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Quality and Safety

QUALITY AND SAFETY

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

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Abstract

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 generalized 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. There were 40 245 (89.8%) patients 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 [odds ratio (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 a systematic review, we screened 3732 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.

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Key words: cohort studies; operative/mortality; postoperative care/methods; postoperative care/statistics and numerical data; surgery; surgical procedures

Editor's key points

- The surgical safety checklist is being promoted as an effective tool to enhance patient safety
- This study provides outcome data from a large and diverse collection of hospitals from around the world
- Surgical safety checklist use was associated with a lower incidence of postoperative mortality, but not of postoperative complications
- A pooled analysis of previous studies found that checklist use was associated with a lower incidence of both postoperative complications and death

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 approximately 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 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 £1 billion each year,[9] and other developed countries are likely to be exposed to similar costs.

Checklists are a simple and reproducible way to standardize selected aspects of patient care. The World Health Organisation (WHO) surgical safety checklist is the most widely used surgical checklist, comprising 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 its inception, the checklist has been adopted in >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 7-day international cohort study, the main results of which have been reported previously.[6] In the UK, the study was approved by the Yorkshire and 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 $\geq$18 years) undergoing elective surgery with a planned overnight stay in hospital. Each participating country selected a single data collection week between April 2014 and August 2014. Patients undergoing emergency surgery, day-case surgery, or radiological procedures were excluded. During the 1-week study period, data were collected for consecutive patients until hospital discharge, using standardized 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 anonymized 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, bloodstream infection, myocardial infarction, arrhythmia, pulmonary oedema, pulmonary embolism, stroke, cardiac arrest, gastro-intestinal bleed, acute kidney injury, postoperative bleed, acute respiratory distress syndrome, anastomotic leak, or other un-categorized 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 $\geq$20 participants, and countries with at least 10 participating hospitals. We dichotomized the sample according to the presence

Table 1 Baseline patient characteristics of patients included in the analysis of the prospective observational cohort (International Surgical Outcomes Study). Data are presented as *n* (%) for categorical variables and as mean with standard deviation (SD) or median with interquartile range (IQR) for continuous variables. Univariable association with exposure to surgical safety checklist presented as odds ratios (OR) with 95% confidence interval (95% CI) and *P*-value. ASA, American Society of Anesthesiologists physical status score; COPD, chronic obstructive pulmonary disease

	Patients *n* (%)	Checklist use (%)	Did not use checklist (%)	OR (95% CI)	P-value
	n = 44 814	*n* = 40 245	*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)	2125 (46.8)	0.95 (0.89–1.01)	0.13
Females, *n* (%)	24 351 (54.3)	21 927 (54.5)	2413 (53.2)	1.05 (0.98–1.13)	0.13
Present smoker, *n* (%)	7931 (17.8)	6942 (17.3)	965 (12.2)	1.04 (0.89–1.22)	0.64
ASA physical status n (%)					
I	11 227 (25.1)	9973 (24.8)	1246 (27.5)	0.97 (0.81–1.16)	0.72
II	22 265 (49.8)	20 300 (50.5)	1956 (43.2)	1.08 (0.94–1.24)	0.28
III	10 193 (22.8)	8991 (22.4)	1194 (26.4)	1.06 (0.92–1.23)	0.41
IV	1038 (2.3)	908 (2.3)	130 (2.9)	0.90 (0.66–1.23)	0.51
Grade of surgery, n (%)					
Minor	8411 (18.8)	7448 (18.5)	960 (21.2)	0.69 (0.63–0.77)	<0.01
Intermediate	20 203 (45.1)	18 051 (44.9)	2137 (47.1)	0.93 (0.86–1.01)	0.11
Major	16 175 (36.1)	14 732 (36.6)	1438 (31.7)	1.54 (1.39–1.72)	<0.01
Surgical specialty, *n* (%)					
Orthopaedic	9459 (21.1)	8683 (21.6)	771 (17.0)	1.18 (1.01–1.39)	0.04
Breast	1538 (3.4)	1393 (3.5)	145 (3.2)	0.86 (0.63–1.18)	0.34
Obstetrics and gynaecology	5674 (12.7)	5123 (12.7)	547 (12.1)	0.92 (0.75–1.12)	0.40
Urology and kidney	4871 (10.9)	4299 (10.7)	570 (12.6)	0.92 (0.76–1.11)	0.37
Upper gastrointestinal	1986 (4.4)	1776 (4.4)	208 (4.6)	1.31 (0.99–1.73)	0.06
Lower gastrointestinal	3073 (6.9)	2711 (6.7)	360 (7.9)	1.06 (0.84–1.33)	0.63
Hepato-biliary	2282 (5.1)	1959 (4.9)	322 (7.1)	1.18 (0.91–1.53)	0.22
Vascular	1599 (3.6)	1436 (3.6)	161 (3.6)	1.17 (0.85–1.61)	0.32
Head and neck	6510 (14.5)	5913 (14.7)	592 (13.1)	0.88 (0.74–1.03)	0.11
Plastic or cutaneous	1670 (3.7)	1386 (3.5)	284 (6.3)	1.01 (0.78–1.31)	0.94
Cardiac	1716 (3.8)	1557 (3.9)	159 (3.5)	0.54 (0.39–0.75)	<0.01
Thoracic (lung and other)	1157 (2.6)	1086 (2.7)	69 (1.5)	1.44 (0.95–2.18)	0.08
Other	3270 (7.3)	2919 (7.3)	350 (7.7)	0.88 (0.72–1.09)	0.24
Laparoscopic surgery, *n* (%)	7087 (15.8)	6472 (16.1)	610 (13.5)	1.37 (1.10–1.69)	<0.01
Comorbid disorder, *n* (%)					
Coronary artery disease	4588 (10.3)	3952 (9.8)	632 (14.0)	1.17 (0.94–1.46)	0.16
Heart failure	1882 (4.2)	1594 (4.0)	287 (6.3)	0.93 (0.70–1.25)	0.65
Diabetes mellitus	5171 (11.6)	4596 (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	1706 (3.8)	1547 (3.9)	159 (3.5)	0.90 (0.67–1.21)	0.48
Stroke	1492 (3.3)	1333 (3.3)	158 (3.5)	1.00 (0.72–1.39)	0.99
COPD	4094 (9.2)	3790 (9.4)	303 (6.7)	1.07 (0.85–1.35)	0.55
Other	3269 (7.3)	16 552 (41.2)	2042 (45.1)	1.00 (0.87–1.16)	0.95
Had a complication	7508 (16.8)	6734 (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

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 generalized 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 factors: age, gender, current smoker, American Society of Anesthesiologists physical status score, grade of surgery, surgical procedure category, and presence of comorbid 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 generalized 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), and 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, TX, USA) for the statistical analysis.

Table 2 Results of the primary and secondary analyses of the prospective International Surgical Outcomes Study (ISOS) cohort. Summary of two separate statistical models, where the dependent variables were either mortality or any postoperative complication (excluding mortality). Generalized 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 physical status and grade of surgery categorical variables where the reference was the average effect across the whole cohort. ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease

	Any complication	P-value	Mortality	P-value
Age (yr)	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 physical status				
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 and gynaecology	0.77 (0.69–0.85)	<0.01	0.80 (0.36–1.76)	0.57
Urology and 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
Hepatobiliary	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 and 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

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 2009–2017 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 (M.P. and A.F.) independently reviewed each record by title and abstract. Papers

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). Generalized 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. ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease

	Any complication	*P*-value	Mortality	*P*-value
Age (yr)	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 physical status				
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 and gynaecology	0.77 (0.69–0.85)	<0.01	0.83 (0.37–1.84)	0.65
Urology and 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
Hepatobiliary	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 and 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

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 (M.G.). Data were extracted from the selected papers by two independent investigators (M.P. and A.F.) to a pre-formatted Excel worksheet (Microsoft, Redmond, WA, 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 randomized 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-randomized studies.[22–24] Between study heterogeneity was assessed with χ^2 test and I^2 test 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 Fig. 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. Some 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 factors [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 quartile 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 3732 records. After removal of duplicates, 3554 abstracts were screened, 41 full-texts were reviewed, and 11 studies (including ISOS) were selected for inclusion (Supplementary Fig. 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. Some 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); $P<0.01$; $I^2=87\%$] (Fig. 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 6043/123 329 (4.9%) of patients not exposed to the checklist. In the random effects meta-analysis, checklist exposure was associated with a reduced incidence of postoperative complications [OR 0.73 (0.61–0.88); $P<0.01$; $I^2=89\%$] (Fig. 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

Table 4 Characteristics of studies included in the systematic review and meta-analysis. GIS, gastrointestinal surgery; GS, general surgery; NCS, non-cardiac surgery; OS, orthopaedic surgery; PS, plastic surgery; SSC, surgical safety checklist; US, urologic surgery

Study ref	In prior review?	Multicentre	Study design	Population	Patients, *n*		Outcomes	
					No checklist	Checklist	Mortality	Complications
Askarian et al.[38]	Y	N	Before/after	GS	144	150	N	Y
Bliss et al.[39]	Y	N	Case/control	GIS/amputations	2079	73	N	Y
Haynes et al.[40]	Y	Y	Before/after	NCS	3733	3955	Y	Y
Jammer et al.[14]	N	Y	Prospective cohort	NCS	15 286	31 038	Y	N
Lacassie et al.[30]	N	N	Retrospective cohort	Any surgery	40 781	29 858	Y	N
Lepanluoma et al.[41]	N	N	Retrospective cohort	Neurosurgery	2665	2753	N	Y
Lubbeke et al.[42]	N	N	Before/after	GS, US, day surgery, elective	609	1818	Y	Y
Mayer et al.[43]	N	Y	Longitudinal	GS, US, OS	220	6494	Y	Y
Urbach et al.[34]	N	Y	Before/after	Any procedure	109 341	106 370	Y	Y
van Klei et al.[44]	Y	N	Retrospective cohort	Non-day case surgery	14 362	11 151	Y	N
ISOS Group	N	Y	Prospective cohort	Inpatient, elective surgery	4538	40245	Y	Y

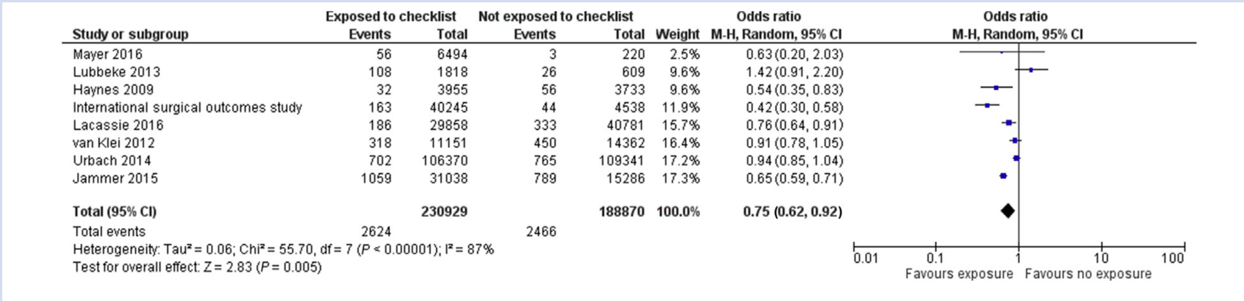

Fig 1. Forest plot for meta-analysis of exposure to surgical safety checklist and relative risk of postoperative mortality.

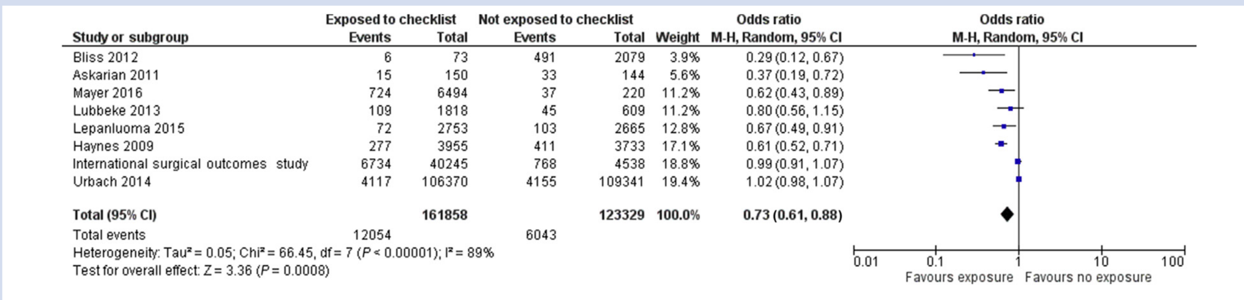

Fig 2. Forest plot for meta-analysis of exposure to surgical safety checklist and relative risk of postoperative complications.

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 randomly assign patients to checklist use because of existing widespread implementation. Therefore, in the absence of data from randomized trials, our analyses may represent the highest currently attainable level of evidence describing the effects of surgical safety checklist use. Future randomized trials may not be possible, but further research should be standardized 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 ISOS 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 generalizable 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 3 months before and after implementation in >200 000 patients. This may be attributable 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 10 patients), making it harder to detect a difference in outcomes between exposed and non-exposed patients. Alternatively, it may be attributable 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] Because of the large number of patients enrolled, we were able to adjust the analysis for a variety of potential confounding factors. However, as with any epidemiological study, we must acknowledge the potential influence of unmeasured confounding. The meta-analysis included more than 10 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 a 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 randomized 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 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 randomized 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

We have provided evidence to show 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.

Authors' contributions

Study design/plan: T.E.F.A., R.P.
Study draft: T.E.F.A., T.A., A.F., M.G., R.P.
Patient recruitment and data collection: members of the ISOS study group (see supplementary file).
Analysis of ISOS data: T.A., T.E.F.A.
Systematic review: A.F., M.P., M.G.
Meta-analysis: A.F., T.E.F.A., M.G.
Writing paper: T.E.F.A., A.F., R.P.
Revised paper: all authors.

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Declaration of interest

R.P. 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. M.S.C. 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.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.bja.2017.08.002.

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