The surgical safety checklist and patient outcomes after surgery: a prospective observational cohort study, systematic review and meta-analysis

T. E. F. Abbott, MRCP;[1] T. Ahmad, MPh;[1] M. K. Phull, FRCA;[2] A. J. Fowler, MBBS;[3] R. Hewson, FRCA;[2] B. M. Biccard, PhD;[4] M. S. Chew, PhD;[5] M. Gillies, MD;[6] and R. M. Pearse, MD;[1] for the International Surgical Outcomes Study (ISOS) group [appendix]

1. William Harvey Research Institute, Queen Mary University of London, EC1M 6BQ, UK
2. The Royal London Hospital, Barts Health NHS Trust, E1 1BB, UK
3. Guys and St. Thomas's NHS Foundation Trust, SE1 7EH, UK
4. Department of Anaesthesia and Perioperative Medicine, Groote Schuur Hospital, Faculty of Health Sciences, University of Cape Town, South Africa
5. Department of Anaesthesia and Intensive Care, faculty of Medicine and Health Sciences, Linköping University, 58185 Linköping, Sweden
6. Department of Anaesthesia, Critical Care and Pain Medicine, University of Edinburgh, EH48 3DF, UK

Correspondence to:
Rupert Pearse,
Adult Critical Care Unit,
The Royal London Hospital,
London,
E1 1BB, UK.
e-mail: r.pearse@qmul.ac.uk Tel: +44 20 3594 0346

Keywords: Cohort Studies; Surgery; Postoperative care/methods; Postoperative care/statistics & numerical data; Surgical Procedures, Operative/mortality

Main text: 2960 words **Summary: 247**

Summary

Background

The Surgical Safety Checklist is widely used to improve the quality of perioperative care. However, clinicians continue to debate the clinical effectiveness of this tool.

Methods

Prospective analysis of data from the International Surgical Outcomes study (ISOS), an international observational study of elective in-patient surgery, accompanied by a systematic review and meta-analysis of published literature. The exposure was surgical safety checklist use. The primary outcome was in-hospital mortality and the secondary outcome was postoperative complications. In the ISOS cohort, a multivariable multi-level generalised linear model was used to test associations. To further contextualise these findings, we included the results from the ISOS cohort in a meta-analysis. Results are reported as odds ratios (OR) with 95% confidence intervals.

Results

We included 44,814 patients from 497 hospitals in 27 countries in the ISOS analysis. 40,245 (89.8%) patients were exposed to the checklist, whilst 7508 (16.8%) sustained ≥1 postoperative complications and 207 (0.5%) died before hospital discharge. Checklist exposure was associated with reduced mortality (OR 0.49 [0.32-0.77]; p<0.01), but no difference in complication rates (OR 1.02 [0.88-1.19]; p=0.75). In the systematic review, we screened 3,732 records and identified 11 eligible studies of 453,292 patients including the ISOS cohort. Checklist exposure was associated with both reduced postoperative mortality (OR 0.75 [0.62-0.92]; p<0.01; I^2=87%) and reduced complication rates (OR 0.73 [0.61-0.88]; p<0.01; I^2=89%).

Conclusions

Patients exposed to a surgical safety checklist experience better postoperative outcomes, but this could simply reflect wider quality of care in hospitals where checklist use is routine.

Introduction

More than 310 million surgical procedures are carried out worldwide every year.[1] Estimates of morbidity and mortality vary.[2-4] However, recent data suggest that ~75 million patients will experience a postoperative complication, leading to two million deaths each year.[5,6] An important cause of avoidable harm is healthcare acquired illness or injury. In the United Kingdom (UK), perioperative adverse events account for one in six patient safety incidents,[7] and as many as half are potentially avoidable.[8] Preventable adverse events are costly in both human and financial terms. The UK Department of Health estimates that iatrogenic harm costs the National Health Service more than £1bn each year,[9] and other developed countries are likely to be exposed to similar costs.

Checklists are a simple and reproducible way to standardise selected aspects of patient care. The World Health Organisation (WHO) Surgical Safety Checklist is the most widely used surgical checklist, consisting of 19 items in three domains: before induction of anaesthesia, before surgical incision, and before the patient leaves the operating theatre. Actions include checks for a variety of items including patient identity, introducing all team members, and antibiotic prophylaxis.[10] Since it's inception, the checklist has been adopted in more than 4000 hospitals worldwide,[11] and is now considered a surrogate marker for quality of patient care.[12] However, there is only limited evidence of any effect of checklist use on health outcomes.[12] A previous meta-analysis reported insufficient high-quality evidence to draw robust conclusions, but there have been further studies since this publication.[12,13] Meanwhile, the clinical effectiveness of the surgical safety checklist remains unclear and some clinicians object to its use.[14,15]

In the recent International Surgical Outcomes Study (ISOS) we collected prospective data describing surgical safety checklist use, along with patient outcomes following elective in-patient surgery in 27 countries.[6] Given the apparent widespread and growing use of the surgical safety checklist and the need for further evidence, we performed a prospective analysis of the effects of checklist exposure on postoperative patient outcomes. To contextualise the results of this analysis and to describe the current evidence for this intervention, we included these findings in a systematic review and meta-analysis of the published literature.

Methods

This was a pre-planned secondary analysis of prospectively collected data as part of ISOS. To complement this we conducted a systematic review of the existing literature and a meta-analysis, in which we included the results of ISOS analysis.

ISOS analysis: design, setting and participants

ISOS was a seven-day international cohort study, the main results of which have been reported previously.[6] In the UK, the study was approved by the Yorkshire & Humber Research Ethics Committee (Reference: 13/YH/0371). In other countries, regulatory requirements varied with some requiring research ethics approval and some requiring only data governance approval. The inclusion criteria were all adult patients (age ≥18 years) undergoing elective surgery with a planned overnight stay in hospital. Each participating country selected a single data collection week between April and August 2014. Patients undergoing emergency surgery, day-case surgery or radiological procedures were excluded. During the one-week study period, data were collected for consecutive patients until hospital discharge, using standardised paper case record forms. Data included baseline demographic information, details of the surgical procedure, postoperative care and in-hospital postoperative clinical outcomes. The use of the surgical safety checklist was collected by study investigators at each site as part of the core dataset. Data were censored at 30 days following surgery for patients who remained in hospital. Data were anonymised and entered onto a purpose-built secure internet database, which included automated checks for plausibility, consistency and completeness.

ISOS analysis: outcome measures

The primary outcome measure for the analysis of the ISOS cohort was in-hospital mortality. The secondary outcome measure was the presence of any postoperative in-hospital complication assessed according to predefined criteria.[6,16] A patient with any of the following complications was deemed to have met the secondary outcome: surgical site infection, body cavity infection, pneumonia, urinary tract infection, blood stream infection, myocardial infarction, arrhythmia, pulmonary oedema, pulmonary embolism, stroke, cardiac arrest, gastro-intestinal bleed, acute kidney injury, postoperative bleed, acute respiratory distress syndrome (ARDS), anastomotic leak or other un-categorised complications. The severity of complications was graded as mild, moderate or severe.[16]

ISOS analysis: statistical methods

Data were included for hospitals returning valid data for ≥20 participants, and countries with at least ten participating hospitals. We dichotomised the sample according to the presence or absence of surgical safety checklist use and presented baseline demographic and clinical characteristics. The outcomes were considered as binary categorical variables. In the primary analysis, we assessed for associations between exposure to a surgical safety checklist and postoperative mortality, compared to no exposure to a surgical safety checklist, before and after adjustment for potential confounding factors. For the adjusted analysis, we used a hierarchical two-level generalised linear model, with patients at the first level and hospitals at the second level; a three-level model with countries at the third level did not converge. We included the following pre-specified covariates to adjust for potential confounding: age, gender, current smoker, American Society of Anesthesiologists (ASA) physical status score, grade of surgery, surgical procedure category, and presence of co-morbid disease (coronary artery disease, heart failure, diabetes mellitus, chronic obstructive pulmonary disease/asthma, cirrhosis, metastatic cancer, stroke and other unspecified chronic disease). These covariates were selected for clinical plausibility and evidence of association with the exposure or outcomes in previous epidemiological research.[4,17-19] The results are presented as odds ratios (OR) with 95% confidence intervals (CI) and associated Wald p-values. The primary analysis was repeated for in-hospital complications as the secondary outcome measure, considered as a binary categorical variable using a three-level generalised linear model, with patients at the first level, hospitals at the second and countries at the third level. Normally distributed continuous variables are presented as mean with standard deviation (SD), non-normally distributed continuous variables are presented as median with interquartile range (IQR), and proportions are presented as n (%). We used STATA version 14 (StataCorp LP, College Station, USA) for the statistical analysis.

ISOS analysis: sensitivity analyses

We were interested to assess whether countries with high checklist usage, as a proportion of the total number of patients (i.e. checklist compliance), were more likely to have lower risk of in-hospital mortality or postoperative complications. We calculated checklist compliance by country as the proportion of patients in each country that were exposed to the checklist. We ranked countries by compliance and divided the sample into four similarly sized quartiles, with quartile one representing lowest compliance and quartile four representing highest compliance. We repeated the primary analysis using quartiles of checklist compliance as the exposure of interest, using a deviation contrast where the mean compliance for the whole cohort was treated as the reference category. Secondly, to identify whether a relationship between checklist use and postoperative complications or mortality differed according to income status of the country of origin, we stratified the sample by country income status (high income or low and middle income), according to the World Bank definition and repeated the analysis.[20]

Evidence synthesis: systematic review and meta-analysis

We undertook a systematic review and meta-analysis of the published literature describing the effects of surgical safety checklist use on patient outcomes, including the results of the ISOS study. We prospectively registered the systematic review with PROSPERO (2016:CRD42016039878). The primary outcome was mortality, which we expected to be the most frequently reported outcome measure. The secondary outcome was postoperative complications. Definitions of complications for included studies are presented in Supplementary table 1. We searched MEDLINE, The Cochrane

Library, EMBASE and CINAHL for the years 2009 to 2017 using Healthcare Database Advanced Search (hdas.nice.org.uk). We scanned the bibliographies of included studies and consulted experts to identify studies that were missed by the search. Full details of the search strategy are provided in supplementary table 2. We extracted records to Mendeley (London, UK) to sort and remove duplicates. Two investigators (MP and AF) independently reviewed each record by title and abstract. Papers identified as potentially relevant were reviewed in full. Papers were selected for inclusion if they described the use of the WHO Surgical Safety Checklist in adult patients (>18 years) undergoing surgery, and reported either complications or mortality as postoperative outcomes. We did not include studies where the surgical safety checklist was tested with another intervention or where the checklist was modified.[21] Differences in opinion were resolved through discussion and referred to a third investigator (MG). Data were extracted from the selected papers by two independent investigators (MP and AF) to a pre-formatted Excel worksheet (Microsoft, Redmond, USA). The meta-analysis was conducted using Review Manager version 5.3 (Cochrane Collaboration, Copenhagen, Denmark). Risk of bias was assessed using the Cochrane tool for randomised controlled trials, the National Institutes of Health 'Quality Assessment of Before-and-after studies' tool for before and after studies, and the Newcastle Ottawa Scale for other non-randomised studies.[22-24] Between study heterogeneity was assessed with Chi-squared and I^2 tests using $p<0.1$ as the pre-defined threshold for statistical significance. A random effects model was used for all analyses. Results are presented as OR with 95% CI, associated p-values, and forest plots.

Results

Surgical safety checklist use in the ISOS cohort

We included 44,814 ISOS participants from 497 hospitals in 27 countries in this analysis (Supplementary figure 1). Eight countries, with 134 participating hospitals, were classed as low or middle income nations.[20] Participating hospitals had a median of 550 (329-850) beds and 21 (10-38) critical care unit beds. 40,245/44,814 (89.8%) patients were exposed to the surgical safety checklist, 7508/44,814 (16.8%) sustained at least one postoperative complication and 207/44,814 (0.5%) died before hospital discharge (Table 1). The results of regression models for surgical safety checklist exposure against postoperative mortality or complications in the ISOS cohort are shown in Table 2. In the unadjusted analysis, exposure to the surgical safety checklist was associated with a reduction in mortality (OR 0.42 [0.33-0.58]; p<0.01), which remained statistically significant after adjustment for confounding (OR 0.49 [0.32-0.77]; p<0.01). Exposure to the checklist was not associated with a reduction in the incidence of postoperative complications in either the unadjusted (OR 0.99 [0.91-1.07]; p=0.74) or the adjusted analyses (OR 1.02 [0.88-1.19]; p=0.75).

Sensitivity analyses of the ISOS cohort

When countries were ranked by compliance with the checklist, the mean compliance in the lowest and highest quartiles were 62.5% and 98.7% respectively (Supplementary table 3). Low checklist use at a national level (quartile 1) was associated with increased mortality (OR 1.80 [1.34-2.41]; p<0.01) and high checklist use at a national level (quartile 4) was associated with reduced mortality (OR 0.61 [0.45-0.83]; p<0.01) (Table 3), with the whole cohort as the reference category. National rates of checklist use (quartile 1 and 4) were not associated with any effects on postoperative complication rates. When we stratified the sample by income status of the participating country and repeated the primary analysis, the findings remained similar (Supplementary tables 4 and 5). To further explore the absence of association between checklist use and reduced incidence of postoperative complications, we conducted a post-hoc sensitivity analysis to see if checklist use was associated with reductions in the incidences of specific severities of complications (either mild or moderate or severe). However, we did not identify any such associations (supplementary table 6).

Systematic review and meta-analysis

Searches identified 3,732 records. After removal of duplicates, 3,554 abstracts were screened, 41 full-texts were reviewed and 11 studies (including ISOS) were selected for inclusion (Supplementary figure 2). Five studies included in previous systematic reviews were excluded because they did not meet our inclusion criteria.[12,13] A summary of the articles included is provided in Table 4. A total of 419,799 patients were included in the meta-analysis for mortality. 2624/230,929 (1.1%) of patients exposed to the checklist died, compared to 2466/188,870 (1.3%) not exposed to the checklist. In the random effects meta-analysis, checklist exposure was associated with reduced mortality (OR 0.75 [0.62-0.92]; $p<0.01$; I^2=87%) (Figure 1). The definition of mortality was 'in-hospital' in two studies, in-hospital restricted to 30 days in five studies, and in-hospital restricted to 60 days in one study. In contrast, 12,054/161,858 (7.4%) of patients exposed to the checklist developed postoperative complications, compared to 6,043/123,329 (4.9%) of patients not exposed to the checklist. In the random effects meta-analysis, checklist exposure was associated with a reduced incidence of post-operative complications (OR 0.73 [0.61-0.88]; $p<0.01$; I^2=89%) (Figure 2). The meta-analysis is weighted according to effect size and the two biggest studies, which account for 38.2% of patients showed no difference in complication rates between exposed and unexposed patients.

The risk of bias was low in all included studies (Supplementary table 7) and visual assessment of funnel plots demonstrated no evidence of publication bias. Compliance with checklist use was variable across studies with no pattern of changing use over time (Supplementary table 8). To account for the possibility that some studies in the meta-analysis included patients exposed to a modified checklist, we repeated the meta-analysis including five studies of modified surgical safety checklists that were excluded from the primary meta-analysis.[25-29] Our findings remained similar for both mortality (OR 0.77 [0.64-0.91]; $p<0.01$; $I^2=83\%$) and complications (OR 0.71 [0.60-0.84]; $p <0.01$, $I^2=92\%$).

Discussion

The principal finding of this research was that patients exposed to a surgical safety checklist had a lower incidence of postoperative complications and death when compared to patients who were not exposed to a checklist. These findings may reflect a higher quality of care in hospitals where checklist use is routine. While the data included in the meta-analyses are primarily observational, this study adds to the overall understanding of the surgical safety checklist, indicating that checklists are widely used internationally, but that in most healthcare settings it is not possible to randomise patients to checklist use because of existing widespread implementation. Therefore, in the absence of data from randomised trials, our analyses may represent the highest currently attainable level of evidence describing the effects of surgical safety checklist use. Future randomised trials may not be possible, but further research should be standardised for individual compliance with the checklist. The findings of the ISOS analysis, where checklist exposure was associated with reduced mortality but not complications, contrasted with the results of the meta-analysis. This is counterintuitive, but not uncommon among meta-analyses, where the results of an individual study may contrast with the overall weighted effect. The results of this meta-analysis suggest that across a range of studies at many hospitals, checklist use is associated with fewer postoperative complications and deaths. However, it is unlikely that it will ever be possible to prove the causality of improved patient outcomes associated with checklist use.

Previous studies in mostly high-income countries have demonstrated associations between checklist use and reduced morbidity and mortality. The European Surgical Outcomes Study, conducted in 426 European hospitals, suggested that checklist exposure was associated with a 19% reduction in the relative risk of in-hospital mortality, while a single centre retrospective cohort study in Chile identified a 27% reduction in mortality.[14,30] However, there is less evidence to support checklist use in low or middle-income countries.[28] Our analysis of the International Surgical Outcomes study is the largest study of which we are aware, to include data from both low-, middle-/high-income countries. Our results are therefore more widely generalisable and indicate a need for research and quality improvement to ensure safe and effective patient care in low- and middle-income countries. Examples may include rapid response systems and early warning scores.[31-33] The largest study to evaluate the surgical safety checklist to date was a cohort study of an implementation project performed in acute care hospitals in Canada.[34] In contrast to our results, the authors did not identify any benefit associated with checklist use, when comparing the three months before and after implementation in more than 200,000 patients. This may be due in part to pre-existing high-quality care at these hospitals. We included this study in our meta-analysis, which may explain, in part, the smaller effect estimates than observed in a previous systematic review.[12] Similarly, the findings of the ISOS analysis contrast with the results of our meta-analysis, which identified a reduction in postoperative complications associated with checklist exposure. This might be explained by the high compliance with checklist use in the ISOS cohort (nine out of ten patients), making it harder to detect a difference in outcomes between exposed and non-exposed patients. Alternatively, it may be due to bias or heterogeneity between studies included in the meta-analysis (supplementary table 6).

This work has several strengths. This was a prospective analysis of the ISOS cohort and a prospective meta-analysis. ISOS is one of the largest prospective international cohort studies of surgical outcomes conducted to date, and in contrast to many other studies, includes data from low, middle and high-income countries.[6] Due to the large number of patients enrolled, we were able to adjust the analysis for a variety of potential confounding factors. Although, as with any epidemiological study, we must acknowledge the potential influence of unmeasured confounding. The meta-analysis included more than ten times as many patients as the previous largest evidence synthesis, and the risk of bias was lower than in previous work.[12,13] Our study also has several weaknesses. The ISOS investigators hoped to include a mix of hospitals from each country. However, it is impossible to say whether the results are representative of practice in any one country. This is particularly pertinent to low- and middle-income countries, where there was a bias towards university hospitals and away from smaller district hospitals. In general, we would expect hospitals that participate in research to offer a better standard of care, since research active hospitals tend to have superior clinical outcomes.[35] There is likely to be heterogeneity of surgical and perioperative care and administrative procedures across hospitals included in the ISOS study, which may influence the results. For example, hospitals in some countries may discharge patients at an earlier stage of the postoperative pathway than others, which may influence the rates of recorded in-hospital complications. This is further illustrated by the variation in compliance with the checklist at a country level, where three quarters of countries used the checklist in >89% of cases, in contrast to wide variation in checklist use among countries in the lowest quartile (27-85%). However, checklist compliance – similar to the heterogeneity of surgical care within and between countries - is unlikely to be uniform across countries and the ISOS sample may not be representative of country-wide practice. Furthermore we did collect data on individual components of the checklist, so it is possible that some sections were completed more frequently than others. The meta-analysis did not include studies of staff training on the use of the surgical safety checklist and we did not differentiate between different types of complications in the analysis. The literature describing the checklist describes a variety of methodologies including randomised trials, prospective and retrospective cohort studies, implementation studies and natural trials. We performed a wide-ranging systematic review and meta-analysis to reflect the breadth of available knowledge. However, while we were able to increase the precision of our effect size estimates compared to previous studies, the population samples of included studies may be quite different, and this is reflected in the between study heterogeneity. An alternative approach is to undertake a meta-analysis based on one methodology only, for example randomised trials. This approach has been helpful, but is limited by the number of available studies and therefore patients.[13] Given the inclusion of three large studies in the meta-analysis, there is the potential that the results may be skewed towards findings of these studies. We were unable to adjust for potential improvements in perioperative care over time or differences in compliance with the checklist between or within included studies.[1,36,37] While several studies have reported compliance rates greater than 90%, the findings of the included studies do not suggest any trend to improved adoption of the checklist over time.

Conclusions

The World Health Organisation and similar surgical safety checklists are simple tools, designed to improve the safety and quality of perioperative care. We have provided evidence that patients exposed to a surgical safety checklist experience better postoperative outcomes. However, it remains uncertain whether these associations are a direct causal effect, or if this simply reflects wider quality of care in hospitals where checklist use is routine.

Conflict of interest statement

RP holds research grants, and has given lectures and/or performed consultancy work for Nestle Health Sciences, BBraun, Medtronic, Glaxo Smithkline and Edwards Lifesciences, and is a member of the Associate editorial board of the British Journal of Anaesthesia. MSC has received unrestricted research grants, and has given lectures and/or performed consultancy work for Thermofisher Scientific, Pulsion Medical Systems and Edwards Lifesciences, and is a member of the Associate editorial board of the European Journal of Anaesthesiology. All other authors declare they have no conflicts of interest.

Contributors

TEFA and RP conceived the analysis. TEFA, TA, AF, MG and RP drafted the analysis plan. Patient recruitment and data collection were performed by the members of the ISOS study group (see supplementary file). TA analysed the ISOS data with input from TEFA. AF and MP performed the systematic review with input from MG. AF performed the meta-analysis with input from TEFA and MG. TEFA, AF and RP drafted the manuscript which was revised following critical review by all authors.

Acknowledgements

The ISOS study was funded through an unrestricted research grant from Nestle Health Sciences. TEFA is supported by a Medical Research Council/British Journal of Anaesthesia clinical research training fellowship. BB is funded by a National Research Foundation rating grant and an MRC(SA) self-initiated research grant. MG is a Chief Scientist Office (Scotland) NHS Research Scheme Clinician. RP is a UK National Institute for Health Research Professor.

References

1. Weiser TG, Haynes AB, Molina G, et al. Estimate of the global volume of surgery in 2012: an assessment supporting improved health outcomes. Lancet 2015;385 Suppl 2:S11.
2. Kable AK, Gibberd RW, Spigelman AD. Adverse events in surgical patients in Australia. International journal for quality in health care : journal of the International Society for Quality in Health Care / ISQua 2002;14:269-76.
3. Mullen R, Scollay JM, Hecht G, McPhillips G, Thompson AM. Death within 48 h--adverse events after general surgical procedures. The surgeon : journal of the Royal Colleges of Surgeons of Edinburgh and Ireland 2012;10:1-5.
4. Pearse RM, Moreno RP, Bauer P, et al. Mortality after surgery in Europe: a 7 day cohort study. Lancet 2012;380:1059-65.
5. Weiser TG, Regenbogen SE, Thompson KD, et al. An estimation of the global volume of surgery: a modelling strategy based on available data. Lancet 2008;372:139-44.
6. International Surgical Outcomes Study g. Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle- and high-income countries. British journal of anaesthesia 2016;117:601-9.
7. Panesar SS, Cleary K, Sheikh A, Donaldson L. The WHO checklist: a global tool to prevent errors in surgery. Patient safety in surgery 2009;3:9.
8. Gawande AA, Thomas EJ, Zinner MJ, Brennan TA. The incidence and nature of surgical adverse events in Colorado and Utah in 1992. Surgery 1999;126:66-75.
9. NHS errors costing billions a year - Jeremy Hunt. 2014. (Accessed 9th May 2017, 2017, at http://www.bbc.co.uk/news/uk-29639383.)
10. WHO Surgical Safety Checklist. 2008. (Accessed 9th May 2017, 2017, at http://www.who.int/patientsafety/safesurgery/checklist/en/.)
11. Putnam LR, Levy SM, Sajid M, et al. Multifaceted interventions improve adherence to the surgical checklist. Surgery 2014;156:336-44.
12. Bergs J, Hellings J, Cleemput I, et al. Systematic review and meta-analysis of the effect of the World Health Organization surgical safety checklist on postoperative complications. The British journal of surgery 2014;101:150-8.
13. Biccard BM, Rodseth R, Cronje L, et al. A meta-analysis of the efficacy of preoperative surgical safety checklists to improve perioperative outcomes. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde 2016;106.
14. Jammer I, Ahmad T, Aldecoa C, et al. Point prevalence of surgical checklist use in Europe: relationship with hospital mortality. British journal of anaesthesia 2015;114:801-7.
15. Vats A, Vincent CA, Nagpal K, Davies RW, Darzi A, Moorthy K. Practical challenges of introducing WHO surgical checklist: UK pilot experience. Bmj 2010;340:b5433.
16. Jammer I, Wickboldt N, Sander M, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: A statement from the ESA-ESICM joint taskforce on perioperative outcome measures. European journal of anaesthesiology 2014.
17. Abbott TE, Ackland GL, Archbold RA, et al. Preoperative heart rate and myocardial injury after non-cardiac surgery: results of a predefined secondary analysis of the VISION study. British journal of anaesthesia 2016;117:172-81.
18. Abbott TEF, Minto G, Lee A, Pearse RM, Ackland GL. Elevated preoperative heart rate is associated with cardiopulmonary and autonomic impairment in high-risk surgical patients. British journal of anaesthesia 2017.
19. Ackland GL, Abbott TEF, Pearse RM, Karmali S, Whittle J. Pulse pressure and postoperative morbidity in high-risk surgical patients. British journal of anaesthesia 2017.

20. World Bank Country and Lending Groups. 2017. (Accessed 09/02/2017, 2017, at https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups.)
21. Kwok AC, Funk LM, Baltaga R, et al. Implementation of the World Health Organization surgical safety checklist, including introduction of pulse oximetry, in a resource-limited setting. Annals of surgery 2013;257:633-9.
22. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. Bmj 2011;343:d5928.
23. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. European journal of epidemiology 2010;25:603-5.
24. NIH - Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group. 2017. (Accessed 02/05/2017, 2017, at https://http://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/before-after))
25. Biskup N, Workman AD, Kutzner E, Adetayo OA, Gupta SC. Perioperative Safety in Plastic Surgery: Is the World Health Organization Checklist Useful in a Broad Practice? Annals of plastic surgery 2016;76:550-5.
26. Boaz M, Bermant A, Ezri T, et al. Effect of Surgical Safety checklist implementation on the occurrence of postoperative complications in orthopedic patients. The Israel Medical Association journal : IMAJ 2014;16:20-5.
27. Bock M, Fanolla A, Segur-Cabanac I, et al. A Comparative Effectiveness Analysis of the Implementation of Surgical Safety Checklists in a Tertiary Care Hospital. JAMA surgery 2016;151:639-46.
28. Chaudhary N, Varma V, Kapoor S, Mehta N, Kumaran V, Nundy S. Implementation of a surgical safety checklist and postoperative outcomes: a prospective randomized controlled study. Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract 2015;19:935-42.
29. Haugen AS, Softeland E, Almeland SK, et al. Effect of the World Health Organization checklist on patient outcomes: a stepped wedge cluster randomized controlled trial. Annals of surgery 2015;261:821-8.
30. Lacassie HJ, Ferdinand C, Guzman S, Camus L, Echevarria GC. World Health Organization (WHO) surgical safety checklist implementation and its impact on perioperative morbidity and mortality in an academic medical center in Chile. Medicine 2016;95:e3844.
31. Abbott TE, Torrance HD, Cron N, Vaid N, Emmanuel J. A single-centre cohort study of National Early Warning Score (NEWS) and near patient testing in acute medical admissions. European journal of internal medicine 2016;35:78-82.
32. Abbott TE, Vaid N, Ip D, et al. A single-centre observational cohort study of admission National Early Warning Score (NEWS). Resuscitation 2015;92:89-93.
33. McGinley A, Pearse RM. A national early warning score for acutely ill patients. Bmj 2012;345:e5310.
34. Urbach DR, Govindarajan A, Saskin R, Wilton AS, Baxter NN. Introduction of surgical safety checklists in Ontario, Canada. The New England journal of medicine 2014;370:1029-38.
35. Ozdemir BA, Karthikesalingam A, Sinha S, et al. Research activity and the association with mortality. PloS one 2015;10:e0118253.
36. Abbott TEF, Fowler AJ, Dobbs T, et al. Frequency of surgical treatment and related hospital procedures in the United Kingdom: A national ecological study using hospital episode statistics. British journal of anaesthesia 2017.
37. Kahan BC, Koulenti D, Arvaniti K, et al. Critical care admission following elective surgery was not associated with survival benefit: prospective analysis of data from 27 countries. Intensive care medicine 2017.

38. Askarian M, Kouchak F, Palenik CJ. Effect of surgical safety checklists on postoperative morbidity and mortality rates, Shiraz, Faghihy Hospital, a 1-year study. Quality management in health care 2011;20:293-7.
39. Bliss LA, Ross-Richardson CB, Sanzari LJ, et al. Thirty-day outcomes support implementation of a surgical safety checklist. Journal of the American College of Surgeons 2012;215:766-76.
40. Haynes AB, Weiser TG, Berry WR, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. The New England journal of medicine 2009;360:491-9.
41. Lepanluoma M, Rahi M, Takala R, Loyttyniemi E, Ikonen TS. Analysis of neurosurgical reoperations: use of a surgical checklist and reduction of infection-related and preventable complication-related reoperations. J Neurosurg 2015;123:145-52.
42. Lubbeke A, Hovaguimian F, Wickboldt N, et al. Effectiveness of the surgical safety checklist in a high standard care environment. Medical care 2013;51:425-9.
43. Mayer EK, Sevdalis N, Rout S, et al. Surgical Checklist Implementation Project: The Impact of Variable WHO Checklist Compliance on Risk-adjusted Clinical Outcomes After National Implementation: A Longitudinal Study. Annals of surgery 2016;263:58-63.
44. van Klei WA, Hoff RG, van Aarnhem EE, et al. Effects of the introduction of the WHO "Surgical Safety Checklist" on in-hospital mortality: a cohort study. Annals of surgery 2012;255:44-9.

Figures

Study or Subgroup	Exposed to checklist Events	Exposed to checklist Total	Not exposed to checklist Events	Not exposed to checklist Total	Weight	Odds Ratio M-H, Random, 95% CI
Mayer 2016	56	6494	3	220	2.5%	0.63 [0.20, 2.03]
Lubbeke 2013	108	1818	26	609	9.6%	1.42 [0.91, 2.20]
Haynes 2009	32	3955	56	3733	9.6%	0.54 [0.35, 0.83]
International Surgical Outcomes Study	163	40245	44	4538	11.9%	0.42 [0.30, 0.58]
Lacassie 2016	186	29858	333	40781	15.7%	0.76 [0.64, 0.91]
van Klei 2012	318	11151	450	14362	16.4%	0.91 [0.78, 1.05]
Urbach 2014	702	106370	765	109341	17.2%	0.94 [0.85, 1.04]
Jammer 2015	1059	31038	789	15286	17.3%	0.65 [0.59, 0.71]
Total (95% CI)		**230929**		**188870**	**100.0%**	**0.75 [0.62, 0.92]**
Total events	2624		2466			

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 55.70$, df = 7 ($P < 0.00001$); $I^2 = 87\%$
Test for overall effect: Z = 2.83 (P = 0.005)

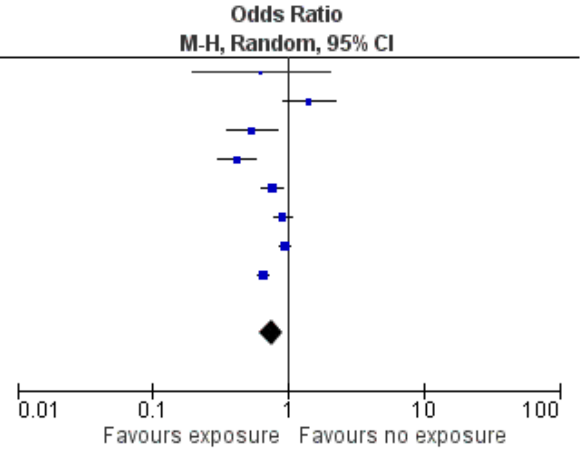

Figure 1. Forest plot for meta-analysis of exposure to surgical safety checklist and relative risk of postoperative mortality.

Study or Subgroup	Exposed to checklist Events	Exposed to checklist Total	Not exposed to checklist Events	Not exposed to checklist Total	Weight	Odds Ratio M-H, Random, 95% CI
Bliss 2012	6	73	491	2079	3.9%	0.29 [0.12, 0.67]
Askarian 2011	15	150	33	144	5.6%	0.37 [0.19, 0.72]
Mayer 2016	724	6494	37	220	11.2%	0.62 [0.43, 0.89]
Lubbeke 2013	109	1818	45	609	11.2%	0.80 [0.56, 1.15]
Lepanluoma 2015	72	2753	103	2665	12.8%	0.67 [0.49, 0.91]
Haynes 2009	277	3955	411	3733	17.1%	0.61 [0.52, 0.71]
International Surgical Outcomes Study	6734	40245	768	4538	18.8%	0.99 [0.91, 1.07]
Urbach 2014	4117	106370	4155	109341	19.4%	1.02 [0.98, 1.07]
Total (95% CI)		**161858**		**123329**	**100.0%**	**0.73 [0.61, 0.88]**
Total events	12054		6043			

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 66.45$, df = 7 (P < 0.00001); $I^2 = 89\%$
Test for overall effect: Z = 3.36 (P = 0.0008)

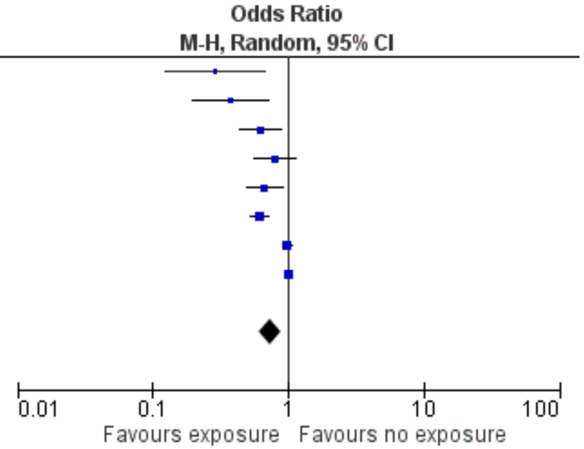

Figure 2. Forest plot for meta-analysis of exposure to surgical safety checklist and relative risk of postoperative complications.

Table 1. Baseline patient characteristics of patients included in the analysis of the prospective observational cohort (International Surgical Outcomes Study).

Data presented as n (%) for categorical variables and as mean with standard deviation (sd) or median with interquartile range (IQR) for continuous variables. ASA, American Society of Anesthesiologists physical status score; COPD, chronic obstructive pulmonary disease. Univariable association with exposure to surgical safety checklist presented as odds ratios (OR) with 95% confidence interval (95% CI) and p-value.

	Number of patients (%)	Checklist use (%)	Did not use checklist (%)	OR (95% CI)	P value
	n = 44814	n = 40245	n = 4538	-	-
Age, Median (IQR)	57 (43 - 69)	57 (43 - 69)	56 (41 - 68)	1.04 (0.87 - 1.23)	0.70
Male, n(%)	20 458 (45.7)	18 317 (45.5)	2 125 (46.8)	0.95 (0.89 - 1.01)	0.13
Females, n(%)	24 351 (54.3)	21 927 (54.5)	2 413 (53.2)	1.05 (0.98 - 1.13)	0.13
Present smoker, n(%)	7 931 (17.8)	6 942 (17.3)	965 (12.2)	1.04 (0.89 - 1.22)	0.64
ASA Score n (%)					
I	11 227 (25.1)	9 973 (24.8)	1 246 (27.5)	0.97 (0.81 - 1.16)	0.72
II	22 265 (49.8)	20 300 (50.5)	1 956 (43.2)	1.08 (0.94 - 1.24)	0.28
III	10 193 (22.8)	8 991 (22.4)	1 194 (26.4)	1.06 (0.92 - 1.23)	0.41
IV	1 038 (2.3)	908 (2.3)	130 (2.9)	0.90 (0.66 - 1.23)	0.51
Grade of surgery, n (%)					
Minor	8 411 (18.8)	7 448 (18.5)	960 (21.2)	0.69 (0.63 - 0.77)	<0.01
Intermediate	20 203 (45.1)	18 051 (44.9)	2 137 (47.1)	0.93 (0.86 - 1.01)	0.11
Major	16 175 (36.1)	14 732 (36.6)	1 438 (31.7)	1.54 (1.39 - 1.72)	<0.01
Surgical Specialty, n (%)					
Orthopaedic	9 459 (21.1)	8 683 (21.6)	771 (17.0)	1.18 (1.01 - 1.39)	0.04
Breast	1 538 (3.4)	1 393 (3.5)	145 (3.2)	0.86 (0.63 - 1.18)	0.34
Obstetrics & Gynaecology	5 674 (12.7)	5 123 (12.7)	547 (12.1)	0.92 (0.75 - 1.12)	0.40
Urology & Kidney	4 871 (10.9)	4 299 (10.7)	570 (12.6)	0.92 (0.76 - 1.11)	0.37
Upper Gastrointestinal	1 986 (4.4)	1 776 (4.4)	208 (4.6)	1.31 (0.99 - 1.73)	0.06
Lower Gastrointestinal	3 073 (6.9)	2 711 (6.7)	360 (7.9)	1.06 (0.84 - 1.33)	0.63
Hepato-biliary	2 282 (5.1)	1 959 (4.9)	322 (7.1)	1.18 (0.91 - 1.53)	0.22
Vascular	1 599 (3.6)	1 436 (3.6)	161 (3.6)	1.17 (0.85 - 1.61)	0.32

Head and neck	6 510 (14.5)	5 913 (14.7)	592 (13.1)	0.88 (0.74 - 1.03)	0.11
Plastic or cutaneous	1 670 (3.7)	1 386 (3.5)	284 (6.3)	1.01 (0.78 - 1.31)	0.94
Cardiac	1 716 (3.8)	1 557 (3.9)	159 (3.5)	0.54 (0.39 - 0.75)	<0.01
Thoracic (lung & other)	1 157 (2.6)	1 086 (2.7)	69 (1.5)	1.44 (0.95 - 2.18)	0.08
Other	3 270 (7.3)	2 919 (7.3)	350 (7.7)	0.88 (0.72 - 1.09)	0.24
Laparoscopic Surgery, n(%)	7 087 (15.8)	6 472 (16.1)	610 (13.5)	1.37 (1.10 - 1.69)	<0.01
Comorbid Disorder, n(%)					
Coronary artery disease	4 588 (10.3)	3 952 (9.8)	632 (14.0)	1.17 (0.94 - 1.46)	0.16
Heart Failure	1 882 (4.2)	1 594 (4.0)	287 (6.3)	0.93 (0.70 - 1.25)	0.65
Diabetes Mellitus	5 171 (11.6)	4 596 (11.4)	571 (12.6)	0.85 (0.70 - 1.03)	0.10
Cirrhosis	342 (0.8)	311 (0.8)	31 (0.7)	1.15 (0.56 - 2.37)	0.70
Metastatic cancer	1 706 (3.8)	1 547 (3.9)	159 (3.5)	0.90 (0.67 - 1.21)	0.48
Stroke	1 492 (3.3)	1 333 (3.3)	158 (3.5)	1.00 (0.72 - 1.39)	0.99
COPD	4 094 (9.2)	3 790 (9.4)	303 (6.7)	1.07 (0.85 - 1.35)	0.55
Other	3269 (7.3)	16 552 (41.2)	2 042 (45.1)	1.00 (0.87 - 1.16)	0.95
Had a complication	7 508 (16.8)	6 734 (16.7)	768 (16.9)	1.04 (0.87 - 1.23)	0.70
In-hospital mortality	207 (0.5)	163 (0.4)	44 (1.0)	0.79 (0.36 - 1.73)	0.55

Table 2. Results of the primary and secondary analysis of the prospective ISOS cohort.

Summary of two separate statistical models, where the dependent variables were either mortality or any postoperative complication (excluding mortality). Generalised linear models, with results presented as odds ratios with 95% confidence intervals and p-values. All variables were binary categorical unless otherwise stated, where exposure to a variable was compared to non-exposure. ASA score and grade of surgery categorical variables where the reference was the average effect across the whole cohort. COPD, Chronic Obstructive Pulmonary Disease; ASA, American Society of Anesthesiologists.

	Any complication	p-value	Mortality	p-value
Age (years)	1.01 (1.00 - 1.01)	<0.01	1.03 (1.02 - 1.04)	<0.01
Male	1.05 (1.02 - 1.08)	<0.01	1.03 (0.89 - 1.21)	0.67
Female	0.95 (0.93 - 0.98)	<0.01	0.97 (0.83 - 1.13)	0.67
Present smoker	0.99 (0.92 - 1.07)	0.84	1.61 (1.12 - 2.31)	0.01
ASA Score				
I	0.54 (0.49 - 0.58)	<0.01	0.09 (0.02 - 0.39)	<0.01
II	0.71 (0.67 - 0.75)	<0.01	0.69 (0.39 - 1.22)	0.20
III	1.21 (1.14 - 1.29)	<0.01	2.20 (1.29 - 3.76)	<0.01
IV	2.17 (1.92 - 2.46)	<0.01	7.54 (4.18 - 13.63)	<0.01
Grade of surgery				
Minor	0.52 (0.49 - 0.56)	<0.01	0.63 (0.43 - 0.93)	0.02
Intermediate	0.91 (0.87 - 0.96)	<0.01	0.92 (0.71 - 1.21)	0.55
Major	2.10 (2.00 - 2.20)	<0.01	1.72 (1.34 - 2.22)	<0.01
Surgical Specialty				
Orthopaedic	0.89 (0.83 - 0.96)	<0.01	0.64 (0.41 - 0.98)	0.04
Breast	0.59 (0.49 - 0.70)	<0.01	0.65 (0.17 - 2.42)	0.52
Obstetrics & Gynaecology	0.77 (0.69 - 0.85)	<0.01	0.80 (0.36 - 1.76)	0.57
Urology & Kidney	0.83 (0.76 - 0.91)	<0.01	0.48 (0.26 - 0.89)	0.02
Upper Gastrointestinal	1.37 (1.23 - 1.53)	<0.01	2.79 (1.85 - 4.22)	<0.01
Lower Gastrointestinal	1.48 (1.34 - 1.62)	<0.01	1.90 (1.27 - 2.84)	<0.01
Hepato-biliary	0.97 (0.86 - 1.10)	0.67	1.61 (0.93 - 2.78)	0.09
Vascular	1.05 (0.93 - 1.19)	0.42	0.96 (0.56 - 1.64)	0.87
Head and neck	0.67 (0.62 - 0.74)	<0.01	0.63 (0.36 - 1.11)	0.11
Plastic or cutaneous	1.01 (0.88 - 1.17)	0.85	0.94 (0.39 - 2.23)	0.88
Cardiac	2.49 (2.20 - 2.80)	<0.01	1.47 (0.95 - 2.28)	0.09
Thoracic (lung & other)	1.25 (1.08 - 1.45)	<0.01	1.19 (0.63 - 2.26)	0.59
Other	0.68 (0.60 - 0.77)	<0.01	0.76 (0.37 - 1.58)	0.46
Comorbid Disorder				
Coronary artery disease	1.04 (0.95 - 1.13)	0.44	0.99 (0.70 - 1.40)	0.96
Heart Failure	1.28 (1.13 - 1.44)	<0.01	1.59 (1.08 - 2.32)	0.02
Diabetes Mellitus	1.10 (1.01 - 1.19)	0.02	1.24 (0.89 - 1.73)	0.20
Cirrhosis	1.45 (1.11 - 1.88)	<0.01	2.77 (1.34 - 5.72)	<0.01
Metastatic cancer	1.45 (1.28 - 1.64)	<0.01	3.41 (2.25 - 5.19)	<0.01
Stroke	1.16 (1.01 - 1.32)	0.03	2.79 (1.88 - 4.14)	<0.01
COPD	1.13 (1.04 - 1.24)	<0.01	1.13 (0.78 - 1.64)	0.52
Other	1.23 (1.15 - 1.31)	<0.01	1.47 (1.07 - 2.01)	0.02
Exposure to checklist	1.02 (0.88 - 1.19)	0.75	0.49 (0.32 - 0.77)	<0.01

Table 3. Compliance with surgical safety checklist by country and postoperative outcomes.
Summary of two separate statistical models, where the dependent variables were either mortality or any postoperative complication (excluding mortality). Generalised linear models, with results presented as odds ratios with 95% confidence intervals and p-values. All variables were binary categorical unless otherwise stated, where exposure to the variable was compared to non-exposure. Checklist compliance, ASA score and grade of surgery categorical variables where the reference was the average effect across the whole cohort. COPD, Chronic Obstructive Pulmonary Disease; ASA, American Society of Anesthesiologists.

	Any complication	p-value	Mortality	P-value
Age (years)	1.01 (1.00 - 1.01)	<0.01	1.03 (1.02 - 1.05)	<0.01
Male	1.05 (1.02 - 1.08)	<0.01	1.05 (0.90 - 1.22)	0.58
Female	0.95 (0.93 - 0.98)	<0.01	0.96 (0.82 - 1.12)	0.58
Present smoker	0.99 (0.92 - 1.07)	0.84	1.58 (1.10 - 2.27)	0.01
ASA Score				
I	0.54 (0.49 - 0.58)	<0.01	0.09 (0.02 - 0.40)	<0.01
II	0.71 (0.67 - 0.75)	<0.01	0.72 (0.41 - 1.26)	0.25
III	1.21 (1.14 - 1.29)	<0.01	2.21 (1.29 - 3.78)	<0.01
IV	2.17 (1.92 - 2.46)	<0.01	7.02 (3.87 - 12.74)	<0.01
Grade of surgery				
Minor	0.52 (0.49 - 0.56)	<0.01	0.64 (0.43 - 0.94)	0.02
Intermediate	0.91 (0.87 - 0.96)	<0.01	0.91 (0.70 - 1.19)	0.5
Major	2.10 (2.00 - 2.20)	<0.01	1.72 (1.33 - 2.22)	<0.01
Surgical Specialty				
Orthopaedic	0.89 (0.83 - 0.96)	<0.01	0.65 (0.42 - 0.99)	0.05
Breast	0.59 (0.49 - 0.70)	<0.01	0.64 (0.17 - 2.40)	0.51
Obstetrics & Gynaecology	0.77 (0.69 - 0.85)	<0.01	0.83 (0.37 - 1.84)	0.65
Urology & Kidney	0.83 (0.76 - 0.91)	<0.01	0.49 (0.26 - 0.91)	0.02
Upper Gastrointestinal	1.37 (1.23 - 1.53)	<0.01	2.69 (1.78 - 4.08)	<0.01
Lower Gastrointestinal	1.48 (1.35 - 1.62)	<0.01	1.89 (1.26 - 2.83)	<0.01
Hepato-biliary	0.98 (0.86 - 1.10)	0.69	1.49 (0.86 - 2.58)	0.16
Vascular	1.05 (0.93 - 1.19)	0.45	0.97 (0.57 - 1.66)	0.92
Head and neck	0.67 (0.62 - 0.73)	<0.01	0.62 (0.35 - 1.10)	0.11
Plastic or cutaneous	1.01 (0.88 - 1.17)	0.88	0.95 (0.40 - 2.26)	0.91
Cardiac	2.49 (2.20 - 2.81)	<0.01	1.60 (1.03 - 2.49)	0.04
Thoracic (lung & other)	1.25 (1.08 - 1.45)	<0.01	1.15 (0.61 - 2.19)	0.66
Other	0.68 (0.60 - 0.77)	<0.01	0.74 (0.36 - 1.54)	0.43
Comorbid Disorder				
Coronary artery disease	1.03 (0.94 - 0.13)	0.48	0.98 (0.69 - 1.39)	0.91
Heart Failure	1.27 (1.13 - 1.44)	<0.01	1.47 (1.00 - 2.16)	0.05
Diabetes Mellitus	1.10 (1.01 - 1.19)	0.03	1.26 (0.90 - 1.75)	0.18
Cirrhosis	1.45 (1.11 - 1.88)	<0.01	2.72 (1.31 - 5.63)	<0.01
Metastatic cancer	1.45 (1.28 - 1.64)	<0.01	3.41 (2.24 - 5.19)	<0.01
Stroke	1.15 (1.01 - 1.32)	0.03	2.80 (1.88 - 4.16)	<0.01
COPD	1.13 (1.04 - 1.24)	<0.01	1.18 (0.81 - 1.72)	0.38
Other	1.22 (1.15 - 1.31)	<0.01	1.42 (1.03 - 1.94)	0.03
Checklist compliance				
Quartile 1 (low)	1.07 (0.94 - 1.23)	0.32	1.80 (1.34 - 2.41)	<0.01
Quartile 2 (medium)	1.17 (1.00 - 1.36)	0.04	1.02 (0.73 - 1.41)	0.93
Quartile 3 (high)	0.87 (0.75 - 1.02)	0.09	0.90 (0.61 - 1.32)	0.58
Quartile 4 (very high)	0.92 (0.81 - 1.03)	0.15	0.61 (0.45 - 0.83)	<0.01

Table 4. Characteristics of studies included in the systematic review and meta-analysis.
GS = General Surgery, PS = Plastic Surgery, GIS = Gastrointestinal Surgery, OS = Orthopaedic Surgery, NCS = Non-Cardiac Surgery, OS = Obstetric Surgery, US = Urologic Surgery, SSC = Surgical Safety Checklist.

Study reference	In prior review?	Multicentre	Study design	Population	Number of Patients		Outcomes	
					No checklist	Checklist	Mortality	Complications
Askarian M[38]	Y	N	Before/After	GS	144	150	NO	YES
Bliss A[39]	Y	N	Case/Control	GIS/Amputations	2079	73	NO	YES
Haynes B[40]	Y	Y	Before/After	NCS	3733	3955	YES	YES
Jammer I[14]	N	Y	Prospective Cohort	NCS	15286	31038	YES	NO
Lacassie J[30]	N	N	Retrospective Cohort	Any Surgery	40781	29858	YES	NO
Lepanuluoma[41]	N	N	Retrospective Cohort	Neurosurgery	2665	2753	NO	YES
Lubbeke A[42]	N	N	Before/After	GS, US, Day Surgery, elective	609	1818	YES	YES
Mayer EK[43]	N	Y	Longitudinal	GS, US, OS	220	6494	Yes	YES
Urbach R[34]	N	Y	Before/After	Any procedure	109341	106370	YES	YES
van Klei WA[44]	Y	N	Retrospective cohort	Non-day case surgery	14362	11151	YES	NO
ISOS Group	N	Y	Prospective Cohort	Inpatient, elective surgery	4538	40245	YES	YES