# High-concentration oxygen and surgical site infections in abdominal surgery: a meta-analysis

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**Background:** There has been recent interest in using high-concentration oxygen to prevent surgical site infections (SSIs). Previous meta-analyses in this area have produced conflicting results. With the publication of 2 new randomized controlled trials (RCTs) that were not included in previous meta-analyses, an updated review is warranted. Our objective was to perform a meta-analysis on RCTs comparing high- and low-concentration oxygen in adults undergoing open abdominal surgery.

**Methods:** We completed independent literature reviews using electronic databases, bibliographies and other sources of grey literature to identify relevant studies. We assessed the overall quality of evidence using grade guidelines. Statistical analysis was performed on pooled data from included studies. A priori subgroup analyses were planned to explain statistical and clinical heterogeneity.

**Results:** Overall, 6 studies involving a total of 2585 patients met the inclusion criteria. There was no evidence of a reduction in SSIs with high-concentration oxygen (risk ratio 0.77, 95% confidence interval 0.50–1.19, $p$ = 0.24). We observed substantial heterogeneity among studies.

**Conclusion:** There is moderate evidence that high-concentration oxygen does not reduce SSIs in adults undergoing open abdominal surgery.

**Contexte :** On observe depuis peu un intérêt à l'endroit de l'oxygène à concentration élevée pour prévenir les infections de plaies opératoires. Les méta-analyses réalisées dans le passé à ce sujet ont donné des résultats divergents. Compte tenu de la publication de 2 nouveaux essais randomisés et contrôlés (ERC) qui n'ont pas été inclus dans les méta-analyses précédentes, une nouvelle revue de la situation s'imposait. Notre objectif était donc d'effectuer une méta-analyse des ERC, qui ont comparé l'oxygène à concentration élevée et faible chez des adultes soumis à une chirurgie abdominale ouverte.

**Méthodes :** Nous avons effectué des analyses indépendantes de la littérature à partir de bases de données électroniques, de bibliographies et autres éléments de la littérature « grise » pour identifier les études pertinentes. Nous avons classé la qualité globale des données probantes selon les lignes directrices de catégorisation. L'analyse statistique a porté sur les données regroupées des études incluses. Des analyses de sous-groupes ont été planifiées a priori pour expliquer l'hétérogénéité statistique et clinique.

**Résultats :** En tout, 6 études regroupant 2585 patients répondaient aux critères d'inclusion. On n'a noté aucune preuve de réduction des infections de plaies opératoires associées à l'oxygène à concentration élevée (risque relatif 0,77, intervalle de confiance de 95 % 0,50–1,19, $p$ = 0,24). Nous avons observé une forte hétérogénéité entre les études.

**Conclusion :** On dispose de données probantes acceptables selon lesquelles l'oxygène à concentration élevée ne réduit pas les infections de plaies opératoires chez les adultes soumis à une chirurgie abdominale ouverte.

Surgical site infections (SSIs) are a source of patient morbidity and mortality. Patients undergoing colorectal surgery have an average risk of 4%–11% for SSIs.[1] The development of an SSI increases the length of hospital stay by 6 days in patients with colorectal disease and 10 days in patients undergoing appendectomy.[2] Patients with an SSI are more likely to be admitted to the intensive care unit and have a higher mortality.[2]

 

The cost associated with SSIs is substantial. Recent systematic reviews evaluating the costs associated with hospital-acquired infections estimated the cost of SSIs to be between US$10 443 and US$25 546[3,4] per patient per SSI in the United States. The total cost of SSIs in the United States has been estimated to be between US$3.45 billion and US$10.07 billion annually (in 2007 dollars).[5]

The use of high-concentration inspired oxygen in the perioperative period has been of recent interest. Oxygen plays an important role in limiting the risk of SSIs. Oxidative killing by neutrophils of pathogenic bacteria is critical in the defence against SSIs. This antimicrobial action relies on the production of superoxide radicals from oxygen, which is dependent on the partial pressure of oxygen within the tissues.[6–8] Increasing the inspired oxygen concentration has been shown to increase tissue oxygen tension.[9]

Randomized controlled trials (RCTs) have been completed in the last decade to determine the effect of high-concentration inspired oxygen on the rate of SSIs in patients undergoing surgery. These RCTs have had conflicting results. As such, 4 meta-analyses have been published in this area. Two exclusively studied patients with colorectal disease[10,11] and had conflicting conclusions.

Two other meta-analyses included patients with colorectal or other types of abdominal disease.[12,13] Al-Niaimi and colleagues[13] included 4 studies and found a significant reduction in SSIs when using a fixed-effects model, but no significant reduction when using a random-effects model. Qadan and colleagues[12] found a significant reduction in SSIs when including an additional trial by Myles and colleagues.[14]

None of the aforementioned meta-analyses included 2 recently published RCTs examining SSIs following abdominal surgery. Meyhoff and colleagues[15] published a large multicentre RCT including patients who had colorectal and noncolorectal surgeries. Bickel and colleagues[16] investigated SSIs in patients undergoing open appendectomies.

An additional criticism of 2 of the meta-analyses[10,12] is their inclusion of the study by Myles and colleagues.[14] The primary intervention in that study was the use of 70% nitrous oxide (with 30% oxygen) compared with a nitrous oxide–free group. Surgical site infections were a secondary outcome. There was no standardization of oxygen concentration in the nitrous oxide–free group (i.e., the high-concentration oxygen group). The inclusion of this trial is questionable and may have had a dramatic effect on the study conclusions owing to its large sample ($n$ = 2050).

Owing to the recent publication of 2 RCTs, as well as the questionable inclusion of the study by Myles an colleagues[14] in previous meta-analyses, an additional meta-analysis of this topic is warranted.

Our study objective was to evaluate whether high-concentration inspired oxygen reduces SSIs in adult patients undergoing open abdominal surgery.

## Methods

### *Inclusion and exclusion criteria*

Studies included in this review were RCTs comparing high-concentration to low-concentration perioperative oxygen in adults undergoing open abdominal surgery. High-concentration perioperative oxygen was defined as fraction of inspired oxygen (FiO2) greater than 60%. Low-concentration perioperative oxygen was defined as FiO2 less than 40%. We excluded observational trials and studies with patients undergoing nonabdominal surgery or laparoscopic procedures. We also excluded studies of patients undergoing cesarean delivery owing to the nature of the anesthetic care in this population. Regional anesthesia is typically used in this group, and control of oxygen delivery during the procedure may be limited. Studies in which there was not a standardized inspired oxygen concentration were also excluded.

### *Outcome*

The primary outcome was SSIs. Diagnosis of SSIs included clinical diagnosis (e.g., purulent drainage, erythema, fever, induration), positive culture, radiologic evidence of infection, or Center for Disease Control and Prevention criteria for SSI.[17]

### *Search methods*

We searched EMBASE (1980–2011), MEDLINE (1948–2011), the Cochrane Central Register of Controlled Trials and the U.S. National Institutes of Health's clinical trials registry (clinicaltrials.gov). Major conference proceedings (including the American College of Surgeons Clinical Congress, International Surgical Congress of the Association of Surgeons of Great Britain and Ireland, The American Society of Anesthesiologists Annual Meeting, The Canadian Surgery Forum) were reviewed for unpublished studies, as were the databases of conference proceedings (proceedings first, papers first). Search terms included "sepsis," "wound infection," "surgical site infection," "hyperoxia," "oxygen," "abdominal surgery" and "laparotomy." Related terms were searched using the "explode" option. Terms were combined using Boolean expressions to widen the search. We searched bibliographies of relevant papers and text books to ensure all relevant studies were identified. The search end date was November 2011.

Two of us (S.V.P. and S.C.) reviewed the studies identified in the search to locate relevant studies. Both reviewers assessed each study to determine if it met the inclusion criteria. The comprehensiveness of this search made it unlikely that any important research was omitted from our review. We used the κ statistic to assess inter-rater agreement.

### Data collection

Data were collected from published works by the primary author and second author independently.

### Quality assessment and data extraction

Two of us (S.V.P. and S.C. C.) independently extracted the data according to predetermined inclusion and exclusion criteria, using a standardized extraction form. We assessed study quality according to the Cochrane Handbook.[18] Randomization, concealment of allocation, blinding, incomplete outcome data and reporting bias were assessed. We categorized the risk of bias as "low," "unclear" or "high" in each category. We performed an overall assessment of the risk of bias for each study. We considered the overall risk of bias to be low when there was a low risk of bias in each category. We considered the overall risk of bias to be high if there was a high risk of bias in 1 or more categories. Finally, we considered the risk of bias to be unclear if there was an unclear risk of bias in 1 or more categories.

The GRADE system was used to rate the overall quality of evidence from this meta-analysis.[19] From this system, RCTs are rated as having a high quality of evidence except in cases of a high likelihood of bias, inconsistent results, uncertainty about directness, imprecise or sparse data, or high probability of publication bias. Concerns in any of these areas can downgrade the evidence from high to moderate, low or very low. The quality of evidence can be improved if there is a dose response, a large magnitude of effect or if confounders would likely reduce the effect.

### Statistical analysis

We analyzed the data using Stata 12 (StataCorp LP). Risk ratios and confidence intervals were calculated using the random-effects model. We used the random-effects model, as there was clinical heterogeneity among studies. Statistical heterogeneity was assessed using the $I^2$ statistic. An $I^2$ less than 40% may not be important, 30%–60% represents moderate heterogeneity and 50%–90% represents substantial heterogeneity.[18]

### Additional analyses

A priori subgroup analyses were planned based on sources of clinical heterogeneity. Early trials looked exclusively at patients undergoing elective colorectal surgery, whereas later trials included patients undergoing other abdominal surgeries. For this reason, we planned a subgroup analysis including only patients undergoing elective colorectal surgeries. We also completed a subgroup analysis based on the quality of studies and standardized prophylactic antibiotic use. The test of interaction was used to assess the difference between effect estimates found in the subgroups.

## Results

There were 683 studies identified through our search. Applying our inclusion and exclusion criteria, we selected 14 studies for full text assessment; 6 of them[9,15,16,20–22] met our inclusion criteria (Fig. 1). The κ statistic was 1, which indicates perfect agreement between reviewers. Study samples ranged from 38 to 1400 patients, and the studies were published between 2000 and 2011.

### Summary of included studies

Study characteristics are summarized in Tables 1 and 2. Three trials[9,15,20] were multicentred RCTs, and 3 trials[16,21,22] were single institution trials. Trials took place across North America, Europe, Asia and Australia. The intervention in all trials was an FiO2 concentration of 80%. The control condition in 5 of the studies[9,15,16,20,21] was an FiO2 of 30%, and 1 trial[22] used an FiO2 of 35% as the control condition. Duration of treatment continued for 2 hours postoperatively in all but 1 study,[20] which continued treatment for 6 hours postoperatively. All trials included high rates of prophylactic antibiotic use, but only 4 trials[15,16,20,21] included prophylactic antibiotics in the study protocol.

### Sources of heterogeneity

We identified potential sources of clinical heterogeneity. The type of procedures included in the studies and the method of diagnosis of SSIs were both sources of clinical heterogeneity. The type of procedures included elective colorectal surgery, emergent and elective abdominal surgery and open appendectomies. Three studies[9,20,21] exclusively included at patients undergoing elective colorectal surgery. Two studies[15,22] included patients who underwent

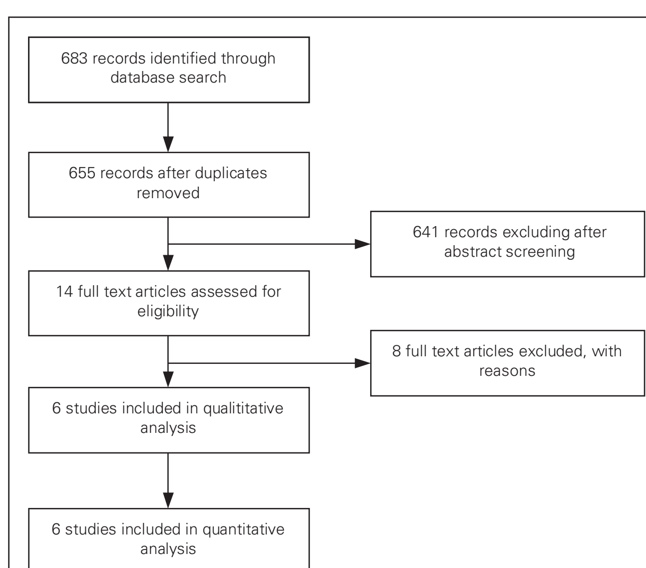


**Fig. 1.** Literature search results.

elective or emergent abdominal procedures, including colorectal procedures. Open appendectomies were assessed in 1 trial.[16] The method of diagnosis of SSIs varied among studies. Most included SSIs diagnosed within 14 days post-procedure. One study[21] included all SSIs diagnosed within 30 days.

Surgical site infections were diagnosed using the CDC criteria[17] or a similar method in 4 of the studies.[15,16,20,21] In the study by Grief and colleagues[9] infections were diagnosed based on positive cultures only. In the study by Pryor and colleagues[22] they were diagnosed through a retrospective chart review after patients were discharged from hospital. Their diagnosis of an SSI required explicit documentation of an SSI by the surgical team and a change in management of the patient. If these 2 criteria were met, 3 objective signs of infection were required, including

**Table 1. Characteristics of included studies**

| Study | No. participants | Methods | Participants | Intervention | Outcomes | Notes |
|---|---|---|---|---|---|---|
| Belda et al.[20] | 300 | Multicentred RCT | Patients aged 18–80 yr undergoing elective open colorectal surgery | Treatment group: FiO2 80%; control: FiO2 30%; duration of treatment was 6 h | SSIs diagnosed within 14 d of surgery | Prophylactic antibiotics standardized |
| Bickel et al.[16] | 210 | Single-centre RCT | Patients, aged > 15 yr undergoing open appendectomy | Treatment group: FiO2 80%; control: FiO2 30%; duration of treatment was 2 h | SSIs diagnosed within 14 d of surgery, | Prophylactic antibiotics standardized |
| Greif et al.[9] | 500 | Multicentred RCT | Patients aged 18–80 yr undergoing elective open colorectal surgery | Treatment group: FiO2 80%;. control: FiO2 30%; duration of treatment was 2 h | SSIs diagnosed within 14 d of surgery by positive culture | — |
| Mayzler et al.[21] | 38 | Single-centre RCT | Patients aged 45–92 yr undergoing elective colorectal surgery | Treatment group: FiO2 80%; control: FiO2 30%; duration of treatment was 2 h | SSIs diagnosed within 30 d of surgery | Control group treated with 30% $O_2$ and 70% nitrous oxide; prophylactic antibiotics standardized |
| Meyhoff et al.[15] | 1400 | Multicentred RCT | Adult patients undergoing elective or emergent abdominal surgery | Treatment group: FiO2 80%; control: FiO2 30%; duration of treatment was 2 h | SSIs diagnosed within 14 d of surgery | Prophylactic antibiotics standardized |
| Pryor et al.[22] | 165 | Single-centre RCT | Adult patients undergoing elective or emergent abdominal surgery | Treatment group: FiO2 80%; control: FiO2 35%; duration of treatment was 2 h | SSIs diagnosed within 14 d of surgery, retrospectively | Laparoscopic procedures included if laparotomy was performed at some point |

FiO2 = fraction of inspired oxygen; $O_2$ = oxygen; RCT = randomized controlled trial; SSI = surgical site infection.

**Table 2. Patient characteristics of participants in studies included in the meta-analysis**

| | Study, group, %* | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Belda et al.[20] | | Bickel et al.[16] | | Greif et al.[9] | | Mayzler et al.[21] | | Meyhoff et al.[15] | | Pryor et al.[22] | |
| Characteristic | Treatment *n* = 148 | Control *n* = 143 | Treatment *n* = 107 | Control *n* = 103 | Treatment *n* = 250 | Control *n* = 250 | Treatment *n* = 19 | Control *n* = 19 | Treatment *n* = 685 | Control *n* = 701 | Treatment *n* = 80 | Control *n* = 80 |
| Age, mean yr | 64 | 62 | 28.5 | 27.6 | 57 | 57 | 67 | 69 | 64† | 64† | 54 | 57 |
| Male sex | 48 | 64 | 75 | 71 | 57 | 55 | 52 | 63 | 42 | 42 | 43 | 43 |
| Operation | | | | | | | | | | | | |
| Colorectal | 100 | 100 | | | 100 | 100 | 100 | 100 | 44 | 47 | 75 | 68 |
| Major gynecologic | | | | | | | | | 20 | 18 | 14 | 19 |
| Appendectomy | | | 100 | 100 | | | | | 9 | 9 | | |
| Other abdominal | | | | | | | | | 27 | 26 | 11 | 14 |
| Prophylactic antibiotics | 100 | 100 | 100 | 100 | "Most" | "Most" | 100 | 100 | 94 | 96 | 100 | 98 |
| BMI, mean | 27 | 27 | | | | | 25 | 27 | 25† | 25† | 27 | 25 |
| BMI > 30 | 18 | 15 | | | | | | | 15 | 16 | 24 | 11 |
| NNISS score | | | | | | | | | | | | |
| M | | | | | | | | | | | 9 | 11 |
| 0 | 17 | 13 | | | 53 | 51 | | | 43 | 44 | 40 | 39 |
| 1 | 58 | 68 | | | 40 | 42 | | | 40 | 41 | 44 | 43 |
| 2 | 25 | 19 | | | 7 | 7 | | | 15 | 13 | 6 | 7 |
| 3 | | | | | | | | | 2 | 2 | 1 | 0 |
| SSI, % | 15 | 24 | 6 | 14 | 5 | 11 | 11 | 16 | 19 | 20 | 25 | 11 |

BMI = body mass index; NNISS = National Nosocomial Infections Surveillance[1]; SSI = surgical site infection.
*Unless otherwise indicated.
†Median value.

elevated white blood cell count, fever, pus from the surgical site, positive culture, erythema and induration, and radiologic evidence of infection.

### *Summary of excluded studies*

We excluded 7 of the studies that were selected for full text review. Two of them were excluded because they involved patients undergoing laparoscopic surgery only.[23,24] One study[25] was excluded as it did not randomize patients to a high-concentration oxygen group. We excluded the study by Myles and colleagues[14] because it had no standardized high-concentration oxygen group and because it included patients undergoing nonabdominal procedures. Four trials[26–29] were excluded because they assessed patients undergoing cesarean delivery.

### *Risk of bias*

A summary of the risk of bias can be found in Table 3. The study by Pryor and colleagues[22] was identified as having an unclear risk of bias. In this trial, SSIs were diagnosed retrospectively through chart review, which raises questions regarding the validity of their results. This trial was the only one that showed an increase in SSIs in the high-concentration oxygen group.

We created a funnel plot, which showed symmetry, reflecting a low likelihood of publication bias. Reporting bias was minimal, as infection rates were reported clearly in all included studies.

### *Analysis*

The results of the 6 studies were combined and are shown in Figure 2. A total of 2585 patients were included, with 1289 patients in the high-concentration oxygen group. The overall infection rate in the high-concentration oxygen group was 15.1% compared with 17.7% in the control group. There was no evidence of a difference between treatment groups (risk ratio [RR] 0.77, 95% confidence interval [CI] 0.50–1.19, $p$ = 0.24). This group had high heterogeneity with an $I^2$ value of 68% ($p$ = 0.008).

### *Subgroup analysis*

Our subgroup analysis assessed the effect of high-concentration oxygen on the SSI rate in patients undergoing elective colorectal surgery (Fig. 3). Three studies[9,20,21] evaluated these patients ($n$ = 829). The infection rate in the high-concentration oxygen group from these studies was 8.8% compared with 16.0% in the control group and represented strong evidence of a decrease in SSIs in the high-concentration oxygen group (RR 0.55, 95% CI 0.38–0.80, $p$ = 0.002). These studies were statistically homogeneous

**Table 3. Risk of bias of included studies**

| | Source of potential bias | | | | | | |
|---|---|---|---|---|---|---|---|
| Study | Randomization | Allocation concealment | Blinding | Incomplete outcome data | Selective reporting | Other | Overall risk of bias |
| Belda et al. 2005[20] | LOW RISK Computerized randomization | LOW RISK Opaque envelopes | LOW RISK Surgeon, wound assessor and patient blinded; | LOW RISK All patients included in analysis | LOW RISK Primary outcome identified in protocol | — | LOW RISK |
| Bickel et al. 2011[16] | LOW RISK Stratified randomization | LOW RISK Sealed envelopes | LOW RISK Surgeon, wound assessor and patient blinded; | LOW RISK All patients included in analysis | LOW RISK Primary outcome identified in protocol | — | LOW RISK |
| Greif et al. 2000[9] | LOW RISK Computerized randomization | LOW RISK Sealed envelopes | LOW RISK Wound assessors and patients blinded | LOW RISK All patients included in analysis | LOW RISK Primary outcome identified in protocol | — | LOW RISK |
| Mayzler et al. 2005[21] | LOW RISK Randomization by lottery | LOW RISK Closed envelopes | LOW RISK Wound assessors blinded | LOW RISK All patients included in analysis | LOW RISK Primary outcome identified in protocol | — | LOW RISK |
| Meyhoff et al. 2009[15] | LOW RISK Computerized Randomization; Stratified by risk factors | LOW RISK Allocation by centralized system | LOW RISK Surgeon, wound assessor and patients blinded | LOW RISK All patients included in analysis | LOW RISK Primary outcome identified in protocol | — | LOW RISK |
| Pryor et al. 2004[22] | LOW RISK Random number table | LOW RISK Sealed envelopes | LOW RISK Surgeon, wound assessor and patient blinded | LOW RISK All patients included in analysis | LOW RISK Primary outcome identified in protocol | UNCLEAR RISK SSI identified retrospectively | UNCLEAR RISK |

SSI = surgical site infection.

($I^2 = 0\%$, $p = 0.78$). A test of subgroup difference did not reveal evidence of a difference in effect between groups ($p = 0.16$).

We conducted subgroup analyses excluding the trial with unclear risk of bias[22] (Fig. 4) and excluding the trials that did not use a protocol of prophylactic antibiotics[9,22] (Fig. 5). Results from the high-quality studies ($n = 2425$), found the infection rate in patients who received high-concentration oxygen was 14.4% compared with 18.2% in the control group. This represented good evidence of a treatment effect (RR 0.66, 95% CI 0.45–0.96, $p = 0.029$). This subgroup analysis showed moderate heterogeneity ($I^2 = 54\%$, $p = 0.07$). The test for interaction showed evidence that the effect within the 2 subgroups was different ($p = 0.003$).

In trials using a protocol for prophylactic antibiotics, there was no evidence of a difference between the high-concentration and low-concentration oxygen groups (RR 0.73, 95% CI 0.50–1.07, $p = 0.10$). These trials were moderately heterogeneous ($I^2 = 42.9\%$, $p = 0.15$) and showed no evidence of a subgroup effect ($p = 0.69$). Comparing the subgroup of trials using standardized prophylactic antibiotics with the overall estimate showed similar risk ratios ($p = 0.94$).

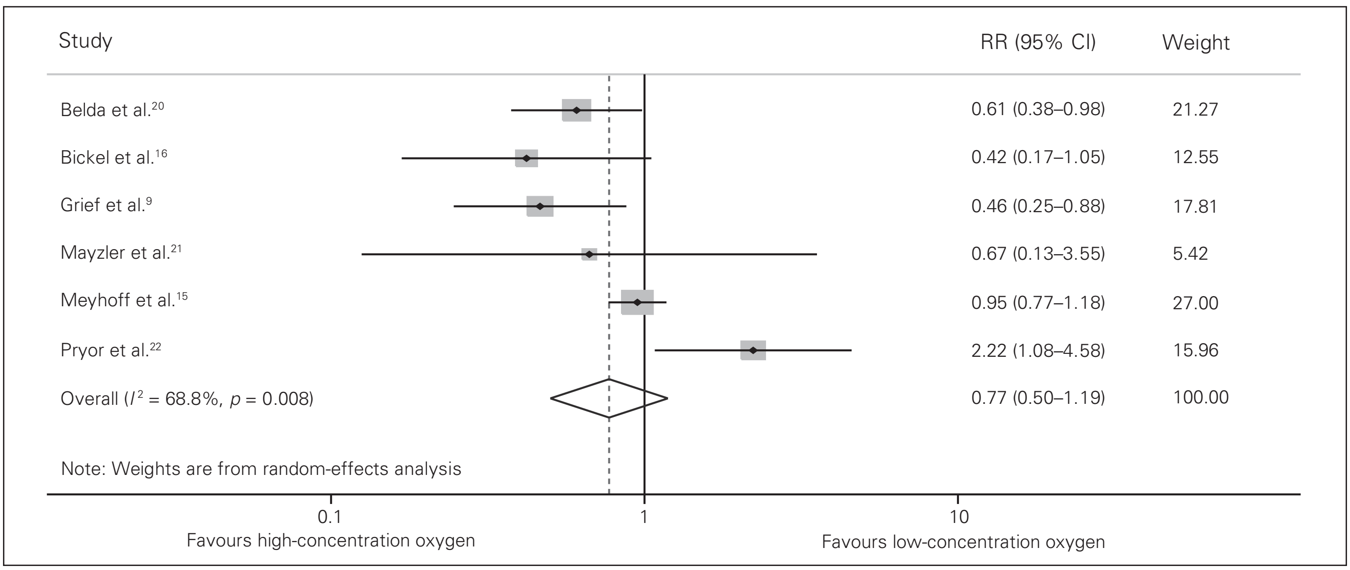


**Fig. 2.** Risk of surgical site infection in high-concentration and low-concentration oxygen groups (pooled risk ratio [RR] 0.77, 95% confidence interval [CI] 0.50–1.19, $p = 0.24$).

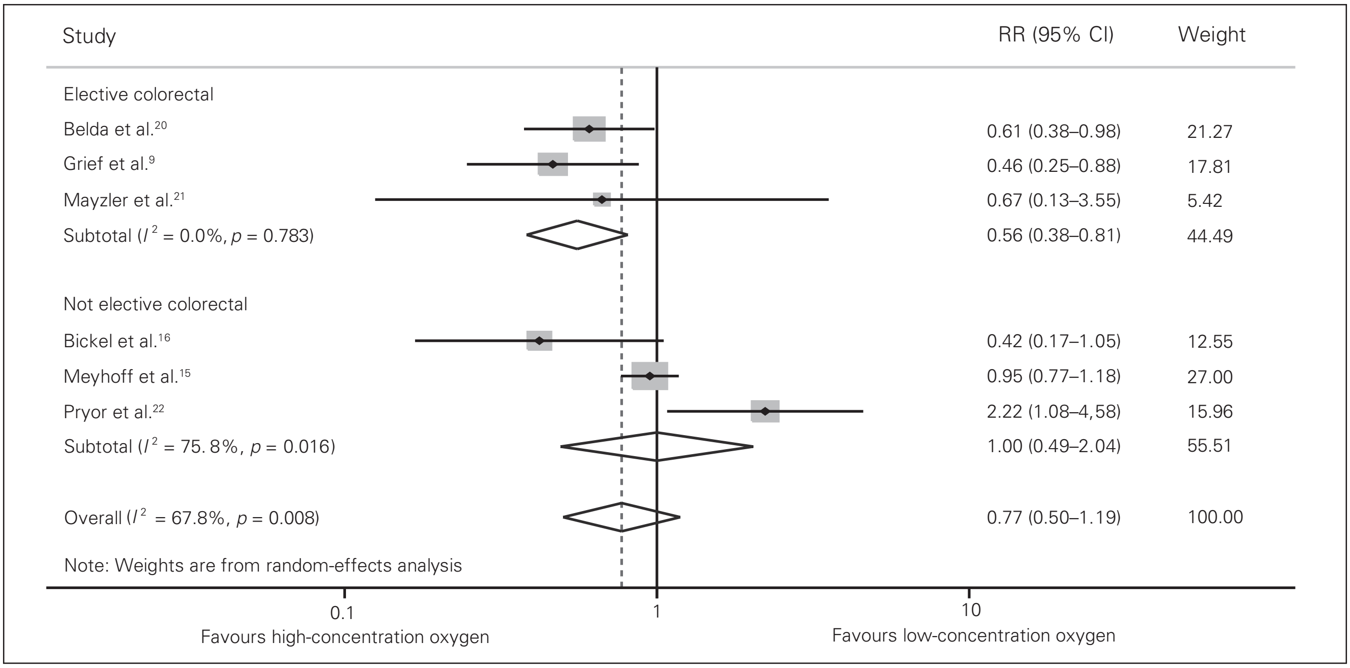


**Fig. 3.** Subgroup analysis of patients who had elective colorectal surgery (rest of subgroup interaction $p = 0.16$). CI = confidence interval; RR = risk ratio.

### *Quality of evidence*

We used the GRADE guidelines to assess the quality of evidence from this review. Table 4 shows the GRADE summary of findings for this study. The quality of evidence was found to be moderate for the outcome addressed in this study. It was downgraded from high for substantial statistical heterogeneity (inconsistency). Moderate quality of evidence indicates that further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

## Discussion

We conducted a meta-analysis to determine whether high-concentration inspired oxygen reduces the risk of

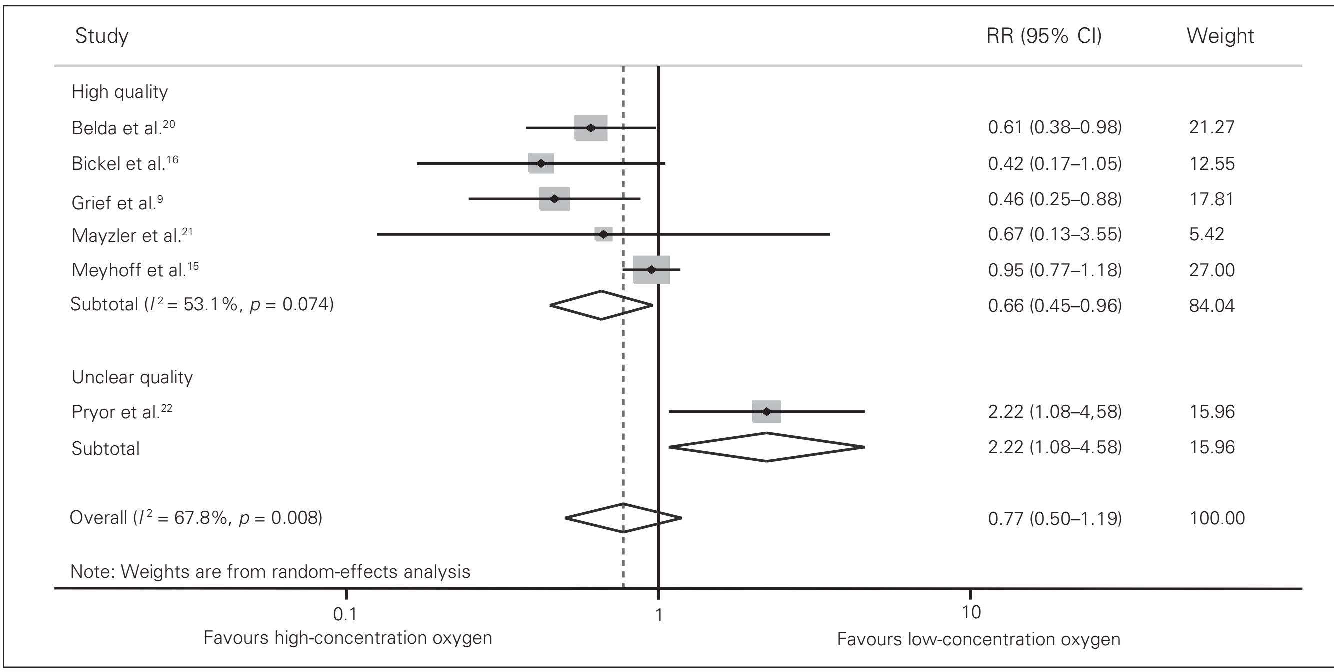


**Fig. 4.** Subgroup analysis excluding the study with unclear risk of bias (test of subgroup interaction $p = 0.003$). CI = confidence interval; RR = risk ratio.

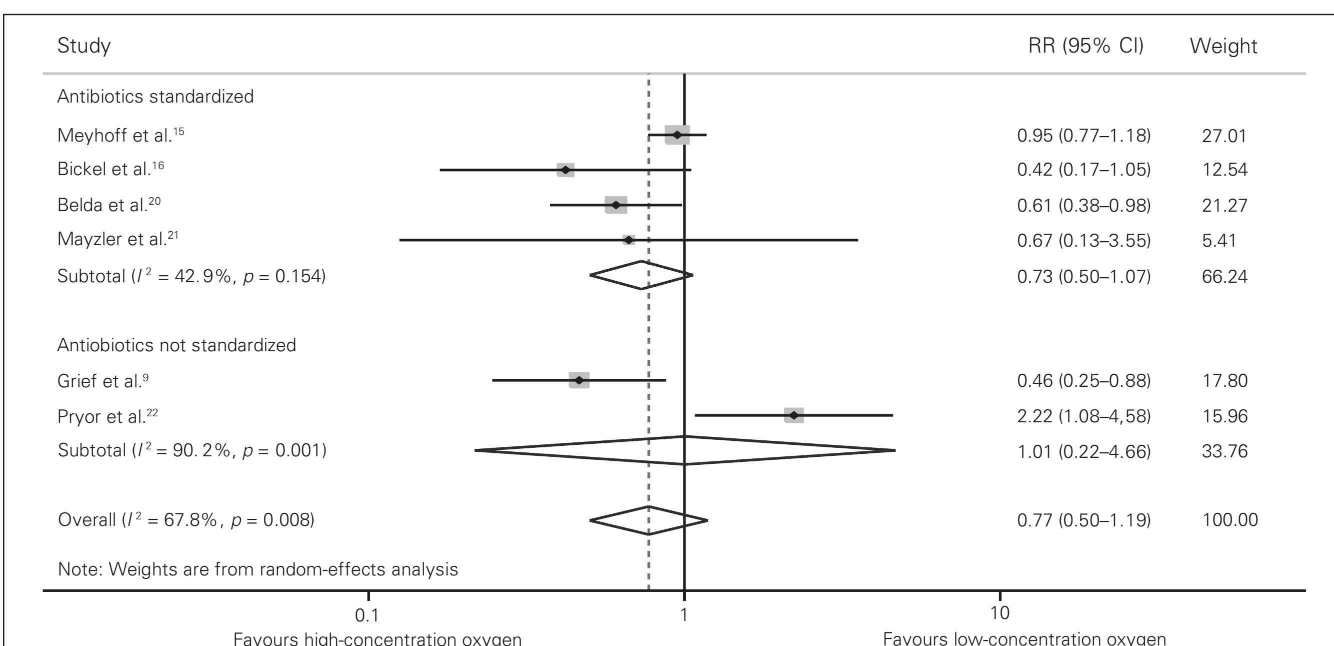


**Fig. 5.** Subgroup analysis including studies with standardized prophylactic antibiotic use (test of subgroup interaction $p = 0.69$). CI = confidence interval; RR = risk ratio.

SSIs in adult patients undergoing open abdominal surgery.

Previous meta-analyses have been inconsistent in their findings. Al-Niaimi and colleagues[13] and Chura and colleagues[10] found conflicting results when using random-effects versus fixed-effects models. Qadan and colleagues[12] found a significant difference in the SSI rates between the 2 groups, while Brar and colleagues[11] found no difference in SSI rates when looking at patients undergoing colorectal surgery.

The inclusion of the study by Myles and colleagues[14] in these meta-analyses is questionable. The primary intervention in that study was nitrous oxide versus no nitrous oxide, with multiple outcomes being assessed (including SSIs). Oxygen concentration was not standardized in the nitrous oxide–free group, which was subsequently analyzed as the "high-concentration oxygen group." Oxygen concentration ranged from 20% to 100%, and averaged 73% in the group. There was a reduced risk of SSIs in this group (odds ratio [OR] 0.72, 95% CI 0.52–0.98, $p$ = 0.036). The reduction in wound infections may have been more attributable to avoiding nitrous oxide than using high-concentration oxygen. In fact, Myles and colleagues[14] examined the independent effect of oxygen concentration on SSIs in their nitrous oxide–free group. This analysis failed to reveal any difference in the SSI rate when comparing 25%–50%, 51%–75%, 76%–85% and 86%–100% oxygen concentration groups. Despite this, the results from this study were used to support the conclusions that high-concentration oxygen reduced SSIs.

Compounding the confusion regarding the recommendations from previous meta-analyses, Meyhoff and colleagues[15] completed a large ($n$ = 1400) multicentred RCT not included in any of the previous reviews. There was not a significant difference in SSIs in their patients (OR 0.94, 95% CI 0.72–1.22, $p$ = 0.64).

Incorporating the 2 most recent trials, and excluding the large study by Myles and colleagues,[14] we found that there was no evidence of a difference in SSI rates between patients receiving high-concentration oxygen and patients receiving low-concentration oxygen who underwent open abdominal surgery (RR 0.77, 95% CI 0.50–1.19, $p$ = 0.24). Our findings are in agreement with those of the largest included RCT by Meyhoff and colleagues.[15]

We attempted to account for the high heterogeneity through subgroup analysis. Studies assessing patients who had elective colorectal surgery were more homogeneous in their results. This subgroup analysis did not reveal a statistical difference between the risk for SSIs in these patients or in those who had nonelective colorectal procedures ($p$ = 0.16). As such, it cannot be confidently concluded that this subgroup of patients had a different risk for SSIs. Excluding the study by Pryor and colleagues,[22] which was the only one that found an increased risk for SSI in the high-concentration oxygen group, did not resolve the heterogeneity seen in the pooled result.

Partial explanation of heterogeneity was achieved through subgroup analysis of trials with standardized prophylactic antibiotics. Despite this, there was no appreciable difference between the subgroup risk ratio and the overall risk ratio ($p$ = 0.94).

### *Limitations*

The strengths of this review include the systematic and explicit application of eligibility criteria, the thorough search of eligible studies, the assessment of bias within the studies, the development and testing of a priori sources of heterogeneity and the transparency of the quality of evidence assessment. Limitations include the high statistical heterogeneity among studies. The RCTs differed in the type of procedures, the acuity of the surgical procedure and how SSIs were diagnosed.

## Conclusion

Overall, there was no evidence of a benefit to using high-concentration oxygen to reduce SSIss following open abdominal surgery. At present, this review is the best evidence of the effect of high-concentration oxygen on SSIs in adult patients undergoing open abdominal surgery. There is a suggestion that high-concentration oxygen may be beneficial in patients undergoing elective colorectal surgery, but this effect does not appear to be generalizable to open abdominal surgery as a whole.

**Competing interests:** None declared.

**Contributors:** S.V. Patel acquired the data. S.V. Patel and S.C. Coughlin wrote the article. All authors designed the study, analyzed data, reviewed the article and approved its publication.

**Table 4. Summary of findings**

| No. studies (No. participants) | Outcome | Estimated risks (95% CI)* | | RR (95% CI) | Quality of evidence |
|---|---|---|---|---|---|
| | | Low-concentration oxygen | High-concentration oxygen | | |
| 6 (2585) | Surgical site infections | 17.7 per 100 | 13.6 per 100 (8.87–21.1) | RR 0.77 (0.50– 1.19) | +++† |

CI = confidence interval; RR = risk ratio.
*Low-concentration oxygen risk based on mean weighted risk, high-concentration oxygen risk based on relative effect.
†Reduced owing to inconsistency.

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