G, Kjonniksen I. Ventilation in operating theatres. Oslo: The Norwegian Knowledge Centre for the Health Services (NOKC) 2001

Ventilation pa operationsstuer – en medicinsk teknologivurdering. [Ventilation systems in operating rooms a health technology assessment] Copenhagen: Danish Centre for Evaluation and Health Technology Assessment (DACEHTA). 13(3). 2011

Excluded studies:

Agarwal R, Volpe MM, Pujols-McKee AL, Umscheid CA, Williams K. Laminar flow in operating rooms to reduce surgical site infections. Philadelphia: Center for Evidence-based Practice (CEP). 2007

Ahl T, Dalen N, Jorbeck H, Hoborn J. Air contamination during hip and knee arthroplasties. Horizontal laminar flow randomized vs. conventional ventilation. Acta Orthop Scand. 1995;66(1):17-20.

Benen T, Wille F, Clausdorff L. Influence of different ventilations systems upon the contamination of medical devices. Hyg Med 2013;38:142-6.

Berg M, Bergman BR, Hoborn J. Ultraviolet radiation compared to an ultra-clean air enclosure. Comparison of air bacteria counts in operating rooms. J Bone Joint Surg Br. 1991;73(5):811-5.

Chidambaram S, Vasudevan MC, Nair MN, Joyce C, Germanwala AV. Impact of Operating Room Environment on Postoperative Central Nervous System Infection in a Resource-Limited Neurosurgical Center in South Asia. World Neurosurg. 2018;110:e239-e44.

Clarke MT, Lee PT, Roberts CP, Gray J, Keene GS, Rushton N. Contamination of primary total hip replacements in standard and ultra-clean operating theaters detected by the polymerase chain reaction. Acta Orthop Scand. 2004;75(5):544-8.

Evans RP. Current concepts for clean air and total joint arthroplasty: laminar airflow and ultraviolet radiation: a systematic review. Clin Orthop. 2011;469(4):945-53.

Feng Y, Geng X, Zhou F, Fu Y. Clinical evaluation of nursing management of laminar flow operating room in controlling hospital infection. Biomedical Research (India). 2017;28(17):7354-7.

Ferretti S, Pasquarella C, Fornia S, Saccani E, Signorelli C, Vitali P, et al. Effect of mobile unidirectional air flow unit on microbial contamination of air in standard urologic procedures. Surg Infect (Larchmt). 2009;10(6):511-6.

Fitzgerald RH, Jr. Total hip arthroplasty sepsis. Prevention and diagnosis. Orthop Clin North Am. 1992;23(2):259-64.

Friberg S, Ardnor B, Lundholm R, Friberg B. The addition of a mobile ultra-clean exponential laminar airflow screen to conventional operating room ventilation reduces bacterial contamination to operating box levels. J Hosp Infect. 2003;55(2):92-7.

Graves N, Wloch C, Wilson J, Barnett A, Sutton A, Cooper N, 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.

Gruenberg MF, Campaner GL, Sola CA, Ortolan EG. Ultraclean air for prevention of postoperative infection after posterior spinal fusion with instrumentation: a comparison between surgeries performed with and without a vertical exponential filtered air-flow system. Spine. 2004;29(20):2330-4.

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.

Herman DC. Safety of a clean air storage hood for ophthalmic instruments in the operating room. Am J Ophthalmol. 1995;119(3):350-4.

Kellam MD, Dieckmann LS, Austin PN. Forced-Air Warming Devices and the Risk of Surgical Site Infections. AORN Journal. 2013;98(4).

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.

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.

Nilsson KG, Lundholm R, Friberg S. Assessment of horizontal laminar air flow instrument table for additional ultraclean space during surgery. J Hosp Infect. 2010;76(3):243-6.

Pasquarella C, Sansebastiano GE, Ferretti S, Saccani E, Fanti M, Moscato U, et al. A mobile laminar airflow unit to reduce air bacterial contamination at surgical area in a conventionally ventilated operating theatre. J Hosp Infect. 2007;66(4):313-9.

Persson U, Persson M, Malchau H. The economics of preventing revisions in total hip replacement. Acta Orthop Scand. 1999;70(2):163-9.

Ritter MA, Olberding EM, Malinzak RA. Ultraviolet lighting during orthopaedic surgery and the rate of infection. J Bone Joint Surg Am. 2007;89(9):1935-40.

Seal DV, Clark RP. Electronic particle counting for evaluating the quality of air in operating theatres: a potential basis for standards? J Appl Bacteriol. 1990;68(3):225-30.

Singh VK, Hussain S, Javed S, Singh I, Mulla R, Kalairajah Y. Sterile surgical helmet system in elective total hip and knee arthroplasty. J Orthop Surg (Hong Kong). 2011;19(2):234-7.

Solomon DH, Losina E, Baron JA, Fossel AH, Guadagnoli E, Lingard EA, et al. Contribution of hospital characteristics to the volume-outcome relationship: dislocation and infection following total hip replacement surgery. Arthritis Rheum. 2002;46(9):2436-44.

Sossai D, Dagnino G, Sanguineti F, Franchin F. Mobile laminar air flow screen for additional operating room ventilation: reduction of intraoperative bacterial contamination during total knee arthroplasty. J Orthop Traumatol. 2011;12(4):207-11.

Stocks GW, O'Connor DP, Self SD, Marcek GA, Thompson BL. Directed air flow to reduce airborne particulate and bacterial contamination in the surgical field during total hip arthroplasty. J Arthroplasty. 2011;26(5):771-6.

Taylor GJ, Bannister GC. Infection and interposition between ultraclean air source and wound. J Bone Joint Surg Br. 1993;75(3):503-4.

Taylor GJS, Bannister GC, Leeming JP. Wound disinfection with ultraviolet radiation. J Hosp Infect. 1995;30(2):85-93.

Wan GH, Chung FF, Tang CS. Long-term surveillance of air quality in medical center operating rooms.[Erratum appears in Am J Infect Control. 2011 Jun;39(5):444]. Am J Infect Control. 2011;39(4):302-8.

Young SW, Zhu M, Shirley OC, Wu Q, Spangehl MJ. Do 'Surgical Helmet Systems' or 'Body Exhaust Suits' Affect Contamination and Deep Infection Rates in Arthroplasty? A Systematic Review. J Arthroplasty. 2016;31(1):225-33.

Zheng H, Barnett AG, Merollini K, Sutton A, Cooper N, Berendt T, et al. Control strategies to prevent total hip replacement-related infections: a systematic review and mixed treatment comparison. BMJ open. 2014;4(3):e003978.

Other references:

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ. 2004 Jun 19;328(7454):1490-4.

Charnley J, Eftekhar N. Postoperative infection in total prosthetic replacement arthroplasty of the hip-joint. With special reference to the bacterial content of the air of the operating room. Br J Surg. 1969 Sep;56(9):641-9.

[Checklist from SBU regarding cohort studies. (Modified) Version 2010:1]. [Internet]. [cited 2018 Oct 10] Available from: https://www2.sahlgrenska.se/upload/SU/HTA-centrum/Hj%c3%a4lpmedel%20under%20projektet/B03_Granskningsmall%20f%c3%b6r%20kohortstudier%20med%20kontrollgrupp%202014-10-29.doc

[Checklists from SBU regarding randomized controlled trials. (Modified) [Internet]. [cited 2018 Oct 10] Available from: https://www2.sahlgrenska.se/upload/SU/HTA-centrum/Hj%c3%a4lpmedel%20under%20projektet/B02_Granskningsmall%20f%c3%b6r%20%20randomiserad%20kontrollerad%20pr%c3%b6vning%20RCT%202014-10-29.doc

Evans RP. Current concepts for clean air and total joint arthroplasty: laminar airflow and ultraviolet radiation: a systematic review. Clin Orthop. 2011;469(4):945-53.

GRADE Working Group. [Internet]. [Place unknown]: GRADE Working Group, c200-2017 [cited 2017 Feb 13]. Available from: http://www.gradeworkinggroup.org

Graves N, Wloch C, Wilson J, Barnett A, Sutton A, Cooper N, 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.

Guren E, Figved W, Frihagen F, Watne LO, Westberg M. Prosthetic joint infection – a devastating complication of hemiarthroplasty for hip fracture. Acta Orthop. 2017 Aug;88(4):383-38

Hart D, MD. Pathogenic bacteria in the air of operating rooms their widespread distribution and the methods of control. Arch surg. 1938;37(4):521-530.

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 Jul 3;285(6334):10-4.

Lister BJ: On the antiseptic principle in the practice of surgery. Br Med J 1867, ii:246.

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.

Segadal L, Andersen B M, Haugsbo A, Hotvedt R, Jacobsen T, Kristiansen I S, Nordsletten L, Sondenaa V G, Kjonniksen I. Ventilation in operating theatres. Oslo: The Norwegian Knowledge Centre for the Health Services (NOKC) 2001

SS-EN ISO 14644-1:2016. Renhetsteknik - Renrum och tillhörande renhetskontrollerade miljöer - Del 1: Klassificering av luftens renhet baserad på partikelkoncentration (ISO 14644-1:2015). Utgåva 2. Stockholm: Swedish Standards Institute (SIS).

Shaw L, Chen IH, Chen CS, Wu HH, Lai LS, Chen YY, et al. Factors influencing microbial colonies in the air of operating rooms. BMC Infect Dis 2018 Jan 2: 18(1): 1-8.

SIS-TS 39:2015. Mikrobiologisk renhet i operationsrum - Förebyggande av luftburen smitta - Vägledning och grundläggande krav. Utgåva 2. Stockholm: Swedish Standards Institute (SIS).

SKL, Sveriges Kommuner och Landsting. Andel med vårdrelaterad infektion [Internet]. Stockholm: SKL; 2018 [cited 2019-02-13]. Available from: https://app.powerbi.com/view?r=eyJrIjoiZWQzM2YxYzItZTUyOS00NWJmLTk0OWItOWE3YTVmN2U2ZDM4IiwidCI6IjE5YjJhNjc2LWRlNTItNGY0NC1hNjdjLTViNzI4NTA3ZDAxNSIsImMiOjh9

WHO World Health Organization. Global Guidelines for the Prevention of Surgical Site Infection [Internet]. Geneva : World Health Organization, 2016. [cited 2019 May 17]. Available from: https://www.who.int/gpsc/global-guidelines-web.pdf?ua=1

Appendix 2: Included studies

Author, Year, Country	Study Design	Study Duration (years)	Study Groups; Intervention vs control	Patients (n)	Mean Age (years)	Gender (M/F)	Outcome variables
Agarwal,2017 U.K.	Cohort	4 years	I= laminar flow C = no laminar flow	I = 85 C= 74 Matched controls	84,8 (I) 85,1 (C)	25/60 (I) 22/52 (C)	Mortality Infection Readmission LOS
Agodi, 2015 Italy	Cohort	1 year 14 hospitals 28 operating theatres	I= laminar flow (U-OT) C= turbulent flow	528 245	Not stated	Not stated	CFU (room air)
Alsved, 2018 Sweden	Cohort		I = laminar flow C = turbulent flow	15 15	Not stated	Not stated	CFU (room air)
Andersen, 1998 Norway	Cohort	14 days	I = laminar flow (cardiac surgery) C = turbulent flow (urology)	11 25	Not stated	Not stated	CFU (room air)
Birgand 2015, France	Cohort	Not stated	I=unidirectional flow C=turbulent flow	25 35	Not stated	Not stated	Comparison between particles and CFU
Bosanquet, 2013 U.K.	Cohort	1 year	I = laminar flow C = non laminar	56 114	64,8 69,1	76/38 33/23	SSI (superficial+deep) Retrospective analysis, vascular surgery
Brandt, 2008 Germany	Cohort	4 years 55 hospitals 63 ORs	I = laminar airflow ventilated C = turbulent ventilated	62130 37100	Not stated	Not stated	SSI+ serious SS 6 operation types Retrospective register.
Breier, 2011 Germany	Cohort	5 years	I = laminar airflow ventilated C = turbulent ventilated	61 766 50144	Not clearly stated	Not clearly stated	Serious SSI Study in 3 separate parts
Dale H, 2009 Norway	Cohort	19 years	I = laminar air flow C = ordinary	45620 48338	Median 70-79	m/f 30/70	Revision due to infection, retrospective register study
Diab-Elschahawi, 2011 Austria	Cohort	N/A	I = laminar air flow (large or small surface area) C = no LAF	40 (21, 19) 40	Not stated	Not stated	CFU (bacterial sedimentation)
Erichsen-Andersson, 2014 Sweden	Cohort	8 months	I = laminar ventilation C = displacement	33 30	Not stated	Not stated	CFU (room air)

Fischer, 2015 Germany	Cohort, before -after	6 years	I = unidirectional displacement ventilation (UDF) C = turbulent mixing ventilation	138 1148	Not stated	Not stated	CFU / m^3 Authors state that UDF is not equivalent to LAF. PICO violation??
Hooper, 2011 New Zealand	Cohort	10 years	I = laminar flow C = conventional ventilation	Not clearly stated	Not stated	Not stated	Serious SSI (need for revision)
Jeong, 2013 S. Korea	Cohort	15 months	I= laminar air flow C=turbulent air flow	1919 172	median 59	Not stated for compared groups	Risk for SSI (NNIS definition)
Kakwani, 2007 U.K.	Cohort	4 years	I= laminar airflow C = non laminar	212 223	84.8 years 84.0 years	Not stated for compared groups. Totally 96 males, 337 females	Revision within 1 year
Kelly, 1996 U.K.	Cohort, before - after	2 x 3months	I = Laminar flow C= Non-laminar flow	I = 8501 143	Not stated	Not stated	Infections (defined) within 1 month
Knobben, 2006 The Netherlands	Cohort	2 years 6 months	I = laminar flow C = Conventional airflow	70 67	Not stated	Not stated	SSI, deep SSI, swabs from instruments and bone chips
Namba, 2012 USA	Cohort (hip)	8 years 9 months	C = other airflow I = laminar airflow	30 491	65,5	43	Deep SSI within one year
Namba, 2013 USA	Cohort (knee)	8 years 9 months	C = other airflow I = laminar airflow	52 216	67,4	37	Deep SSI within one year
Oguz, 2017 Austria	Cohort (randomized for additional external heating blanket or not)		I = laminar flow C = no laminar flow	20 with, 20 without blanket 20 with, 20 without blanket	42;36 48;35	10/10; 16;6 12/8;7/13	CFU (sedimentation)
Pedersen, 2010 Denmark	Cohort	13 years	I = laminar airflow ventilation C = conventional ventilation	 72423 8333	Median 70 - 79	42	Time to failure (= time to first revision)
Pinder, 2016, U.K.	Cohort + before-and-after	5 years	I = laminar flow ventilation C = plenum ventilation	507024 81509	0-44 years: 36.4% 45-64 years: 16.3% 65+: 47.3% 0-44 years: 36.4% 45-64 years: 16.3% 65+: 47.3%	M: 44.2% F: 55.8% M: 44.1% F: 55.9%	Infections(SS19 codes stated) 90 days after surgery

Simsek-Yavuz, 2006 Turkey	Cohort	5 months	I = newer OR with laminar airflow ventilation C = older OR without LAF	546 445	Not stated for compared groups	Not stated for compared groups	SSI (NNIS codes)
Singh, 2017 U.K.	Cohort	10 years 6 months	I = hospital with LAF C = hospital without LAF	3986 6837	Median 70 Median 71 years	M: 38.5% F: &1.5% M: 38.4% F: 61.6%	SSI or need for revision
Song, 2012 S. Korea	Cohort	3 years	I = Hepa filtered laminar flow C = HEPA filtered turbulent air flow	4188 2086	Not stated for compared groups	Not stated for compared groups	SSI
Stather U.K.	Cohort		I = laminar flow ventilation (orthopedic surgery) C = conventional plenum ventilation (vascular surgery)	24 21	75 years 73 years	Not stated	CFU (cultures)
Tayton, 2016 New Zealand.	Cohort	13 years	I = laminar air flow C = Conventional air flow	27663 36903	Not stated for compared groups	Not stated for compared groups	Revision 6 months and 12 months after surgery
Van Griethuysen 1996, The Netherlands	Cohort	10 months + 10 months	I = laminar air flow C = conventional air flow	2935 2905	Not stated	Not stated	SSI , deep SSI, bacterial cultures (CFU). Follow up 1 year for prostheses, 1 month for other groups

Appendix 3: Excluded studies

Agarwal 2007 HTA	Exclude (SR, majority of included articles published before 1990)
Ahl 1995	Exclude (wrong intervention, horizontal ventilation)
Benen 2013	Exclude (wrong outcome)
Berg 1991	Exclude (wrong intervention)
Chidambaram 2018	Exclude (unclear intervention, probably not LAF)
Clarke 2004	Exclude (wrong outcome)
Evans 2011	Exclude (non-systematic review)
Feng 2017	Exclude (unclear I and C)
Feretti 2009	Exclude (wrong I, not vertical)
Fitzgerald 1992	Exclude (not vertical flow)
Friberg 2003	Exclude (mobile laminar flow)
Graves 2016	Exclude (cost effectiveness modelling study) Other references
Gruenberg 2004	Exclude (wrong intervention, LAF+"space suit")
Hansen 2005	Exclude (wrong comparison, hospital rooms)
Herman 1995	Exclude (wrong I)
Kellam 2013	Exclude (wrong intervention)
Merollini 2013	Exclude (simulering). Other references
Miner 2007	Exclude, wrong I (both horisontal and laminar flow)
Nilsson2010	Exclude (wrong intervention, horizontal LAF, wrong outcome)
Pasquarella 2007	Exclude (wrong I, mobile unit+horisontal)
Persson 1999	Wrong/unclear I ("surgical enclosure")
Ritter 2007	Exclude (wrong I, horizontal)
Seal 1990	Exclude (wrong I, method evaluation)
Singh 2011	Exclude (wrong outcome)
Solomon 2002	Exclude (wrong outcome)
Sossai 2011	Exclude (wrong I, mobile system)
Stocks 2011	Exclude (wrong intervention, horisontal)
Taylor 1993	Exclude (wrong comparison)
Taylor 1995	Exclude (wrong comparison)
Wan 2011	Exclude (wrong comparison)
Young 2016	Exclude (wrong comparison)
Zheng 2014	SR. Exclude (many studies published before 1990)

Appendix 4: Outcome tables (see separate documents)

* + No or minor problems
? Some problems
- Major problems

Appendix 4.1.1
Outcome variable: mortality

Author year country	Patient group	Intervention	Study type	Setting	Absolute effects (events/total, %)		OR[CI low, CI high], p-value	Directness *	Study limitations *	Precision *
					Intervention (LAF)	Control (Non-LAF)				
Agarwal 2017, United Kingdom	P2 (non-implant orthopaedic surgery)	I3 (LAF + volume flow not stated)	Cohort with matched controls	General district hospital	5/85 6.2%	4/74 5.2%	1.09[0.28, 4.23] p=0.90	+	+	-

* + No or minor problems
? Some problems
- Major problems

Appendix 4.1.2.
Outcome variable: Serious surgical site infection

Author year country	Patient group	Intervention	Study type	Setting	Absolute effects (events/total, %)		OR[95% CI], p-value	Directness *	Study limitations *	Precision *
					Intervention (LAF)	Control (Non-LAF)				
Implant orthopaedics (hip or knee)										
Brandt 2008 Germany	P1 (Hip implant)	I3 (air changes not described)	Cohort	National registry	242/17657 1.37%	99/10966 0.90%	OR=1.53[1.21, 1.93] p<0.0001	+	-	+
Breier 2011 Germany	P1 (Hip surgery, arthrosis)	I2 (air changes described)	Cohort	National registry	196/23017 0.85%	52/10446 0.50%	Adj OR= 1.10[0.56, 2.17] n.s.	+	-	+
Breier 2011 Germany	P1 (Hip surgery, fracture)	I2 (air changes described)	Cohort	National registry	160/6513 2.46%	25/1236 2.02%	adj OR: 1.28 [0.67, 2.43] n.s.	+	-	+
Breier 2011 Germany	P1 (Knee surgery)	I2 (air changes described)	Cohort	National registry	93/14456 0.64%	36/6098 0.59%	adj OR: 0.95 [0.37, 2.41] n.s.	+	-	+
Dale 2009 Norway	P1 (Hip surgery)	I2 (air changes described)	Cohort	National registry	324/45620 0.71%	260/48338 0.54%	OR=1.32[1.12, 1.56] P=0.006	+	-	+
Hooper 2011 New Zealand	P1 (Hip surgery)	I3 (air changes not described)	Cohort	National registry	9/16990 0.05%	0/3958 0%	OR=4.03[0.23, 69.2] n.s.	**+**	**?**	+
Kakwani 2007 Hip	P1 (Hip surgery)	I3 (air changes not described)	Cohort, before-and-after	District general hospital	0/212 0%	9/223 4.04%	OR=0.05[0.00, 0.92] p=0.04	+	?	-
Knobben 2006 Hip	P1 (Hip surgery)	I3 (air changes not described)	Cohort, before-and-after	University hospital	1/70 1.43%	3/67 4.48%	OR=0.31[0.03, 3.05] n.s.	+	?	-

* + No or minor problems
? Some problems
- Major problems

Nambda 2012 USA	P1 (Hip surgery)	I3 (air changes not described)	Cohort	Multicentre registry	46/8478 0.54%	109/22013 0.50%	OR=1.10[0.78, 1.15] n.s.	+	?	?
Nambda 2013 USA	P1 (Knee surgery)	I3 (air changes not described)	Cohort	Multicentre registry	105/16693 0.63%	299/39523 0.76%	OR=0.83[0.68, 1.08] n.s.	+	?	+
Pedersen 2010 Denmark	P1 (Hip surgery)	I3 (air changes not described)	Cohort	National registry	517/72423 0.71%	80/8333 0.96%	OR=0.74[0.59, 0.94] p=0.01	+	?	+
Singh 2017 United Kingdom	P1 (Hip surgery)	I3 (air changes not described)	Cohort	General district hospital	5/1752 0.29%	12/3163 0.38%	ORn=0.75[0.26, 2.14] n.s.	+	-	-
Singh 2017 United Kingdom	P1 (Knee surgery)	I3 (air changes not described)	Cohort	General district hospital	16/2234 0.72%	19/3674 0.52%	OR=1.39[0.71, 2.70] n.s.	+	-	+
Taynton 2016 New Zealand	P1 (Knee surgery)	I3 (air changes not described)	Cohort	General district and university hospitals	64/27663 0.23%	6 mo data: 42/36903 0.11%	OR=2.04[1.38, 3.00] p<0.001	+	-	+
Van Grietshuysen 1996 Holland	P1 (Hip surgery)	I3 (air changes not described)	Cohort	Teaching hospital	1/139	1/135	OR=0.97[0.06, 15.68] n.s.	-	-	-
Van Grietshuysen 1996 Knee	P1 (Knee surgery)	I3 (air changes not described)	Cohort	Teaching hospital	0/113 0%	0/88 0%	Not estimable	-	-	-
Other orthopedic										
Agarwal 2017 United Kingdom	P2 (trauma surgery, proximal femur fracture)	I3 (air changes not describexd)	Cohort	General district hospital	1/85 1.18%	0/85 0%	OR=3.04[0.12, 75.6] n.s.	+	+	-
Kelly 1996 United Kingdom	P2 (mixed orthopaedic)	I3 (air changes not describexd)	Cohort	General district hospital	17/851 2.00%	0/143 0%	OR=6.02[0.36, 100.64] n.s.	+	-	?
Pinder EM 2016, United Kingdom	P2 (orthopaedic trauma)	I3 (air changes not described)	Cohort	National registry, hospital episodes	13690/507024 2.70%	1956/81509 2.40%	OR=1.13[1.08, 1.18] P<0.0001	+	+	+

* + No or minor problems
? Some problems
- Major problems

GI/vascular/mixed										
Bosanquet 2013 United Kingdom	P2 (vascular)	I3 (air changes not describexd)	Cohort	District hospital, one surgeon	4/56 7.14%	8/114 7.02%	OR=1.02[0.29, 3.54] n.s.	+	-	+
Brandt 2008 Germany	P2 (mixed GI)	I3 (air changes not describexd)	Cohort	National registry	413/38480 1.07%	178/22731 0.78%	OR=1.37[1.15, 1.64] p<0.001	+	-	+
Simsek Yavuz 2006 Turkey	P2 (cardiac surgery, sternotomy)	I3 (air changes not describexd)	Cohort	General district	25/546 4.58%	26/445 5.62%	OR=0.77[0.44, 1.36] n.s.	?	?	+
Van Griethuysen 1996 Holland	P2 (general surgery)	I3 (air changes not describexd)	Cohort	Teaching hospital	35/1891 1.85%	28/1909 1.47%	OR=1.27[0.77, 2.09] n.s.	?	-	+

* + No or minor problems
? Some problems
- Major problems

Appendix 4.1.3.
Surgical site infection

Author year country	Patient group	Intervention	Study type	Setting	Absolute effects (events/total, %)		OR[CI low, CI high], p-value	Directness *	Study limitations *	Precision *
					Intervention (LAF)	Control (Non-LAF)				
4.1.3. Outcome surgical site infection										
Orthopedic implant surgery										
Brandt 2008 Germany	P1 (Hip implant)	I3 (air changes not described)	Cohort	National registry	326/17657 1.86%	144/10966 1.31%	OR=1.41[1.16, 1.72] p <0.001	+	-	+
Brandt 2008 Knee	P1 (Knee implant)	I3 (air changes not described)	Cohort	National registry	80/5993 1.33%	28/3403 0.82%	OR=1.63[1.06, 3.51] p=0.03	+	-	+
Song KH 2012, S. Korea	P1 (Hip implant)	I3 (air changes not described)	Cohort	National registry	50/2037 2.45%	20/1149 1.74%	OR=1.42[0.84, 2.41] n.s.	+	?	+
Song KH 2012, S. Korea	P1 (Knee implant)	I3 (air changes not described)	Cohort	National registry	37/2151 1.72%	29/937 3.09%	OR=0.55[0.33, 0.90] p=0.02	+	?	+
Other orthopedic										
Kelly 1996 United Kingdom	P2 (mixed orthopaedic)	I3 (air changes not describexd)	Cohort	General district hospital	47/851 5.52%	6/143 4.2%	OR=1.33[0.56, 3.18] n.s.	+	-	?
Van Grietshuysen 1996 Holland	P2 (mixed orthopaedic)	I3 (air changes not described)	Cohort	Teaching hospital	13/823 1.58%	10/873 1.15%	OR=1.39[0.60, 3.18] n.s.	+	?	?

* + No or minor problems
? Some problems
- Major problems

GI/vascular/mixed										
Bosanquet 2013 United Kingdom	P2 (vascular)	I3 (air changes not describexd)	Cohort	District hospital, one surgeon	4/56 7.14%	19/114 16.7%	OR=0.38[0.12, 1.19] n.s.	+	-	+
Brandt 2008 Germany	P2 (mixed GI)	I3 (air changes not describexd)	Cohort	National registry	486/38480 1.26%	246/22731 1.08%	OR=1,17[1.00, 1.36] p=0.05	+	-	+
Jeong 2013 Korea	P2 (gastric surgery)	I2 (air changes described)	Cohort	10 hospitals in Korea	45/1919 2.1%	26/172 15.1%	OR=0.13[0.08, 0.22] p <0.0001	+	-	?
Simsek Yavuz 2006 Turkey	P2 (cardiac surgery, sternotomy)	I3 (air changes not describexd)	Cohort	General district	11/546 2.01%	30/415 7.23%	OR=0.26[0.13, 0.53] p<0.001	**?**	**?**	+
Van Griethuysen 1996 Holland	P2 (general surgery)	I3 (air changes not describexd)	Cohort	Teaching hospital	64/2935 2.18%	70/2905 2.41%	OR=0.90[0.64, 1.27] n.s.	?	-	+

Appendix 4.1.4.

Outcome variable:CFU/m3 in room air

* + No or minor problems
? Some problems
- Major problems

Author year country	Patient group	Intervention	Study type	Setting	Mean CFUs/m^3 +/- SD		Mean difference [95% CI, p-value	Directness *	Study limitations *	Precision *
					Intervention (LAF)	Control (Non-LAF)				
Orthopedic implant surgery										
Agodi 2015 Hip Italy	Elective hip prothesis	LAF vs No LAF	Cohort	14 "hospitals"	23 +/- 33	58 +/-39	MD = -35[-48, -22] p <0.0001	+	-	+
Agodi 2015 knee Italy	Elective knee prothesis	LAF vs No LAF	Cohort	14 "hospitals"	20+/-37	70+/-56	MD = -51 [-77, -24] p <0.0001	+	-	+
Erichsen Andersson 2014 Sweden	Orthopedic trauma implants	LAF vs No LAF	Cohort	University Hospital	5 +/- 5	60 +/- 56	MD = -55 [-78, -32] p <0.0001	+	?	+

Other types of surgery										
Alsved 2018 Sweden	Wrist fractures, shoulder arthroscopies, hip fracture dislocations	LAF vs No LAF	Cohort	Hospital "acute care"	0 +/- 10	22 +/- 25	MD = -22 [-28, -16] p <0.0001	**+**	**-**	?
Andersen 1998 Norway	Cardiothoracic and urological	LAF vs No LAF	Cohort	University Hospital	2 +/- 1	45+/-15	MD = -43 [-49, -37] p <0.0001	**-**	**-**	-

Appendix 4.1.5

Outcome variable: Passive bacterial sampling

* + No or minor problems
? Some problems
- Major problems

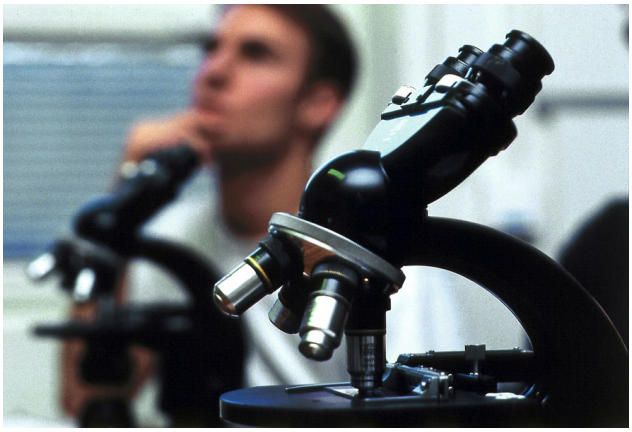
Author year country	Patient group	Intervention	Study type	Set ting	Mode of sampling,unit	Intervention		Directness	Study limitations *	Precision *
						LAF	Non-LAF			
Orthopedic implant surgery										
Knobben 2006 Netherlands	Knee or hip implants	LAF vs turbulent ventilation	Cohort (before-and-after)	University Hospital	Swabs from used+unused instruments, removed bone "% contaminated" (definition not stated)	Instrument (early): 4/70 Instrument (late): 3/70 p =0.001	Instrument (early): 20/67 Instrument (late): 9/67	+	+	-
Other types of surgery										
Birgand 2015 France	Cardiac (n=26) and orthopaedic (n=34)	LAF versus turbulent ventilation	cohort	5 university + 5 private hospitals	Pads from operating wound CFU/m^2	0 CFU/$m^{2:}$ 19 1-10 CFU/$m^{2:}$ 6 >10 CFU/$m^{2:}$ 0 p=0.01	0 CFU/$m^{2:}$ 14 1-10 CFU/$m^{2:}$ 15 >10 CFU/$m^{2:}$ 6	**?**	**-**	+

Diab-Elschahawi 2011	Various orthopedic	LAF of different sizes, No LAF	cohort	2137 bed tertiary care hospital	Sedimentation sampling (agar plates around patient) CFU/m^2*hr mean+/- SD	Large LAF roof data: 100 cm above floor: 452+/-710 150 cm above floor: 19+/-62 120 cm above floor, right side of patient:97+/-182 On instrument table: 48+/-153* *= p<0.001	 1992+/-1258 1536+/-1789 1178+/-1153 2159+/-1337	**+**	**-**	-
Fischer 2015 Germany	Not stated	LAF vs turbulent	Cohort, before-and-after	Not stated	Sedimentation plates on instrument table CFU/h	0.3+/-0.7 p<0.05	5+/-5.3	-	-	+
Oguz 2017 Austria	"Minor orthopaedics"	LAF versus turbulent ventilation	Cohort (randomized for blanket warming or not)	University Hospital	4 agar plates and 2 nitrocellulose membranes on instrumentation table OR (CI) for bacterial deposition	All LAF theaters relative OR=1.00 (set as reference) p <_0.05	Plate 1 (floor): 2.42(1.00-5.83) Plate 2 (at head of patient: 3.70(2.05-6.67) Plate 3 (150 cm at head): 3.48(1.61-7.51) Plate 4 (table level, 50 cm from wound): 5.10(2.59-10.06) Plate 5 and 6: at sterile instrumentation table): 2.18(1.13-4.20)	-	-	?
Stather 2017 UK	Orthopedic implant and vascular graft surgery	LAF versus turbulent ventilation	Cohort (also different types of surgery in groups)	General district	"Bacterial fallout" with 10 agar settle plates at various positions Counts/plate, median and IQR	Median 2, IQR 1-4 p <0.001	Median 17, IQR 9-24	-	-	-

Van Griethuysen1996 Netherlands	General + orthopaedic surgery	Howorth system/downflow vs no ventilation/ inlet clean air/downflow	Cohort, before-and-after	Teaching hospital	Microorganisms isolated from wound infections	Orthopedic surgery: 13 General surgery: 64 n.s.	Orthopedic surgery: 10 General surgery: 70	-	-	-

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

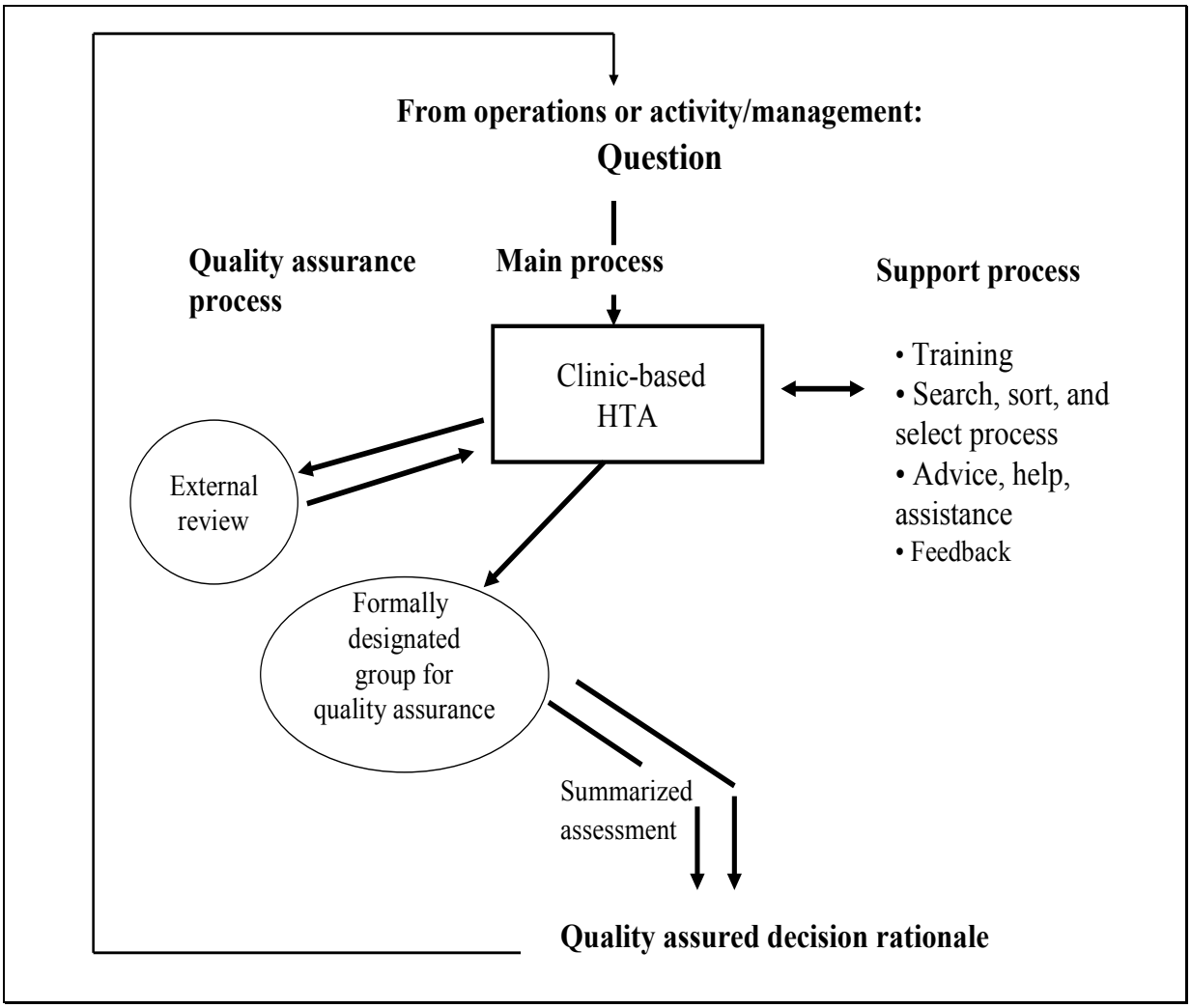
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the certainty of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High certainty of evidence	= (GRADE⊕⊕⊕⊕)
Moderate certainty of evidence	= (GRADE ⊕⊕⊕O)
Low certainty of evidence	= (GRADE ⊕⊕OO)
Very low certainty of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh
Professor, MD
Head of HTA-centrum


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Sahlgrenska Universitetssjukhuset, HTA-centrum
Röda Stråket 8, 413 45 Göteborg
www.sahlgrenska.se/htacentrum