Effect of intraoperative hyperoxia on the incidence of surgical site infections: a meta-analysis

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Abstract

Background: Whether supplemental intraoperative oxygen reduces surgical site infections remains unclear. Recent recommendations from the World Health Organization and Center for Disease Control to routinely use high inspired oxygen concentrations to reduce infection risk have been widely criticized. We therefore performed a meta-analysis to evaluate the influence of inspired oxygen on infection risk, including a recent large trial.

Methods: A systematic literature search was performed. Primary analysis included all eligible trials. Sensitivity analyses distinguished studies of colorectal and non-colorectal surgeries, and excluded studies with high risk of bias. Another post-hoc sensitivity analysis excluded studies from one author that appear questionable.

Results: The primary analysis included 26 trials (N=14,710). The RR [95%CI] for wound infection was 0.81 [0.70, 0.94] in the high vs. low inspired oxygen groups. The effect remained significant in colorectal patients (N=10,469), 0.79 [0.66, 0.96], but not in other patients (N=4,241), 0.86 [0.69, 1.09]. When restricting the analysis to studies with low risk of bias, either by strict inclusion criteria (N=5,047) or by researchers’ judgment (N=12,547), no significant benefit remained: 0.84 [0.67, 1.06] and 0.89 [0.76, 1.05], respectively.

Conclusions: When considering all available data, intraoperative hyperoxia reduced wound infection incidence. However, no significant benefit remained when analysis was restricted to objective- or investigator-identified low-bias studies, although those analyses were not as well-powered. Meta-analysis of the most reliable studies does not suggest that supplemental oxygen substantively reduces wound infection risk, but more research is needed to fully answer this question.

Keywords: anaesthesia; hyperoxia; meta-analysis; surgical wound infection

All surgical wounds become contaminated, but effective host defences usually prevent contamination from progressing to clinical infection. The most important defence against bacterial contamination is oxidative killing by neutrophils.¹³ Killing
Editor’s key points

- Whether supplemental intraoperative oxygen reduces surgical site infections remains unclear despite recent publication of a very large trial.
- The authors conducted a meta-analysis of relevant trials, including sensitivity analyses restricted to higher-quality trials.
- The primary analysis included more than 14,000 subjects, and indicated that the relative risk for wound infection was 0.70–0.94 (95% confidence interval, high vs low inspired oxygen groups). However, when analysis was restricted to studies with low risk of bias no significant benefit remained.

Supplemental oxygen is inexpensive and easy to provide, reduces infection risk, thus remains in dispute. Consistent with heterogeneous underlying reports, recent meta-analyses conflict, with some emphasizing a possible beneficial effect of high inspired oxygen fraction (FiO₂) on SSI while others emphasize possible detrimental effects. Despite obvious uncertainty, the World Health Organization recently published recommendations for the prevention of SSI that include use of inspired FiO₂ of 0.8 during surgery, and when possible for several hours thereafter. This recommendation was apparently largely based on a meta-analysis that omitted a recent 560 patient randomized trial that reported no benefit from supplemental oxygen. The World Health Organization recommendation was widely criticized. Curiously, the US Centers for Disease Control recently promulgated similar guidelines despite divergent trial results and lack of general consensus.

In a recent, alternating-intervention trial, we assigned more than 5,700 colorectal patients to 30% or 80% intraoperative inspired oxygen. Supplemental oxygen did not reduce the primary composite of deep- and organ-space infection and major healing-related complications. Our recent trial is by far the largest. It is thus of considerable interest to include these new data in a meta-analysis of supplemental oxygen and SSI in adults having non-cardiac surgery. Secondly, we evaluated the influence of intraoperative FiO₂ on SSI in patients having colorectal surgery and when analysis was restricted to higher-reliability trials.

Methods

We performed a systematic literature review and meta-analysis of trials in which investigators assigned patients to high or low intraoperative inspired oxygen and assessed SSIs. The last Cochrane meta-analysis was published in 2015. We used similar searching rules, as detailed in the Appendix. As the Cochrane review was based on a search concluded in February 2014, we limited our search to studies published since January 2014. Our last search date was January 11, 2017. To those results, we added our recent alternating intervention trial.

Eligibility criteria

After performing the preliminary search, two authors (B.C and Y.N.S) independently reviewed the search results for studies fulfilling all the following criteria:

- randomised clinical trial;
- adults aged 18 yr or older;
- elective or urgent surgeries with general or neuraxial anaesthesia;
- comparison of high FiO₂ >60% to low FiO₂ ≤40% with a high/low FiO₂ ratio ≥2;
- designated FiO₂ maintained intraoperatively, with or without postoperative oxygen manipulation;
- SSI reported as an outcome.

Disputes about qualification for inclusion were adjudicated by a third investigator (D.I.S). Blinding was not required and we considered any language. Results presented only as abstractions or in conference proceedings were included.

Data sources

Our search included the electronic databases Medline, Embase, Central, Cinahl, Web of science, and Google scholar and relevant articles’ reference lists and the investigators’ personal reference collections. We were not able to search the Chinese Biomedical Literature Database and the Latin American Caribbean Health Sciences Literature (LILACS). Our main search strategies relied on the previous meta-analysis by Wetterslev and colleagues extended from January 2014 to January 2017 and are detailed in the Appendix.

Extracted data included the number of participants and their demographic characteristics along with the type of surgery. We also recorded intervention details including the FiO₂ in each group, use of N₂O, continuation of the intervention into the postoperative period, and duration of anaesthesia. We considered study methodology including randomisation method, allocation concealment, blinding, completeness of primary outcome availability and reporting, and how SSIs were defined. Finally, we evaluated statistical methodology including appropriate sample size calculations and sufficient power, the number of patients included in analysis, and whether analysis was conducted on an intention-to-treat basis.

Eligible trials were evaluated for methodological strength according to a priori domains based on the Cochrane Handbook for Systematic Reviews of Interventions version 5.1.0. Each domain was ranked as having low, unclear, or high risk of bias. Then, an overall risk of bias was evaluated as low or high using two distinct approaches: first, using strict criteria according to which any single domain rated as having either high or unclear risk of bias was sufficient to rank the study as having an overall high risk of bias. Second, using the investigators’ clinical judgment and perception of the potential effect of every domain on each study’s actual risk of bias. This process was independently performed by two investigators (B.C and Y.N.S). Interevaluator discrepancies were adjudicated by another investigator (D.I.S).
Risk of bias considerations for the entire meta-analysis

Treat anaesthesiologists were never blinded, and we chose not to consider this issue by itself as lack of blinding. Some studies were performed in centres in which electronic anaesthesia records were already in use which make complete blinding impossible because any caregiver in such centres has potential access to the participants’ records. Again, this issue by itself was not considered as high-risk for un-blinding. Although some studies in which the intervention continued into the postanaesthesia care unit took extra measures to make sure patients and outcome assessors remain blinded, this was not the case in the majority of studies, potentially introducing a significant degree of bias to the results.

Although our cohort included many studies with negative results, it remains likely that other studies, probably small underpowered ones with negative results, were never published. We reduced the risk of publication bias by including studies that were only presented as abstracts or in conference proceedings even though the works were never peer-reviewed.

Statistical methods for the meta-analysis

Our primary outcome was postoperative SSI. The meta-analysis was performed on qualifying studies to assess the association between SSI and levels of intraoperative FiO₂. DerSimonian and Laird random-effects models were used with inverse variance weighting were performed to pool the relative risks (RR) and their corresponding 95% confidence intervals (CI). Statistical heterogeneity across the various trials was assessed using the Cochrane Q statistic and quantified by the I² value, with a value exceeding 25% considered as representing substantial heterogeneity.

Publication bias was assessed using funnel plot asymmetry. We also used the Duval and Tweedie non-parametric ‘trim and fill’ method to further evaluate the possibility of publication bias (i.e., a sensitivity analysis). This approach estimates the number and effect size of studies missing from the meta-analysis if in fact there were no publication bias, treats them as actually existing studies, imputes their relative risks, and recalculates an adjusted RR.

Sensitivity analyses

Several sensitivity analyses were performed. The first three analyses were predefined, while the fourth was added after reviewing the preplanned results.

First, sensitivity analyses were performed to include only studies that were judged to have a low risk of bias and high-quality methodology, with risk of bias separately evaluated using objective criteria and the investigators’ judgement.

Second, a sensitivity analysis was performed including only studies that evaluated colorectal surgeries. Studies that enrolled both colorectal and non-colorectal cases were included in this analysis if they provided data regarding the colorectal cases separately. Appendectomies were considered as colorectal, as their clean-contaminated (or often contaminated) nature probably puts them at a similar high risk for SSI as other colorectal surgeries. We then performed a sensitivity analysis including only colorectal studies with low risk of bias, as ranked by evaluators’ judgment.

A third analysis included only studies enrolling non-colorectal cases. Studies that enrolled both colorectal and non-colorectal cases were included only if the non-colorectal cases were reported separately. A similar sensitivity analysis including only studies with low risk of bias was also performed.

Lastly, a post hoc sensitivity analysis was performed after excluding studies authored by Schietroma and colleagues because one of his studies was challenged by Meyhoff and colleagues, who pointed out that although data were presented as statistically significant, they actually were not. More importantly, one of Schietroma’s studies was retracted by the editor-in-chief for suspected similarities with works previously presented by other authors. We also have concerns about some of Schietroma’s other publications. For example, Schietroma reports use of an implausibly precise and constant anaesthetic regimen including thiopental, remifentanil, and sevoflurane in a study that recruited patients over a 10-year period from 2004 to 2013. We also note reported use of computer-generated randomisation, concealed allocation, and CDC definitions of SSI in this study, which started enrolling patients in 2004 and was published in 2016, although Schietroma used cruder methods in studies that started much later. We also note that this author reports relative risks that seem inaccurate and results that are deemed statistically significant despite confidence intervals that cross the reference value of 1.

Sample size justification and power analyses

We performed a poststudy power analysis to roughly assess (i.e., assuming data independence across studies) available power with the given sample sizes to detect relative reductions of 10% and 20% in the primary outcome of infection, assuming the observed incidence in the 30% oxygen group. For the primary analysis (total \(n = 14,710\), incidence of 13% in the 30% oxygen group), we had 67% power to detect relative reductions of 10% and 99% power to detect relative reductions of 20%.

For the sensitivity analyses assessing low risk of bias, we had only 33% power at 10%, but 88% power at 20% using the objective criteria (total \(n = 5047\)). Using the investigators’ judgement (\(n = 12,546\)) to assess low risk of bias, we had 58% power at 10% and 99% power at 20%. When the analysis was restricted to colorectal surgery (\(n = 10,469\)), we had 49% power at 10% and 99% power at 20%. And finally, for non-colorectal surgery (\(n = 4241\)), we had 23% power at 10% and 71% power at 20% reduction.

We also conducted a trial sequential analysis to evaluate whether this meta-analysis contains sufficient information to make a definitive conclusion on the research question, controlling for the repeated testing implicit in a meta-analysis and considering a relative risk reduction of 20% as clinically important. We used conservative O’Brien–Fleming \(z\) spending (for monitoring efficacy) and \(\beta\) spending (for monitoring futility) functions and DerSimonian and Laird random-effects models.

All study analyses were performed using the R (R Development Core Team, 2008) and Metafor package and TSA software.

Results

Ten new randomised trials fulfilling the eligibility criteria were found, \(7,20–22,26–31\), of more than 500 results of the literature search conducted between 2014 and 2017. The Preferred
Primary analysis

Analysis of all 26 studies included 14,710 cases with a general SSI incidence of 12%. A random-effects model was used as moderate heterogeneity was found with $I^2 = 41\%$, $Q = 43$, $P = 0.015$. The incidence of SSI was 11.0% and 13.0% in the high and low FiO$_2$ groups. The pooled RR (95%CI) of 0.81 (0.70, 0.94) indicated that the higher level of FiO$_2$ decreased SSI infection ($P = 0.0057$, Fig. 2).

Visual inspection of the funnel plot and Begg adjusted rank correlation test did not reveal apparent publication bias ($P = 0.23$; Supplementary Fig. S2). The estimated number of missing studies on the right side was five. With the missing studies filled in as described above, the estimated effect was...
still significant ($P=0.039$), suggesting that publication bias did not much influence our analysis.

### Sensitivity analyses

Seven studies including 5047 patients fulfilled the strict inclusion rule for low overall risk of bias (having no high or unclear risk score in any domain). The overall incidence was 12.5% in the high FiO$_2$ group and 14.7% in the low FiO$_2$ group. No significant association between levels of FiO$_2$ and SSI was found, with an adjusted pooled RR of 0.84 (95% CI, 0.67, 1.06; $P=0.15$; Supplementary Fig. S3).

When using the investigators’ judgment of overall low risk of bias, 13 studies including 12 547 patients were included. The overall incidence was 11.1% in the high FiO$_2$ group and 12.4% in the low FiO$_2$ group. No association was found, with an adjusted RR (95%CI) of 0.89 (0.76, 1.05; $P=0.16$; Fig. 3). When Schietroma and colleagues’ studies were included, their 576 patients were excluded, the RR (95% CI) was 0.88 (0.77, 1.01; $P=0.08$).

Thirteen studies enrolling 10 469 patients were included in the sensitivity analysis of colorectal surgeries (including 633 colorectal cases from the PROXI trial). The general incidence of SSI after colorectal surgeries was found to be 11.9%. Higher FiO$_2$ was associated with lower incidence of SSI. The pooled RR (95%CI) for the high FiO$_2$ vs low was 0.79 (0.66, 0.96; $P=0.015$; Supplementary Fig. S4). However, the sensitivity analysis including only colorectal studies with low risk of bias showed no effect: 0.84 (0.68, 1.03; $P=0.09$; Supplementary Fig. S5).

Fourteen studies and 4241 patients were included in the non-colorectal sensitivity analysis, demonstrating a RR (95% CI) of 0.86 (0.69, 1.09) for high FiO$_2$ vs low ($P=0.21$), indicating no association between SSI and levels of FiO$_2$ (Supplementary Fig. S6). Again, the sensitivity analysis including only studies with low risk of bias also showed no association: 1.01 (0.81, 1.25; $P=0.93$; Supplementary Fig. S7).

Our trial sequential analyses using all studies indicated that the efficacy boundary was crossed when assuming that a relative 20% reduction is clinically important (Supplementary Fig. S8). When including studies judged by the investigators as having low risk of bias, the futility threshold was nearly met, suggesting no evidence of beneficial effect of hyperoxia on SSI (Fig. 4). When removing studies deemed to be at higher risk of bias by the strict exclusion criteria, only about 5000 patients remained and the trial sequential analysis indicated that approximately 13 000 more patients will be needed to make a definitive conclusion on the benefits of supplemental oxygen (Supplementary Fig. S9).
Discussion

Supplemental oxygen is inexpensive and trivial to provide, at least intraoperatively. Oxygen at 100%, as given to nearly all patients during induction of general anaesthesia, provokes atelectasis with just a breath or two—and is easily reversed with an expansion manoeuvre. When oxygen concentration is restricted to 80%, there is no more atelectasis than with 30% oxygen. Although an initial report claimed that supplemental oxygen increases long-term mortality, there was no obvious mechanistic explanation and a subsequent study found no difference whatsoever. While it remains possible that supplemental perioperative oxygen causes harm, there is not currently convincing evidence to support the theory, but the fact that supplemental oxygen does not cause substantive harm is insufficient justification for its use; the treatment should also provide benefit.

Both the World Health Organization and US Centers for Disease Control recently recommended providing 80% inspired oxygen during and after surgery to reduce the risk of SSI. The guidance appeared ill-considered based on data available at the time. Our recent large alternating intervention study confirmed that supplemental oxygen does not reduce the risk of deep and organ-space infections even in colorectal patients who have a high infection risk and are perhaps most likely to benefit, and only slightly reduced the superficial infections. The primary analysis including all available data from eligible studies and an analysis restricted to colorectal patients showed mild beneficial effects of hyperoxia on SSI incidence. But after eliminating studies with high risk of bias, no significant benefit of supplemental oxygen on SSI remained.

A limitation inherent in any meta-analysis is potential bias in selecting studies for inclusion. Although we had a priori rules for selecting studies, some decisions remained challenging. For example, strictly excluding all studies with even a single unclear or high risk score in any methodologic domain is not necessarily clinically sensible. For example, our large alternating-intervention study was ranked as having high risk for selection bias as individual patients were not randomised (in this respect, being like a cluster-randomised trial), and for measurement bias as investigators were not blinded. Nonetheless, unique study design features effectively allocated patients randomly to comparable groups and the registry outcomes seem unlikely to be biased. In contrast, studies by Schietroma and colleagues appear methodologically excellent as reported but are nonetheless suspect for many reasons. To evaluate the consequences of various inclusion approaches, we conducted several sensitivity analyses, especially related to individual studies at high risk of bias. Using either of two distinct definitions of low bias risk, there was no longer a significant benefit from supplemental oxygen.

![Fig 2. Forest plot of all eligible studies on the association of high intraoperative FiO2 and SSI incidence. RE, random-effects. A significant association was found (P=0.0057). Lines indicate 95% confidence intervals (CIs). The diamond represents the pooled relative risks and 95% CI of the overall population. The arrows represent trimmed 95% CIs. SSI, surgical site infection.](image-url)
Perhaps the major limitation to any meta-analysis is publication bias. The general danger is that small negative studies are often unpublished, leading meta-analyses to sometimes falsely conclude that treatments are beneficial. Our analysis differs somewhat in including many negative studies, including the three largest. It nonetheless remains probable that at least a degree of publication bias remains. To the extent that negative studies were unpublished, the true relative risk point estimates would be closer to 1, and P-values consequently larger.

The studies included in our meta-analysis are heterogeneous, with treatment effects ranging from relative risk reductions of >50% with supplemental oxygen to one reporting a wildly implausible two-fold risk increase. Possible explanations include heterogeneous patient populations, methodologies, definitions of SSI, and baseline incidence of the outcome. For example, major colorectal operations differ from elective Caesarean deliveries in many aspects including patients’ baseline medical condition, length of surgery, use of general vs regional anaesthesia, the baseline risk of SSI, the length and timing of the intervention, the method of oxygen administration, and so on. Urological, breast, and orthopaedic surgeries each have their own unique characteristics. It is also obvious that medical practices and the incidence and definition of SSI have changed over the 18 yr of publications included in our meta-analysis. As many of these data were not available in the trial reports, we could not adjust for these differences.

The incidence of SSI also varied substantially from study to study, ranging from negligible rates to more than 50%. The US Centers for Disease Control reported an SSI incidence of about 3% in colon surgery, but newer reports based on the American College of Surgeons’ National Surgical Quality Improvement Program have reported an overall SSI incidence of 13–15% after colorectal surgery. The overall incidence for a study matters as variance for individual proportions and relative risks are smallest when proportions are near 0.50, and larger as they approach 0 or 1. Thus, it is possible for small studies reporting a high outcome incidence to be weighted in the analysis similarly to much larger studies that report sparse outcomes. For example, Schietroma and colleagues reported baseline infection incidences up to 50% which was partly responsible for this small trial (total n=239) being weighted 65% as high in our random-effects model as the largest study, which had 24 times as many patients. For comparison, Tajne and colleagues had a total n=240, but was assigned a weight one-third as large as the Schietroma study due mainly to the incidence being 10% rather than 50%. However, a more general phenomenon is that weights in a random effects model combine the within-trial variance and the between-trial variance, which results in the weights across studies being more similar to each other than in a fixed effects model (which ignores between-trial variance). Although statistically more appropriate, giving an apparently disproportionate weight to some smaller studies in the meta-analysis effectively discounted larger robust trials, including

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**Fig 3.** Forest plot of studies with low overall risk of bias according to investigators’ judgment (total n=12 547). SSI, surgical site infection, RE, random-effects model. Lines indicate 95% confidence intervals (CIs). The diamond represents the pooled relative risk and 95% CI of the overall population. The arrows represent trimmed 95% CIs. No significant association was found (P=0.16).
many that did not identify any benefit from supplemental oxygen. Because of the heterogeneity amongst published trials, it is important to look beyond the strict meta-analytic results to the ‘sense’ of the data. Doing so shows that most large trials (n>300) demonstrate no benefit from supplemental oxygen.

Our primary analysis was fairly well powered, but the sensitivity analyses were less so, mainly because there were fewer data for them. As shown in our power analysis details (see end of ‘Statistical methods for the meta-analysis’ section), we had about 99% power to detect a relative 20% reduction in SSI and 67% to detect a 10% reduction. Although we found a difference when using all data, power was considerably lower for some of the sensitivity analyses, such as 71% to detect a 20% relative reduction in non-colorectal surgeries, and 88% when removing studies with higher chance of bias using objective criteria. Therefore, negative results for our sensitivity analyses should not be considered definitive.

We also conducted a trial sequential analysis to assess whether available studies contain enough information to definitively assess the effect of supplemental oxygen on SSI while adjusting for repeated testing over time, analogous to what is commonly done in a group sequential trial designs to account for multiple interim analyses. The trial sequential analysis similarly showed that more information (in the form of more patients and thus more studies) is needed to definitely determine whether supplemental oxygen reduces the risk of SSI when analysis is restricted to studies with low risk of bias. Two relatively large on-going trials will hopefully add power to future analyses: the iPROVE-O2 study aims to randomise 756 patients undergoing abdominal surgery to 80% or 30% intraoperative inspiratory oxygen concentrations, and the OXYGEN study aims to randomise 1000 patients to 80% or 30% inspiratory oxygen concentration during, and for 2 h after, orthopaedic surgery.

In summary, published trials are heterogeneous. Our primary analysis using all qualifying trials shows that supplemental oxygen significantly reduces SSIs by about 20%. However, many trials appear to be at substantial risk of bias. Supplemental oxygen no longer significantly reduced infections after studies at high risk of bias were excluded. Trial sequential analysis indicates that our sensitivity analyses were underpowered, especially when restricted to objectively defined studies with low risk of bias. Nonetheless, the preponderance of available high-quality evidence and the largest trials suggest that supplemental oxygen has little or no effect on the risk of SSI.

**Author’s contributions**

B.C.: Study design, data review, writing paper, review and approval of final manuscript.

Y.S.: Study design, data review, review and approval of final manuscript.

K.R.: Data review, review and approval of final manuscript.

S.A.: Data review, review and approval of final manuscript.

D.Y.: Data analysis, review and approval of final manuscript.

E.M.: Data analysis, review and approval of final manuscript.

A.B.: Data review, review and approval of final manuscript.
M.H.: Study design, data review, review and approval of final manuscript.
D.S.: Study design, data review, data analysis, writing paper, review and approval of final manuscript.

Declaration of interest
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Supplementary material
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Appendix

Literature search details

Ovid Medline, Epub ahead of print, In-process and other non-indexed Citations, Ovid Medline Daily

Searched January 11, 2017:
1. Exp wound infection
2. (((surgic* adj5 wound*) or (surgic* adj5 site*)) and infect*).mp. or (site* or wound*) adj5 infect*.ti,ab. or (operat* adj3 wound*).mp.
3. 1 or 2
4. oxygen/ or exp oxygen inhalation therapy/ or hyperoxia/
5. (((inspirator* or fraction* or supplement* or concentrat*) adj5 oxygen*) or hyperoxia or oxygenat*).mp.
6. 4 or 5
7. 3 and 6
8. ((randomized controlled trial or controlled clinical trial)pt. or (randomized or placebo)ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (animals not (humans and animals)).sh.
9. 7 and 8
10. limit 9 to yr=“2014 -Current”

Ovid EMBASE, 1974 to January 10, 2017

Searched January 11, 2017:
1. surgical infection/ or wound infection/
2. (((surgic* adj5 wound*) or (surgic* adj5 site*)) and infect*).mp. or (site* or wound*) adj5 infect*.ti,ab. or (operat* adj3 wound*).mp.
3. 1 or 2
4. oxygen/ or exp oxygen therapy/ or hyperoxia/
5. (((inspirator* or fraction* or supplement* or concentrat*) adj5 oxygen*) or hyperoxia or oxygenat*).mp.
6. 4 or 5
7. 3 and 6
8. ((randomized controlled trial or controlled clinical trial).pt. or (randomized or placebo).ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (animals not (humans and animals)).sh.
9. 7 and 8
10. limit 9 to yr=“2014 -Current”

Google Scholar Advanced

Searched January 11, 2017:
Find articles with all of the words in the title of the article:
surgical infection oxygen
Limit to articles dated between 2014 and 2017

CINAHL Ebsco

Searched January 13, 2017:
1. (MH “Surgical Wound Care”) OR (MH “Wound Infection”) OR (MH “Surgical Wound Infection”)
2. surgic* AND ((wound* or site*)) AND infect*
3. ((site* or wound*)) AND infect*
4. operat* and wound*
5. S1 AND S2 AND S3 AND S4
6. (MH “Oxygen”) OR (MH “Hyperbaric Oxygenation”)
7. (MH “Hyperoxia”)
8. (((inspirator* or fraction* or supplement* or concentrat*)) AND oxygen
9. hyperoxia or oxygenat*
10. S5 OR S7 OR S8 OR S9
11. S5 AND S10, Limiters - Published Date: 20140101-20171231

Cochrane CENTRAL

Searched January 13, 2017:
#1 MeSH descriptor: [Surgical Wound Infection] explode all trees
#2 MeSH descriptor: [Wound Infection] explode all trees
#3 (surgic* adj5 wound*) or (surgic* adj5 near site*) and infect*) or ((site* or wound*) near infect*) or (operat* near wound*)
#4 #1 or #2 or #3
#5 MeSH descriptor: [Oxygen] explode all trees
#6 MeSH descriptor: [Oxygen Inhalation Therapy] explode all trees
#7 MeSH descriptor: [Hyperoxia] explode all trees
#8 (((inspirator* or fraction* or supplement* or concentrat*) near oxygen*) or hyperoxia or oxygenat*)
#9 #5 or #6 or #7 or #8
#10 #4 and #9 Publication Year from 2014 to 2017, in Trials

Handling editor: J.G. Hardman