environment, and computerised decision support will further expand these possibilities.[7] Similarly, high-quality, adequately powered, and influential clinical trials of decompressive craniectomy,[8] hypertonic saline,[9] tranexamic acid,[10] and intramedullary nails,[11] for example, used national and international networks that have, so far, been mobilised infrequently.

An international research agenda setting initiative is now needed that engages key civilian and military stakeholders involved in trauma research, practice, and policy. The aims should include gaining of consensus about the most important and feasible collaborative research priorities, and charting of a strategy for global trauma research that can be resourced, implemented, and translated to improve outcomes for injured patients. The Series points to some promising topics in brain injury, fracture healing, coagulopathy, and the immune–inflammatory response to severe injury. Because studies of monotherapies to target discrete mechanisms have often yielded disappointing results, future clinical studies should explore broad-acting therapeutic strategies and treatment combinations.

Deaths, disability, and costs can all be reduced with improved trauma care. Research is needed to develop and assess new treatments, improve clinical care, and strengthen trauma systems. The time has come for injured people to benefit from research-based advances on a scale similar to that which has transformed other domains of health-care.

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We declare that we have no conflicts of interest.

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What factors affect mortality after surgery?

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For decades, researchers have used mortality as an objective outcome measure in medicine. The difference in mortality after surgery between countries, hospitals, and surgeons is of interest to all parties, including patients, health-care providers and payers, and governments. In *The Lancet*, Rupert Pearse and colleagues[1] present results of a large prospective analysis measuring national in-hospital mortality and investigating allocation of critical care resources. The study was done during 7 days in April, 2011, during which almost 50 000 surgical patients were enrolled from nearly 500 hospitals in 28 European countries. The study population underwent various non-cardiac procedures and was followed up for 60 days. A median of 1045 patients (IQR 455–1732) were included per country, and 281 hospitals (56%) were affiliated to a university. Median hospital stay was 3 days (IQR 1·0–7·0), and admission to a critical care unit varied from 0% in Cyprus to 16·1% (95% CI 14·1–18·1) in Romania.

The key finding was an overall crude mortality of 4%, which is double that expected from national registries. Another important finding was the wide range of mortality between countries (from 1·2% [0·0–3·0] for Iceland to 21·5% [16·9–26·2] for Latvia). Pearse and colleagues postulated that an insufficient number of intensive-care unit (ICU) beds would result in increased mortality. This notion was corroborated by the finding that three quarters of patients who died were never admitted to an ICU. The investigators also note that the high mortality identified contrasts with that of 2% for

patients undergoing cardiac surgery, who are routinely admitted to the ICU.[1] On this basis, they argue that availability and use of ICU beds are crucial for improved survival in patients undergoing non-cardiac surgery.

The strength of this study is the objective snapshot of postoperative mortality in a large sample of non-selected surgical patients throughout Europe. However, the actual rationale for the differences identified remains speculative. Although Pearse and colleagues used strategies to enhance comparability, such as adjustment for baseline confounders (eg, urgency and surgical procedure category, age, American Society of Anesthesiologists score, metastatic disease, and cirrhosis), various aspects must be considered when ranking countries by mortality rates and ICU beds. The definition of ICU beds might differ between countries. In many large centres, patients spend postoperative time in a recovery room or intermediate care unit before admission to a ward. These units are often well managed by an interdisciplinary team of surgeons and anaesthesiologists, and might be associated with better care than formal ICU beds elsewhere. Resources allocated to ICUs differ between countries, with variation in the ratios of total hospital beds to ICU beds[2] and of nurses to patients ranging from 1:1 to 1:3.[3] Furthermore, the qualifications of care providers and surgeons were unclear in Pearse and colleagues' study.

Evidence shows that several factors affect postoperative course, such as routine use of surgical safety checklists,[4] clinical pathways,[5] enhanced recovery strategy[6] (previously called fast track surgery), volume of cases,[7] presence of general versus specialised surgeons,[8] and ability to recognise and manage complications.[9] Although these factors have been shown to affect the postoperative course of complex procedures, of great interest is whether they might also apply to the general surgical population and their respective importance compared with availability of ICU beds.

Pearse and colleagues attempted to measure national surgical and perioperative performance and quality by assessing mortality rates. Yet, for this endpoint to be a useful measure of performance, the procedure must have a high mortality rate and be done frequently.[10] Consequently, the investigators calculated that they needed to include at least 20 000 patients to obtain meaningful results. A more sensitive and relevant marker of quality of care is morbidity, which can be measured in a quantitative and reproducible way.[11]

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Morbidity information can easily be collected, both prospectively in a database or retrospectively from discharge notes, because severity of a complication is closely associated with the corrective treatment used. Measurement of complication rates could provide further information about the magnitude of differences among centres or countries from a much smaller sample size of patients than that used by Pearse and colleagues. Although mortality rates are used in reports of health outcome measures, difficulties in conclusive risk adjustment often preclude meaningful interpretation.[12] Another endpoint testifying to the quality of care is failure to cure,[13] which is especially relevant after cancer surgery. Such data, however, require long-term follow-up. Some investigators have examined incidence of recurrent tumours to suggest ways to improve care.[14]

Pearse and colleagues' results show that the poorest outcomes correspond to economically underdeveloped countries, such as in eastern Europe. Therefore, can outcomes be improved in countries with scarce resources? The most important factor affecting cost is the severity of postoperative complications.[15] For example, surgery on the pancreas with a grade IV complication (requiring ICU management) can increase the cost of the procedure by a factor of five. We suggest that even use of expensive resources, such as additional ICU beds, could rapidly become cost effective by reducing complications. This message should be delivered to those who fund medical care. The recommendation might be difficult to test, but is supported by results of studies showing costs associated with poor postoperative outcomes.[16] Measures of cost

associated with death are inconsistent, because cost can be high, for example with death after many days in the ICU, or low with sudden postoperative death.

How can we reconcile Pearse and colleagues' study with that by Wunsch and colleagues,[2] who looked at variation in critical care services across the USA, Canada, and western Europe? Wunsch identified a substantial difference in ICU admissions, for example a ten-times difference between the USA and Germany, and a seven-times difference between the UK and Germany. The Netherlands, with one of the lowest mortality rates in Pearse and colleagues' study, was in the lowest rank in terms of availability of ICU beds of the eight countries assessed by Wunsch and colleagues. Such data suggest that quality assurance in surgery relies on several factors, of which the availability of ICU beds is only one. In future studies, we need to learn more about the relevant issues and optimum processes to secure quality. Targets could include the type of intensive care beds needed, volume, university versus community hospitals, and surgeons' qualifications. Costs for the overall postoperative course would also be key, to allow us to propose cost-effective and relevant corrective measures.

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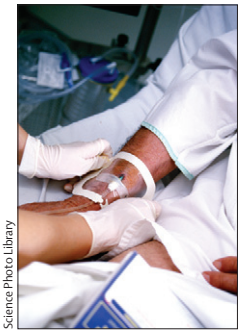
Should intravenous catheters be replaced routinely?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Currently the US Centers for Disease Control and Prevention (CDC) state that peripheral catheters do not need to be replaced more frequently than every 72–96 h to reduce the risk of infection and phlebitis in adults.[1] Although results from some observational studies have shown that the risk of phlebitis rises with increasing catheter dwell time,[2–4] other studies have not confirmed this finding.[5–8] Catheter replacement trials are frequently limited by study design and small sample size.[6,8] Therefore, the study in *The Lancet* by Claire Rickard and colleagues,[9] which compares intravenous catheter replacement in adults every 3 days with replacement when clinically indicated, is a major contribution to this debate. It is a large (3283 patients), multisite, randomised trial with high quality methods, excellent enrolment (97%) and follow-up (100%), and broad inclusion criteria.

The investigators postulated that occurrence of phlebitis and other complications would be equivalent when intravenous catheters were replaced when clinically indicated compared with routine changes every third day. Indeed, the occurrence of the primary outcome of phlebitis was 7% in both groups (absolute risk difference 0·41%, 95% CI –1·33 to 2·15). Rickard and colleagues acknowledge that the non-masking of research nurses was a limitation that could have biased the recording of phlebitis. However, the high quality of this study provides a strong basis for their

Mortality after surgery in Europe: a 7 day cohort study

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Summary

Background **Clinical outcomes after major surgery are poorly described at the national level. Evidence of heterogeneity between hospitals and health-care systems suggests potential to improve care for patients but this potential remains unconfirmed. The European Surgical Outcomes Study was an international study designed to assess outcomes after non-cardiac surgery in Europe.**

Methods **We did this 7 day cohort study between April 4 and April 11, 2011. We collected data describing consecutive patients aged 16 years and older undergoing inpatient non-cardiac surgery in 498 hospitals across 28 European nations. Patients were followed up for a maximum of 60 days. The primary endpoint was in-hospital mortality. Secondary outcome measures were duration of hospital stay and admission to critical care. We used χ^2 and Fisher's exact tests to compare categorical variables and the *t* test or the Mann-Whitney *U* test to compare continuous variables. Significance was set at p<0·05. We constructed multilevel logistic regression models to adjust for the differences in mortality rates between countries.**

Findings **We included 46 539 patients, of whom 1855 (4%) died before hospital discharge. 3599 (8%) patients were admitted to critical care after surgery with a median length of stay of 1·2 days (IQR 0·9–3·6). 1358 (73%) patients who died were not admitted to critical care at any stage after surgery. Crude mortality rates varied widely between countries (from 1·2% [95% CI 0·0–3·0] for Iceland to 21·5% [16·9–26·2] for Latvia). After adjustment for confounding variables, important differences remained between countries when compared with the UK, the country with the largest dataset (OR range from 0·44 [95% CI 0·19–1·05; p=0·06] for Finland to 6·92 [2·37–20·27; p=0·0004] for Poland).**

Interpretation **The mortality rate for patients undergoing inpatient non-cardiac surgery was higher than anticipated. Variations in mortality between countries suggest the need for national and international strategies to improve care for this group of patients.**

Funding **European Society of Intensive Care Medicine, European Society of Anaesthesiology.**

Introduction

More than 230 million major surgical procedures are undertaken worldwide each year.[1] For most patients, risks of surgery are low and yet evidence increasingly suggests that complications after surgery are an important cause of death.[2–5] About 10% of patients undergoing surgery in the UK are at high risk of complications, accounting for 80% of postoperative deaths.[2–4] If this rate is applicable worldwide, up to 25 million patients undergo high-risk surgical procedures each year, of whom 3 million do not survive until hospital discharge. Patients who develop complications but survive to leave hospital often have reduced functional independence and long-term survival.[5–8]

Despite obvious differences in procedure-related and patient-related mortality risks, most surgical patients use one care pathway, sharing standard facilities for pre-operative assessment, anaesthesia, operating rooms, post-anaesthetic recovery, and hospital wards. This approach is adequate for most patients but might not meet the needs of the small number of patients at high risk of complications and death. In the USA, evidence of variations in postoperative mortality within health-care systems suggest the potential to implement measures that improve patient outcomes.[9] Low rates of admission to critical care for patients at high risk of complications undergoing non-cardiac surgery are of particular concern,[2–4] and might be affected by international differences in the provision of critical care.[10,11] With high volumes of surgery undertaken, even a low rate of avoidable harm will be associated with many preventable deaths.

International comparative data might provide important insights into delivery of health care for surgical patients. However, little or no data are available describing provision of care or outcomes for unselected surgical patients. The objective of the European Surgical Outcomes Study (EuSOS) was to describe mortality rates and patterns of critical care resource use for patients undergoing non-cardiac surgery across several European nations.

Methods

Study design and participants

We did this European cohort study between 0900 h (local time) on April 4, 2011, and 0859 h on April 11, 2011. All adult patients (older than 16 years) admitted to participating centres for elective or non-elective inpatient surgery commencing during the 7 day cohort period were

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eligible for inclusion. Patients undergoing planned day-case surgery, cardiac surgery, neurosurgery, radiological, or obstetric procedures were excluded because these patients receive care within separate, dedicated pathways. Participating hospitals (appendix pp 11–68) were a voluntary convenience sample, identified through membership of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology and by direct approach from national study coordinators. Ethics requirements differed by country. In Denmark, centres were exempt from ethics approval because this study was deemed to be a clinical audit. In all other nations formal ethics approval was applied for and given. In Finland alone we were required to obtain written informed consent from individual patients.

Procedures

For the **EuSoS study protocol** see http://eusos.esicm.org

Local investigators were supported by national coordinators and via a website that provided key documentation, including the protocol and guidance on study procedures. We obtained data describing perioperative care facilities once for each hospital at the beginning of the study. We collected data describing consecutive patients with paper case record forms, which we made anonymous before entering the information onto a secure internet-based electronic case record form (OpenClinica, Boston, MA, USA). We completed an operating theatre case report form for each eligible patient who we then followed up until hospital discharge for data describing hospital stay, admission to critical care, and in-hospital mortality. We completed a critical care case record form to capture data describing the first admission to critical care for any individual patient at any time during the follow-up period. Example case record forms are available from the study website.

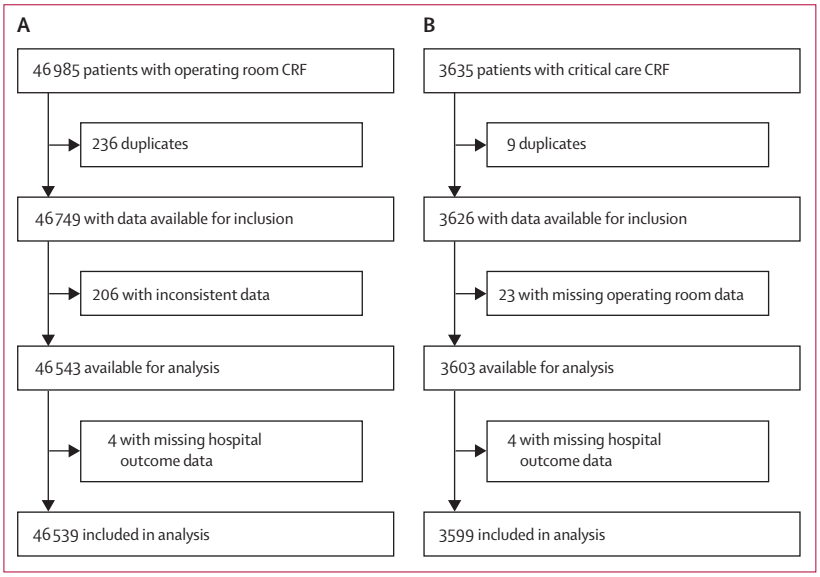

Figure 1: **Study profile**
(A) All patients. (B) Patients admitted to critical care. CRF=case report form.

We selected patient-level variables on the basis that they were objective, routinely collected for clinical reasons, could be transcribed with a high level of accuracy, and would be relevant to a risk adjustment model in most patients. We censored critical care and hospital discharge data at 60 days after surgery. We assessed data for completeness and then checked for plausibility and consistency with prospectively defined ranges.[12]

The primary endpoint was in-hospital mortality. Secondary outcome measures were duration of hospital stay and admission to critical care.

Statistical analysis

Our aim was to recruit as many participating hospitals as possible and to recruit every eligible patient in those hospitals. We anticipated that a minimum sample size of 20 000 patients would enable a precise estimate of mortality. This sample size was also expected to provide a sufficient number of events (>200) for construction of a robust logistic regression model for mortality.

We used SPSS (version 19.0) for data analysis. Categorical variables are presented as number (%) and continuous variables as mean (SD) when normally distributed or median (IQR) when not. We used χ^2 and Fisher's exact tests to compare categorical variables and the *t* test or the Mann-Whitney *U* test to compare continuous variables. Significance was set at $p<0\cdot05$. We constructed several binary logistic regression models to identify factors independently associated with hospital mortality and to adjust for differences in confounding factors between countries. These included a one-level model and a hierarchical two-level generalised linear mixed model, with patients being at the first level and hospital at the second. Factors were entered into the model based on their univariate relation to outcome ($p<0\cdot05$). All factors were biologically plausible with a sound scientific rationale and a low rate of missing data. The results of the model are reported as adjusted odds ratios (OR) with 95% CI. We assessed the models through sensitivity analyses with three random (disjoint) subsamples of countries and a fourth sample removing all patients from the largest country in the dataset (the UK). We explored all possible interacting factors and examined how they might have affected the final results.

This study is registered with ClinicalTrials.gov, number NCT01203605.

Role of the funding source

The study was funded by the European Society of Intensive Care Medicine and the European Society of Anaesthesiology who appointed an independent steering committee (appendix p 11), who were responsible for study design, conduct, and data analysis. Members of the steering committee had full access to the study data and were solely responsible for interpretation of the data, drafting and critical revision of the report, and the decision to submit for publication.

Results

We collected data describing patients undergoing in-patient surgery in 498 hospitals across 28 European nations. Median number of operating theatres in each hospital was 15 (IQR 10–22) and median number of critical care beds was 19 (9–40). Data were returned for 46 985 cases of which 446 were removed having been identified as duplicates or having missing critical care or mortality data, leaving 46 539 for analysis (figure 1). A median number of 83 (39–125) patients were included per hospital and 1045 (455–1732) per country. 281 (56%) hospitals were affiliated to a university, recruiting 31 132 patients (68% of total, appendix p 2).

Table 1 shows baseline data for all patients. Overall crude mortality was 4·0% and the median duration of hospital stay was 3·0 days (IQR 1·0–7·0). Prevalence of comorbid disease, grade of surgery, crude mortality rates, duration of hospital stay, and number of critical care admissions differed substantially between countries (table 2, appendix p 2). Table 2 shows unadjusted OR for hospital mortality by country. 3599 patients (8%) were admitted to critical care at some point during hospital stay, of whom 2555 (71%) had planned admissions (figure 2). Median stay in critical care was 1·2 days (0·9–3·6). 1358 patients who died were not admitted to critical care at any stage after surgery (73% of all deaths). 506 patients (14%) admitted to critical care died before hospital discharge, of whom 218 (43%) died after the first admission to critical care was complete.

We explored variables associated with hospital mortality in a univariate analysis, the findings of which were much the same as for a sensitivity analysis of different subsets of the database (table 1, appendix pp 3–4). We then constructed several binary logistic regression models to adjust for baseline differences that might explain the unadjusted OR for individual countries (table 2). We developed both single-level and multilevel models (appendix pp 5–8) with variables that were significant in the univariate analysis. The point estimates for the OR did not differ greatly between the one-level and two-level models, but the hierarchical model consistently provided a more conservative estimate of country effects across the sensitivity tests (appendix p 9).

We constructed a further model including all significant interacting factors (appendix p 10). Since this increased model complexity did not substantially change the country-level estimates, we report results of the more parsimonious two-level model without interactions (figure 3). Factors that were independently associated with mortality and that we therefore used to adjust for baseline confounders were: country where surgery was done, urgency of surgery, grade of surgery, surgical procedure category, age, American Society of Anesthesiologists (ASA) score, metastatic disease, and cirrhosis (appendix pp 7–8). We entered ASA score rather than the Lee Revised Cardiac Index because, although the two were highly correlated, less data describing ASA score were missing.

	All patients (n=46 539)	Died in hospital (n=1864)	Survived to hospital discharge (n=44 657)	Odds ratio (95% CI)	p value
Age (years)	56·7 (18·5)	61·0 (18·7)	56·6 (18·5)	1·01 (1·01–1·02)	<0·0001
Men	22 607	968	21 629	1·15 (1·05–1·26)	0·003
Present smoker	9872	363	9503	0·90 (0·80–-1·01)	0·07
ASA score					
1	11 642	362	11 280	Reference	..
2	21 582	633	20 944	0·94 (0·83–1·07)	0·36
3	11 574	539	11 025	1·51 (1·32–1·73)	<0·0001
4	1559	279	1277	6·75 (5·71–7·97)	<0·0001
5	90	49	41	35·61 (23·23–54·59)	<0·0001
Grade of surgery					
Minor	12 041	431	11 608	Reference	..
Intermediate	22 231	741	21 483	0·93 (0·82–1·05)	0·22
Major	12 170	685	11 476	1·59 (1·40–1·80)	<0·0001
Urgency of surgery					
Elective	35 049	1129	33 908	Reference	..
Urgent	8923	483	8436	1·71 (1·52–1·91)	<0·0001
Emergency	2557	249	2303	3·20 (2·77–3·70)	<0·0001
Surgical specialty					
Orthopaedics	12 214	468	11 744	1·02 (0·84–1·24)	0·85
Breast	1500	43	1456	0·76 (0·53–1·07)	0·12
Gynaecology	3972	115	3857	0·76 (0·59–0·99)	0·04
Vascular	2376	140	2233	1·61 (1·26–2·05)	0·0001
Upper gastrointestinal	2228	155	2071	1·88 (1·48–2·39)	0·0001
Lower gastrointestinal	4972	284	4683	1·54 (1·25–1·91)	0·0001
Hepato-biliary	2247	113	2134	1·35 (1·04–1·74)	0·025
Plastic or cutaneous	2432	73	2356	0·79 (0·59–1·06)	0·12
Urology	4881	144	4737	0·78 (0·61–0·99)	0·042
Kidney	463	9	454	0·51 (0·26–1·01)	0·05
Head and neck	5640	174	5466	0·82 (0·65–1·03)	0·09
Other	3463	132	3329	Reference	
Laparoscopic surgery	5510	160	5350	0·69 (0·59–0·82)	<0·0001
Comorbid disorder					
Cirrhosis	498	65	433	3·64 (2·79–4·76)	<0·0001
Congestive heart failure	2154	166	1985	2·10 (1·78–2·48)	<0·0001
COPD	5162	244	4912	1·21 (1·05–2·48)	0·008
Coronary artery disease	6274	387	5881	1·73 (1·54–1·94)	<0·0001
Diabetes (taking insulin)	2081	135	1939	1·73 (1·44–2·07)	<0·0001
Diabetes (not taking insulin)	3495	147	3348	1·05 (0·88–1·24)	0·61
Metastatic cancer	2173	155	2017	1·91 (1·61–2·27)	<0·0001
Stroke	2006	120	1884	1·57 (1·30–1·90)	<0·0001

Data are mean (SD) or n unless otherwise specified. Odds ratios were constructed for in-hospital mortality with univariate binary logistic regression analysis. ASA=American Society of Anesthesiologists. COPD=chronic obstructive pulmonary disease.

Table 1: **Description of cohort**

	Number of patients	Median days in hospital (IQR)	Number admitted to critical care	Percentage admitted to critical care (95% CI)	Number died in hospital	Percentage died in hospital (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p value
Belgium	1486	3·0 (1·0–6·0)	136	9·2% (7·7–10·6)	47	3·2% (2·3–4·1)	0·89 (0·65–1·21)	1·65 (0·81–3·40)	0·17
Croatia	1767	4·0 (2·0–7·0)	166	9·4% (8·0–10·8)	131	7·4% (6·2–8·6)	2·17 (1·77–2·67)	1·89 (0·94–3·80)	0·07
Cyprus	45	1·0 (1·0–3·0)	0	0	1	2·2% (0·0–6·7)	0·62 (0·09–4·48)	0·82 (0·04–16·70)	0·90
Czech Republic	434	4·0 (2·0–9·0)	21	4·8% (2·8–6·9)	10	2·3% (0·9–3·7)	0·64 (0·34–1·21)	1·30 (0·23–7·46)	0·77
Denmark	1000	2·0 (1·0–5·0)	36	3·6% (2·4–4·8)	32	3·2% (2·1–4·3)	0·90 (0·62–1·29)	1·16 (0·52–2·61)	0·72
Estonia	727	3·0 (1·0–6·0)	51	7·0% (5·2–8·9)	11	1·5% (0·6–2·4)	0·42 (0·23–0·76)	0·60 (0·16–2·28)	0·45
Finland	1071	2·0 (1·0–5·0)	43	4·0% (2·8–5·6)	21	2·0% (1·1–2·8)	0·54 (0·35–0·85)	0·44 (0·19–1·05)	0·06
France	2278	3·0 (1·0–6·0)	132	5·8% (4·8–6·8)	73	3·2% (2·5–3·9)	0·90 (0·70–1·16)	1·36 (0·72–2·56)	0·34
Germany	5284	4·0 (2·0–9·0)	611	11·6% (10·7–12·4)	133	2·5% (2·1–2·9)	0·70 (0·57–0·86)	0·85 (0·50–1·43)	0·54
Greece	1803	3·0 (2·0–7·0)	63	3·5% (2·7–4·3)	65	3·6% (2·7–4·5)	1·01 (0·78–1·33)	1·20 (0·66–2·16)	0·55
Hungary	621	4·0 (2·0–7·0)	44	7·1% (5·1–9·1)	20	3·2% (1·8–4·6)	0·90 (0·57–1·43)	1·23 (0·43–3·50)	0·69
Iceland	162	2·0 (1·0–4·0)	15	9·3% (4·8–13·8)	2	1·2% (0·0–3·0)	0·34 (0·08–1·37)	0·47 (0·07–3·41)	0·46
Ireland	856	3·0 (1·0–6·0)	66	7·7% (5·9–9·5)	55	6·4% (4·8–8·1)	1·86 (1·39–2·49)	2·61 (1·30–5·27)	0·007
Italy	2673	3·0 (2·0–7·0)	200	7·5% (6·5–8·5)	141	5·3% (4·4–6·1)	1·51 (1·24–1·84)	1·70 (0·97–2·97)	0·06
Latvia	302	4·0 (2·0–8·0)	19	6·3% (3·5–9·1)	65	21·5% (16·9–26·2)	7·44 (5·55–9·97)	4·98 (1·22–20·29)	0·025
Lithuania	375	3·0 (2·0–5·0)	14	3·7% (1·8–5·7)	10	2·7% (1·0–4·3)	0·74 (0·39–1·40)	1·21 (0·21–6·95)	0·83
Netherlands	1627	3·0 (1·0–6·0)	126	7·7% (6·4–9·0)	32	2·0% (1·3–2·7)	0·55 (0·38–0·78)	0·63 (0·28–1·41)	0·26
Norway	689	3·0 (1·0–6·0)	31	4·5% (3·0–6·1)	10	1·5% (0·6–2·4)	0·40 (0·21–0·75)	0·51 (0·17–1·49)	0·22
Poland	397	5·0 (2·0–7·5)	8	2·0% (0·6–3·4)	71	17·9% (14·1–21·7)	5·91 (4·48–7·79)	6·92 (2·37–20·27)	0·0004
Portugal	1489	3·0 (1·0–7·0)	103	6·9% (5·6–8·2)	61	4·1% (3·1–5·1)	1·16 (0·88–1·53)	1·43 (0·72–2·83)	0·31
Romania	1298	5·0 (3·0–8·0)	209	16·1% (14·1–18·1)	88	6·8% (5·4–8·2)	1·97 (1·55–2·51)	3·19 (1·61–6·29)	0·001
Serbia	85	5·0 (3·0–7·0)	1	1·2% (0·0–3·5)	2	2·4% (0·0–5·6)	0·65 (0·16–2·67)	1·06 (0·11–10·04)	0·96
Slovakia	1156	3·0 (2·0–7·0)	22	1·9% (1·1–2·7)	129	11·2% (9·3–13·0)	3·41 (2·76–4·20)	2·15 (0·91–5·07)	0·08
Slovenia	518	3·0 (1·0–7·0)	13	2·5% (1·2–3·9)	15	2·9% (1·5–4·3)	0·81 (0·48–1·37)	1·12 (0·30–4·22)	0·86
Spain	5433	3·0 (1·0–7·0)	677	12·5% (11·6–13·3)	208	3·8% (3·3–4·3)	1·08 (0·91–1·28)	1·39 (0·89–2·18)	0·15
Sweden	1314	2·0 (1·0–6·0)	42	3·2% (2·2–4·2)	24	1·8% (1·1–2·6)	0·50 (0·33–0·77)	0·58 (0·23–1·49)	0·26
Switzerland	1019	4·0 (2·0–8·0)	79	7·8% (6·1–9·4)	20	2·0% (1·1–2·8)	0·54 (0·35–0·86)	0·86 (0·25–2·97)	0·81
UK	10 630	2·0 (1·0–6·0)	671	6·3% (5·9–6·8)	378	3·6% (3·2–3·9)	1·00	..	..

Odds ratios (OR) referenced against the UK and adjusted for age, American Society of Anesthesiologists' score, urgency of surgery, grade of surgery (minor, intermediate, major), surgical specialty, and the presence of either metastatic disease or cirrhosis in a two-level binary logistic regression model (with patient at the first level and hospital at the second).

Table 2: **Relation between country and in-hospital mortality**

With the UK study population as the reference category, we identified higher unexplained rates of mortality in Poland, Romania, Latvia, and Ireland (table 2, figure 3).

Discussion

This international prospective study has provided data for a population of more than 46 000 unselected patients undergoing inpatient surgery from 28 European countries. 4% of included patients died before hospital discharge, which was a higher mortality rate than expected.[2,3,6,13–16] We identified substantial differences in crude and risk adjusted mortality rates between countries. When compared with the UK, the recorded mortality rates for Poland, Latvia, Romania, and Ireland were higher even after adjustment for all identified confounding variables. This pattern could relate to cultural, demographic, socioeconomic, and political differences between nations, which might affect population health and health-care outcomes.

A major strength of our study was the large number of consecutive unselected patients enrolled in a multicentre and multinational setting. A vigorous approach to follow-up for missing and incomplete data provided a high-quality dataset for analysis. The dataset allowed us to explore probable prognostic factors and to adjust crude mortality rates to describe differences in outcomes between countries. Our analysis identified several factors associated with increased mortality. These findings suggest that surgery-related and patient-related factors interact to increase mortality risk. Only two comorbid disease categories were identified as independent variables. This finding probably arose because the ASA score was designed to describe the severity of coexisting medical disease.

Evidence suggests that critical-care-based cardiorespiratory interventions can improve outcomes among high-risk surgical patients.[17–21] However, in our study, only 5% of patients underwent a planned admission to critical care with a median stay of about 1 day. Unplanned admissions to critical care were associated with higher mortality rates than were planned admissions. Remarkably, most patients who died (73%) were not admitted to critical care at any

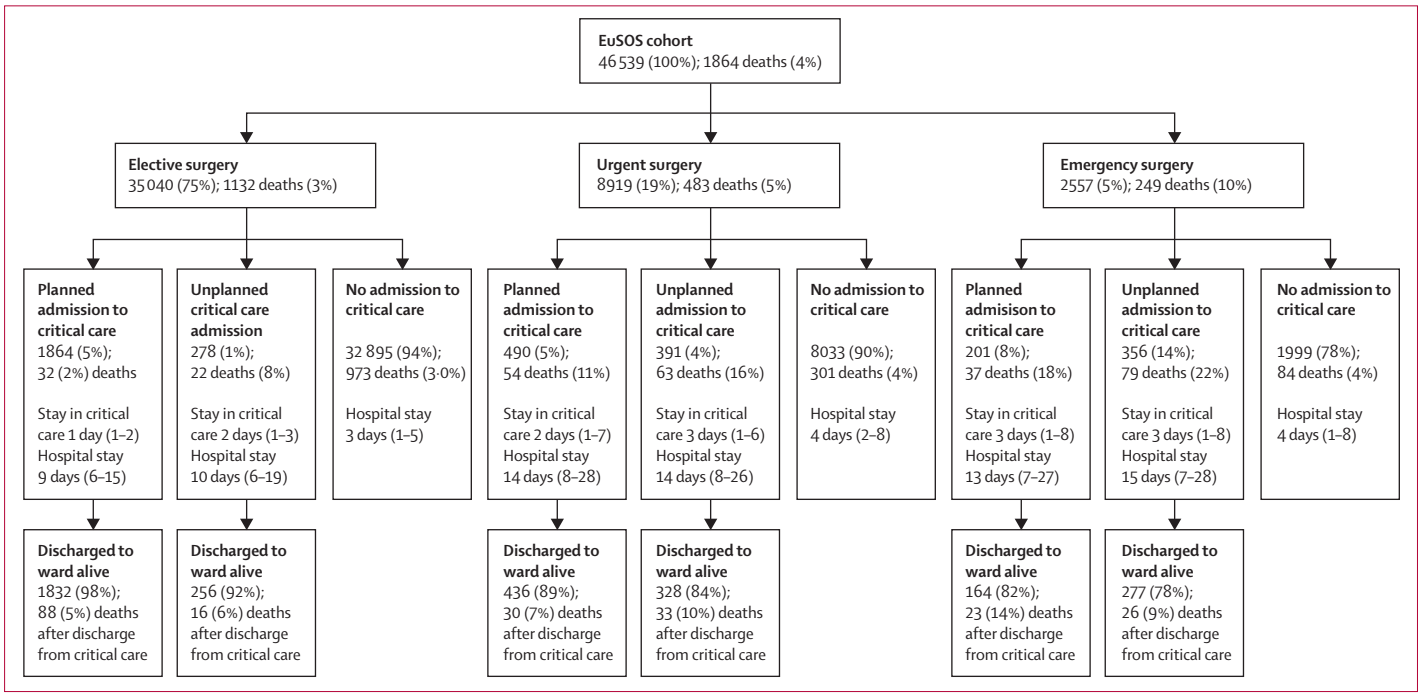

Figure 2: **Planned and unplanned admission to a critical-care unit according to urgency of surgery**
Data are n (%) or median (IQR). We collected data describing the first critical care admission for any individual patient. The data presented do not describe readmission to critical care. Because of incomplete data for admission planning, 19 admissions to critical care are not presented in this figure. EuSOS=European Surgical Outcomes Study. Elective=not immediately life saving; planned within months or weeks. Urgent=planned surgery within hours or days of the decision to operate. Emergency=as soon as possible; no delay to plan care; ideally within 24 h.

stage after surgery. Of patients who died after admission to critical care, 43% did so after the initial episode was complete and the patient had been discharged to a standard ward. These findings suggest a systematic failure in the process of allocation of critical care resources. This notion is consistent with previous reports of a failure to rescue deteriorating surgical patients with a detrimental effect on patient outcomes[22] and the high incidence of myocardial injury in the days after surgery.[23] For some patients with a poor prognosis, postoperative admission to critical care might have been deemed inappropriate—eg, after palliative surgery for disseminated malignancy. However, our data suggest these cases are few in number (<5% of patients had malignancy, table 1). Meanwhile other investigators have challenged the suggestion that patients should be offered surgery when the standard of postoperative care is unlikely to be adequate for their needs.[2] The low rate of admission to critical care prevents any detailed comparison of this resource between nations. Further research is needed to better understand whether early admission to critical care can improve survival after major surgery.

Despite the large sample size, our study might not be truly representative of current practice across Europe because only a small proportion of European hospitals took part. Although in some countries the patient sample was large enough to show national practice, the high proportion of patients enrolled in university hospitals in other countries suggests a degree of selection bias. In particular, our data might not show the true surgical

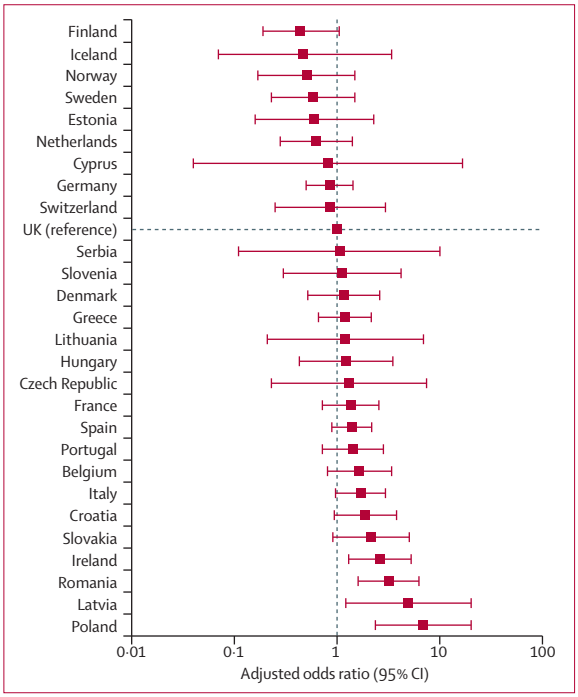

Figure 3: **Adjusted odds ratio for death in hospital after surgery for each country**

***Panel:* Research in context**

Systematic review

We searched Medline for original research from the past 10 years describing mortality rates in large unselected national and international populations of patients undergoing non-cardiac surgery. We used the search terms "surgery", "mortality", and "complications" and widened our search to include retrospective analyses of health-care registries and prospective epidemiological studies. Publications were screened by title and then by abstract for relevance to the objectives of our study. Additionally, coinvestigators in various European nations searched for publicly available registry analyses reporting mortality rates for unselected populations of surgical patients. We identified seven large national studies[2,3,6,13-16] describing mortality rates for the population of interest, three of which involved prospective data collection. No studies were identified that provided international comparative data. The last search was done on June 15, 2012.

Interpretation

As far as we are aware, this was the first large prospective international epidemiological study of unselected non-cardiac surgical patients and as such it provides a new perspective on mortality after surgery. A few national reports describe mortality rates from 1·3% to 2·0%.[2,3,6,13-16] In our study, the overall crude mortality rate of 4% was higher than anticipated. We identified important variations in risk-adjusted mortality rates between nations, and critical care resources did not seem to be allocated to patients at greatest risk of death. Our findings raise important public health concerns about the provision of care for patients undergoing surgery in Europe.

case-mix and standards of care in countries with a small number of participating hospitals. Although we planned to enrol every eligible patient undergoing surgery during the study period, we cannot be sure of the exact proportion of eligible patients included. Nonetheless, assuming the volume of surgery during the cohort week is typical of the participating hospitals, these centres undertake more than 2·3 million inpatient surgical procedures each year, which is 1% of the estimated volume of surgery taking place worldwide.[1] Whether truly representative or not, our findings clearly describe a large cross-section of health care in Europe.

Some of our findings might be indicative of limitations of commonly used risk-adjustment variables with unexpected patterns of survival across categories for both ASA score and grade of surgery. This finding could result from the poor ability of clinicians to discriminate between the less severe categories of these variables. Random partitioning of the countries into three equal groups and repetition of the modelling exercise showed much the same results with regards to the OR of the relevant effect factors, showing some stability of the risk adjustment in subsets of countries. This stability was further confirmed in more complex models that included interactions between variables for which none of the interactions with the country factor contributed significantly to prediction. We identified other interactions that did significantly contribute to prediction but we did not record a substantial change in country effects when estimated from the extended model including these interactions. We therefore decided to use the simpler of the hierarchical models for the final analysis because our aim had been to construct a parsimonious model that practising clinicians would easily understand.

As far as we are aware, this was the first large, prospective, international assessment of surgical outcomes (panel). In some countries, data are available that describe survival after specific procedures such as vascular, joint replacement, or bowel cancer surgery.[24–26] However, these audits are poorly representative of overall national surgical populations because high-risk patients are under-represented. The few previous estimates suggest an overall mortality for unselected inpatient surgery of between 1% and 2%,[2,3,6,13–16] but these values are representative of only a few health-care systems. In a previous study[13] of national registry data from the Netherlands, 30 day mortality was reported as 1·85%, which is much the same as the crude hospital mortality of 2% for this country in the EuSOS study. In the UK, a prospective investigation[2] with a very similar methods to EuSOS identified a postoperative critical care admission rate of 6·7%, which is much the same as to the value of 6% for EuSOS in the UK.[2] However, 30 day mortality was 1·6% compared with 3·6% for 60 day in-hospital mortality for UK patients in EuSOS. Reports from nations outside Europe describe 30 day mortality rates from 1·3% to 2·0%.[6,14,15]

Previous investigators have described the differences in provision of health services across Europe, in particular numbers of critical care beds.[10,11] The reported seven-times greater provision of critical care beds for Germany than for the UK is likely to affect rates of admission to critical care and postoperative outcomes.[10,11,27] This finding is in keeping with our present data that show a greater rate of admission to critical care after surgery in Germany than in the UK. Other studies have shown that fewer than a third of high-risk non-cardiac surgical patients are admitted to critical care after surgery in the UK despite high mortality rates,[2–4] which is consistent with the results of our study; across Europe 73% of surgical patients who died were never admitted to critical care. This situation contrasts with perioperative care for cardiac surgical patients who by definition have severe comorbid disease and undergo major body cavity surgery followed by routine admission to critical care with mortality rates of less than 2%.[28] Several reasons could explain why outcomes for cardiac and non-cardiac surgical patients differ but the quality of perioperative care is likely to be among the most important. The heath-care community increasingly recognises the importance of the entire perioperative care pathway including preoperative assessment, optimisation of coexisting medical disease, integrated care pathways relevant to the surgical procedure, WHO surgical checklists, advanced haemodynamic monitoring during surgery, early admission to critical care, acute pain management and critical-care outreach services, and hospital discharge planning together with the

primary care physician.[20,21] Routine audit and reporting of data for clinical outcomes has also proved a highly effective instrument for improvement of the quality of perioperative care.[29]

Our findings suggest both the need and potential to implement measures to improve postoperative outcomes. In addition to further research in this discipline, the root causes of this problem could be better understood through increased use of high-quality registries designed to capture robust data describing quality of care and clinical outcomes for surgical patients. This step would require increased funding for this specific area of health services research. The high mortality rate after surgery might be modified by changes in the organisation of care.[20]

Contributors

All authors were involved in the design and conduct of the study. Data collection and collation was done by the members of the EuSOS study group. AR, RM, and PB did the data analysis with input from RP. The report was drafted by RP and AR and revised following critical review by all authors.

Conflicts of interest

We declare that we have no conflicts of interest.

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Mortality after surgery in Europe

The Association of Anaesthesiologists and Reanimatologists of Latvia and the Latvian Association of Surgeons would like to state that the mortality data published in the paper by Rupert Pearse and colleagues (Sept 22, p 1059)[1] were completely incorrect regarding Latvia.

During the 7-day cohort study between April 4 and April 11, 2011, there was one death out of 85 patients at the Paul Stradins Clinical University Hospital; one death out of 104 patients at the Riga East Clinical University Hospital "Gailezers"; and no deaths out of 113 patients at the Traumatology-Orthopaedic Hospital in Riga. Therefore, during this period, only two of 302 patients who were enrolled in this study actually died, giving a mortality rate of 0·66%, not 21·5% as published by Pearse and colleagues. The heads of these departments undertook an internal audit and they did not find any errors.

The important issue is the fact that Pearse and colleagues' data were not controlled and verified by the Latvian coordinator before publication, despite repeated requests. Such highly unusual and unlikely results were published without further clarification and confirmation from the original source.

We declare that we have no conflicts of interest.

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1 Pearse RM, Moreno RP, Bauer P, et al, for the European Surgical Outcomes Study (EuSOS) group for the Trials groups of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology. Mortality after surgery in Europe: a 7 day cohort study. *Lancet* 2012; **380:** 1059–65.

I was asked by Rupert Pearse to participate in the European Surgical Outcomes Study (EuSOS)[1] as a national coordinator and to propose other Polish participants for the trial. Unfortunately, Pearse and colleagues did not give me the opportunity to see the results before submitting the paper, so I was not able to review the results of the study before publication.

Seeing the published results with respect to Poland, I have to state that the striking rate of mortality given for Poland (17·9%) is significantly higher than the actual rate. I collected information on the number of deaths at the hospitals that had participated in the study. According to these data, during the period of study, only two deaths were reported of 397 patients included (mortality rate 0·5%). The incredibility and incoherence of the data presented in the paper are further demonstrated by the number of 71 deaths, when there were only eight patients in intensive-care units (ICUs). The number of ICU patients and the number of postoperative deaths should be proportional, because if a patient's condition deteriorates, he or she is transferred to the ICU.

The data reported by Pearse and colleagues have the potential to mislead the medical community and should be corrected.

I declare that I have no conflicts of interest.

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Rupert Pearse and colleagues[1] present a study assessing in-hospital deaths after surgical procedures in Europe, which shows rather high average mortality (4%). This rate is partly driven by very high mortality in some countries—eg, Poland at 17·9%. Such a figure does not seem to reflect reality. A death rate of 17·9% would be unacceptable in any hospital, and the extrapolation of the results from a 7-day study in six hospitals in Poland to the whole country, as Pearse and colleagues have done, seems inappropriate.

We assessed data for 2011 from the database of the National Health Foundation (NHF) in Poland. The database, which is not publicly accessible, includes almost all major and most minor surgical procedures (it does not cover obstetric, radiological, or paediatric procedures, nor the usually minor procedures done privately, but does cover planned 1-day, cardiac, and neurological surgery, which were excluded by Pearse and colleagues). We noted the type of discharge from hospital (in this case "death"), predefined in the computer system and reported to the NHF.

As shown in the table, the average in-hospital mortality for all surgical procedures in 2011 in Poland was 0·98%—ie, 18 times lower than that shown by Pearse and colleagues.[1] Additionally, we have extracted from the NHF database the data on mortality in the six hospitals in Poland that took part in Pearse and colleagues' study. In those six hospitals, average in-hospital mortality after all surgical procedures in 2011 was 1·07%, which is very similar to the whole-country rate.

We suggest that Pearse and colleagues' methods are misleading

	Number of procedures	Number of in-hospital deaths
Vascular	100 792	1964 (1·9%)
Eye	216 208	104 (0·005%)
Skin and mammary gland	107 896	355 (0·33%)
Gastrointestinal tract	335 706	7501 (2·2%)
Head and neck	123 864	98 (0·08%)
Endocrinological	23 381	26 (0·11%)
Heart and circulation	235 891	4129 (1·8%)
Bone and muscle	422 329	2948 (0·70%)
Genitourinary tract	125 641	308 (0·25%)
Neurosurgery	42 763	2591 (6·1%)
Respiratory system	27 537	464 (1·7%)
Liver, pancreas, and spleen	118 070	1391 (1·2%)
Female genital tract	361 033	109 (0·03%)
Polytrauma	146	40 (27·4%)
Total	2 241 257	22 028 (0·98%)

Table: **In-hospital mortality after surgical procedures in Poland in 2011, according to surgical specialty**

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and insufficient to draw conclusions valid for whole countries. The results might therefore be unreliable not only for Poland but also for other European countries.

We declare that we have no conflicts of interest.

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We have three concerns about Rupert Pearse and colleagues' groundbreaking EuSOS study.[1]

First, the use of in-hospital mortality is not robust, since local behaviour introduces substantial bias.[2] The use of 30-day mortality would remove this problem. The registration details of the study[3] specify "28-day mortality" as a secondary outcome, a measure absent from the study documentation[4] and report.[1]

Second, it is reasonable to adjust mortality with the UK as the reference standard. Less reasonable is to use the UK (22·8% of all data) as a benchmark for statistical comparison. Table 4 in the EuSOS appendix supports this contention, since Pearse and colleagues' regression model shows a p value of <0·0001 for "country" versus the UK. With an appropriate analysis that uses the whole study population as a reference standard, the UK is likely to be an outlier, which is clearly impossible if it is used as the reference standard.

Third, Pearse and colleagues state that low rates of admission to critical care prevent "any detailed comparison of this resource between nations", but postulate that availability of intensive-care facilities affects outcomes, citing Germany versus the UK. Examination of their data, however, seems to refute their hypothesis—for example, Sweden has both a low mortality rate (1·8%) and a low rate of admission to critical care (3·2%). More formal analysis of this relation seems appropriate, with adjustment for confounding variables.

Pearse and colleagues might be able to respond to our concerns by re-examining their data, and applying the suggested analyses.

We declare that we have no conflicts of interest.

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In their study on postoperative mortality in Europe,[1] Rupert Pearse and colleagues point out that international comparative data might provide important insights into the delivery of health care for patients undergoing surgery. As a consequence, they provide estimates for in-hospital mortality in 28 European countries. Unadjusted mortality rates differed substantially, ranging from 1·2% in Iceland to 21·5% in Latvia. Poland, Latvia, Romania, and Ireland had higher mortality rates than the UK even after adjustment for confounding variables.

However, the representativeness of the samples and comparability of countries seems questionable: in Poland, only six hospitals (including one university hospital) took part in the study, whereas in the UK, the reference country, 100 hospitals (including 52 university hospitals) were studied.

The observation period of 7 days is also probably not representative of the volume of surgery in a hospital. It seems highly unlikely that every fifth or sixth patient dies after an operation, as described for Latvia or Poland. Thus conclusions about any difference between countries remain speculative.

Nonetheless, this dataset clearly describes a large cross-section of health care in Europe and provides relevant information on the drivers of postoperative mortality. However, it would have been worthwhile to get more detailed information on other influencing factors—eg, preoperative assessment, checking of equipment and drugs, syringe labelling, and infection control—as described in the Helsinki Declaration on Patient Safety in Anaesthesiology.[2]

We declare that we have no conflicts of interest.

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Authors' reply

We did a large study to provide data at a European level on mortality after surgery.[1] We are not aware of any previous work exploring surgical outcomes on an international basis. However, the 7-day cohort design does not provide definitive data. The intention was to inform and stimulate

the design of further research to improve outcomes for patients undergoing surgery.

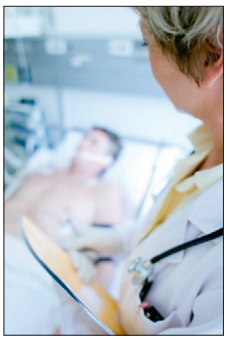
We specifically state in the paper that these data cannot be used as an accurate indication of mortality in individual countries. There are obvious risks of overgeneralising small cohorts with likely selection bias. Some correspondents suggest that mortality has been over-reported in some centres. During the data cleaning process we asked local investigators to complete a large number of validation checks and also asked national coordinators to facilitate this process.

We are aware that the mortality rates in the EuSOS study have subsequently been compared to registry data in some countries. Such a comparison could stimulate helpful debate as we attempt to understand surgical outcomes in individual countries. Indeed, we requested the help of national coordinators in identifying any publicly available data against which our data should be compared. We presented all such evidence where it was made available. Nonetheless, we advocate caution because differences in estimates are not unexpected when comparing mortality estimates calculated by use of very different methods. Our selection criteria excluded low-mortality patients who receive care in dedicated care pathways such as obstetrics, day case, and cardiac surgery. It is unclear to us whether comparisons with registry data allow correct application of the same selection criteria used in our study. We also note that most national health-care registries were not designed to audit patient outcome and might underestimate mortality.[2]

To further inform the discussion of our findings, we have done an additional, more conservative, sensitivity analysis in which we excluded hospitals above the 95th centile for mortality and also those that recruited ten patients or fewer during the 7-day study period. This process excludes 72 centres and 944 patients from the cohort, leaving 426 centres and 45 595 patients to be analysed. Since high-mortality centres were excluded, we saw an overall reduction in mortality from 4% to 3%. The findings of this sensitivity analysis remain consistent with our original conclusion that mortality was higher than expected, with significant variations between nations. In this analysis, outcomes in Finland were better than the UK (odds ratio 0·5, 95% CI 0·2–0·9]), whereas outcomes in Romania were worse (2·8, 1·7–4·6).

We agree that the overall patient population could also be used as a reference in making such comparisons. This has very little effect, however, on the relative position of nations and does not alter our conclusions. We reported data as in-hospital mortality censored at 60 days. The great majority of deaths occurred within 14 days of surgery. The primary and secondary outcome measures are clearly described in the full protocol, which is available online and has also been published in summary form in a peer-reviewed journal.[3] Any exploration of the effect of critical-care admission on postoperative mortality is affected by the definition used. We predefined critical care as a facility routinely capable of admitting patients who require invasive ventilation overnight. We suspect that, in some countries, at least a proportion of postanaesthetic recovery units meet these criteria but are not locally regarded as critical care. Meanwhile, in other nations, there is evidence to suggest that some facilities are identified as intensive-care units but do not offer organ support.[4] We did collect data of relevance to the Helsinki Declaration on Patient Safety in Anaesthesiology and we plan to explore this in the near future.

In summary, the findings of our study indicate that mortality rates after non-cardiac surgery were higher than expected, that variations in mortality between nations suggest that some deaths might be preventable, and that there is evidence of process failure in the allocation of critical-care resources among surgical patients. We would welcome robust public audit of patient outcomes, because only this can provide an accurate indication of these factors. We also encourage ongoing research to identify more effective approaches to perioperative care for high-risk patients. Given that the surgical population is very large, these measures could prevent a substantial number of deaths.



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For the **EuSOS website** see http://eusos.esicm.org/

We declare that we have no conflicts of interest.

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Mortality after surgery in Ireland

The European Surgical Outcomes Study (EuSOS)[1] shows mortality rate in Ireland of 6·4% (95% CI 4·8–8·1%) for all elective and non-elective inpatient surgery, excluding planned day-case surgery, cardiac surgery, neurosurgery, radiological surgery, and obstetric surgery, during a week in April, 2011. This rate was significantly higher than that of 3·6% (95% CI: 3·2–3·9%) for the UK, which was the reference country. If true, these data have serious implications for the Irish health-care system.

There were repeated unsuccessful requests to the EuSOS authors by the Royal College of Surgeons in Ireland (RCSI) and the College of Anaesthetists of Ireland to get access to the EuSOS data. In view of the inability to validate the Irish EuSOS data and the importance of the findings, a direct replication study—the Irish Surgical Outcomes Study (ISOS)—was done (appendix). This study involved all 17 Irish hospitals that participated in EuSOS, and we applied the same methods (details were available from the EuSOS website) and covered the same period in April, 2011.

The ISOS findings showed substantial differences from the EuSOS data for the same period. An additional 215 eligible patients were identified, but fewer deaths (table).

These substantial differences raise serious concerns regarding the quality and completeness of EuSOS. Ireland is not the only country to dispute EuSOS findings;[2–4] at least three countries (of 28) have publicly challenged the integrity of EuSOS data. These concerns call into question the propriety of retaining the original paper in the literature and plans for the original team to continue to produce a series of further papers from this dataset.

We declare that we have no conflicts of interest.

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Authors' reply

Sally Doherty and colleagues report the findings of a retrospective study of surgical mortality in Ireland during the same period studied in our prospective European study (EuSOS).[1] Using a different method, the authors collected data describing a larger cohort of patients and identified fewer deaths, resulting in a different mortality estimate. While the authors use the original EuSOS data as a reference for their findings, they also suggest these data are inaccurate. The overall mortality for any large population of surgical patients is crucially dependent on the representation of high-risk surgical patients within it. The lower numbers of critical-care admissions and deaths suggest the high-risk group was not so strongly represented in this repeat study population. This difference might also represent a stronger tendency for investigators to include patients undergoing complex surgery in the prospective study. Nonetheless, the hospital mortality of 2·5% is higher than previous estimates, which range from 1 to 2%,[2–4] and remains a cause for concern.

The authors sought our assistance with their study and we encouraged them to make full use of our original protocol and case record form. We also confirmed which Irish hospitals took part in our original study. The authors did request the EuSOS data for Ireland but, despite our repeated requests, were unable to provide a prospective statistical analysis plan. We remain prepared to share the data provided this basic methodological standard is met. Since publication of the report, we have worked with various groups to further analyse the EuSOS data and better understand our findings. Prospectively defined analyses of the relation between mortality and haemoglobin, serum sodium, surgery at nighttime, and use of the WHO checklist have all generated important findings and confirmed the validity of our data. Notably, prospective linkage with Swedish registry data has confirmed the accuracy of the stated hospital mortality and shows a four-fold increase in mortality within 1 year of surgery. Therefore, surgical patients could remain at risk even in nations with low early postoperative mortality rates.

We previously acknowledged[1,5] the pragmatic nature of the EuSOS study. We have repeatedly indicated that our study does not provide a definitive mortality estimate, particularly in countries that contributed few patients, but that it demonstrates the need for further research and audit of

See Online for appendix

	EuSOS	ISOS
Patients identified	856	1071
Median hospital stay	3 (1–6)	3 (1–7)
Admitted to critical care	66	56
Percentage admitted to critical care	7·7% (5·9–9·5)	5·3% (4·0–6·9)
Number died in hospital	55	27
Percentage died in hospital	6·4% (4·8–8·1)	2·5% (1·9–3·4)
Unadjusted odds ratio*	1·86 (1·39–2·49)	0·70 (0·45–1·04)

Data are n, median (IQR), or % (95% CI), unless otherwise stated. For the details of the ISOS study, see appendix. ISOS= Irish Surgical Outcomes Study. EuSOS=European Surgical Outcomes Study. *UK as reference.

Table: **The ISOS data compared with the EuSOS findings**

outcomes for this population. In view of the very large size of the surgical population, such measures might lead to a substantial reduction in the number of deaths.

We declare that we have no conflicts of interest.

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E anophelis outbreak in an intensive-care unit

We read with interest Jeanette Teo and colleagues' report (Sept 7, p 855)[1] of the first outbreak of *Elizabethkingia anophelis* identified by 16SrRNA sequencing and whole-genome alignment. The subgroup of isolates had been previously identified as *Elizabethkingia meningoseptica* on the basis of matrix-assisted laser desorption-ionisation time-of-flight (MALDITOF) mass spectrometry analysis.

The history of this microorganism starts with its description as a cause of infant meningitis by Elizabeth O King at the US Centers for Disease Control and Prevention (CDC). She first isolated an organism referred to as CDC group IIa in 1959 and named it *Flavobacterium meningosepticum*. It was subsequently renamed *Chryseobacterium meningosepticum*, and classified in the new genus *Elizabethkingia*, in 2005.[2]

We believe that modern techniques (such as MALDITOF and sequencing) might generate more and more pseudo first outbreaks. Outbreaks of *F meningosepticum*, *C meningosepticum*, and *E meningoseptica* have been described in several patient settings, including intensive-care units.[3–5] Thus, what is new here, except the name? To be considered as new outbreaks, future reports should describe a new source or pathway of transmission and not merely one that appears new because of the diagnostic methods presently used.

We declare that we have no conflicts of interest.

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Authors' reply

Andreas Voss and colleagues have alluded to the fact that 16SrRNA sequencing in the early 2000s allowed *Elizabethkingia* to be placed separately from the genus of *Chryseobacterium*. Next-generation sequencing has facilitated a higher level of differentiation between two very distinct species of *Elizabethkingia*, namely *Elizabethkingia meningoseptica* and *Elizabethkingia anophelis*.[1,2] Our analyses identifying the intensive-care unit outbreak strain as *E anophelis* is not just a reclassification of an old species as Voss and colleagues suggest. *E anophelis* is an entirely separate species with infection potential. *E anophelis* is presently understudied but should not be considered irrelevant in the clinical setting. Our sequencing data suggest the presence of a substantial number of virulence determinants, and studies to assess *E anophelis*' virulence potential in animal are in progress.

Investigation of novel outbreaks when paired with comparative genome sequencing data provides important information to understand transmission of a pathogen, and especially so for rare organisms. Comparative genomics is a crucial approach in the discovery of virulence determinants and genetic markers of uncharacterised bacterial species. Genome-based approaches can be associated with other omics-based approaches (eg, transcriptomics and proteomics)[3] to analyse bacterial physiology and pathogenesis mechanisms.

An intriguing and important issue is the transmission pathway of *E anophelis*. We speculate that malaria carriage in patients might be at the origin of *E anophelis* transmission in the hospital setting, which we are investigating.

We declare that we have no conflicts of interest.

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The measles crisis in Europe—the need for a joined-up approach

Measles elimination in Europe is in crisis. More than 80 000 confirmed cases were reported in 2018 in the 53 countries in the WHO European Region,[1] the highest figure for 20 years. 14 countries in the region reported more than 500 confirmed cases, including four countries that were previously deemed to have eliminated measles (Greece, Albania, Israel, and the UK), meaning interrupted transmission for 3 years. New strategies are urgently needed to put measles elimination in Europe back on track.

In theory, controlling measles should be straightforward. Two doses of the measles, mumps, and rubella (MMR) vaccine provide highly efficacious protection that is long lasting.[2] Yet, in practice, achieving elimination has proven challenging. One of the most contagious diseases, measles can strike susceptible pockets even if vaccination coverage on a national level is high. Although asserting elimination status for individual nations might serve as a motivational tool, countries can experience large outbreaks even after several years of interrupted transmission. Countries such as Greece, Germany, and Kyrgyzstan reported consistently high MMR uptake over the past decade but are still experiencing outbreaks. Moreover, outbreaks do not occur in isolation: they traverse country borders, sometimes lasting years, and affecting different countries at different times.[3]

In light of these issues, there is a need to link efforts across the continent. The Pan American Health Organization[4] interrupted measles transmission in the early 2000s through combined strategies, including high routine immunisation, catch-up campaigns during periods of low transmission, and follow-up campaigns ensuring high levels of immunity at the age of school entry, all applied uniformly across the Americas. Applying a similar joined-up approach in Europe would serve the dual purpose of increasing immunity in the general population while reducing the chance of imported cases reaching susceptible pockets.

Epidemiological investigation would also benefit from combined efforts. Linking genetic and case data to better understand chains of transmission has proven successful for other diseases[2] and might reveal the interconnectivity of measles across Europe.[5] Subnational seroprevalence studies could be used to better identify pockets of susceptibles.[6] Improved vaccine supply, advocacy, and communication to population groups found to be most at risk could help increase immunity to the levels required.[7] Such efforts would come at a fraction of the cost of responding to outbreaks.[8] The Americas have shown that elimination of measles is feasible through a combination of political willpower, targeted interventions, and concerted effort. If Europe can sustain a similar approach, it might still follow suit.

We declare no competing interests.

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Media for Medical/Getty Images

Post-surgery mortality in Poland

In 2012, *The Lancet* published the results of a 7 day cohort study on mortality after surgery in Europe (Sept 22, 2012, p 1059).[1] The Article contained information that was inappropriately used in Poland to promote a film, *Botoks*, which was watched by more than 2 million people. I am concerned that these data could still be used in similar ways.

According to table 2,[1] post-surgery mortality in the Polish sample was 17·9%. According to data collected at the behest of the Polish Society of Anaesthesiology and Intensive Therapy,[2] post-surgery mortality was just 0·5%. The authors[1] also reported that post-surgery mortality in Latvia was 21%, whereas the data collected for the Polish Society of Anaesthesiology and Intensive Therapy suggest that it is actually 0·66%.[2] If mortality was so high, even in select hospitals, one would expect this to be a major topic of health-care discussions in both countries.

According to Patryk Vega, director of *Botoks*,[3] the film was watched by 1 458 609 people within its first 10 days; subsequent media reports[4] said that it attracted over 2 million views in its first month. *The Guardian*[5] reported that *Botoks* was also the third highest grossing

foreign-language film in the UK and Ireland in 2017.

The film's trailer opens with the statement that "17% of patients did not survive a surgery in Poland last year". Some Polish commentators[6] and media[7] were quick to point out how similar this number was to the 17·9%, as shown in *The Lancet*.[1] This is an example of how data from the Article can be used in unfair criticism of the Polish health system, both at home and abroad, which can ultimately result in less trust for doctors and thus, sadly, in more deaths.

I am not sure that revising the data for Poland and Latvia would be enough to mitigate this problem. As Maria Wujtewicz and Mariusz Piechota[2] noted, "Since two national coordinators reported serious reservations regarding the data presented by Rupert M Pearse MD and colleagues…the remaining data on postoperative hospital mortality (from all 28 countries participating in the study) provided in this article should be verified based on the information sent by local coordinators. Verification ought to be supervised by national EuSOS coordinators." This line of criticism does not seem to have been addressed in any of the Authors' Replies[8,9] to readers' Correspondence. I believe that it should be addressed, and that, at the very least, the data for Poland and Latvia ought to be corrected.

I declare no competing interests.

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Author's reply

Stanislaw Krawczyk refers to the director Patryk Vega and his film *Botoks*, which provides a fictional account of the experiences of individuals receiving health care in Poland. The film, which has been widely viewed, caused outrage among health-care workers in Poland, who are depicted in an extremely negative way, perhaps the most striking example being the serious sexual assault of a patient by a member of hospital staff. The film is provocative to say the least, and some consider it deliberately misleading. I understand from colleagues in Poland that the film director was subject to legal action by several organisations relating to misrepresentation of various statistics about the Polish health-care system. The film does include a statistic regarding postoperative mortality but does not cite our Article[1] as a source.

As with any epidemiological research, we can only describe patterns in the data collected. We must be cautious in making any generalisation to the wider population we sample from. In our Article,[1] we recognised that our overall mortality figure was at the higher end of published estimates, and we made it clear that readers should not draw conclusions about outcomes in individual countries, especially those with a small number of participating hospitals. These mortality estimates cannot be considered representative of the entirety of the health-care systems in question. Our focus was instead placed on the variation in outcomes between countries that sampled their surgical populations in the same way.

In the 5 years since the publication of this work, epidemiological studies[2–5] from several international groups have revealed more about outcomes after surgery. The consistent message is that a high-risk subpopulation of surgical patients exists that accounts for about 10–15% of inpatient procedures. High-risk patients are typically older with severe chronic disease. In a technical sense, surgery and anaesthesia are safe throughout Europe, yet high-risk patients still frequently develop medical complications, such as pneumonia or myocardial infarction, in the days following surgery.

Postoperative complications in high-risk patients are widely agreed to be the primary cause of preventable deaths after surgery in high-income countries. The proportion of such patients included in any epidemiological sample has a considerable effect on the overall mortality estimate. It is now clear that the findings of large epidemiological studies of surgical populations are very susceptible to this source of bias. We studied all surgical procedures (ie, the entire population, not a sample) performed in UK National Health Service hospitals in a 5-year period from 2009 to 2014.[2] Among the 39 million procedures performed, the overall 30-day mortality was 1·1% (twice the mortality quoted for Poland by Krawczyk), increasing to 2·3% after 90 days. Importantly, these findings were very sensitive to how surgery was defined and categorised. Using the broadest definition of which procedures count as surgery, 12 500 procedures are performed per 100 000 population, but this falls to

just 2 400 procedures for the strictest definition. Confusion is caused by the large volume of very minor procedures, which might or might not take place in an operating theatre, sometimes under anaesthesia and sometimes not. The inclusion or exclusion of low-risk day-case surgery or high-risk emergency surgery has a considerable effect on both the apparent number of procedures and the apparent mortality. This is highly relevant to our 2012 Article[1] because we excluded day-case surgery but included emergency surgery. Furthermore, we now believe that local investigators in Poland and elsewhere took much more trouble to collect data describing major surgeries at the expense of omitting minor (low-risk) procedures. This explains the face validity of numerous secondary analyses of these data for risk factors such as anaemia and serum sodium,[6,7] through to standards of care such as use of the WHO safe surgery checklist.[8] In a subsequent international study of elective surgery only,[3] we did not identify such high mortality. Despite offering assurances of complete data control, we were unable to persuade societies in Poland and Ireland to participate in this comparative study, and an opportunity for clarification was missed.

It has been my continued personal career aim to promote better perioperative care in order to improve outcomes for high-risk surgical patients. This is embodied in the concept of perioperative medicine, which is now being widely adopted throughout the world as an approach to improving short-term and long-term patient outcomes, and hence the success of surgery as a treatment. Epidemiological research provides essential information by describing which patients experience poor outcomes, thus guiding subsequent interventional trials and quality improvement programmes. Among numerous examples of positive international effects, the aforementioned work has driven a major national campaign to promote perioperative medicine led by the Royal College of Anaesthetists in the UK, and was used to make the case to the Romanian Ministry for Health for more investment in perioperative care resources. In these examples, discussion of the research did not centre on specific mortality estimates, nor on technical error by surgeons and anaesthetists, but on whether the paper provided evidence of a need to improve the quality of perioperative care. I share Krawczyk's frustration with the way these research findings have been misrepresented. However, I feel I must also emphasise the considerable positive effects the work has had in many countries.

I hold various grants from public and commercial funders for research into better ways to care for high-risk surgical patients.

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Rheumatoid arthritis-associated bronchiectasis


Science Photo Library/Getty Images

We read with great interest the comprehensive review of diffuse bronchiectasis by Patrick Flume and colleagues (Sept 8, 2018, p880).[1] The authors mentioned the autoimmune diseases (most notably, rheumatoid arthritis and ulcerative colitis) that can be associated with bronchiectasis and for which causative genes have not yet been identified. We agree with their conclusion; however, as they exclusively detailed the associated genetic risk loci in inflammatory bowel diseases, we would like to add that, to our knowledge, the only family-based association study in patients with non-cystic fibrosis diffuse bronchiectasis was done in patients with rheumatoid arthritis.[2] We found that the frequency of *CFTR* gene variants was higher in family members with rheumatoid arthritis-diffuse bronchiectasis than in unaffected relatives or in unrelated healthy controls, but not in family members with rheumatoid arthritis only.[2] *CFTR* variants were also more frequent in family members with rheumatoid arthritis diffuse bronchiectasis compared with those with rheumatoid arthritis only (odds ratio 5·3, 95% CI 2·48–11·33; p<0·0001), and this feature co-segregated with rheumatoid arthritis diffuse bronchiectasis in the families.[2] We therefore believe that *CFTR* variants in patients with rheumatoid arthritis appear to be important markers of the risk of associated diffuse bronchiectasis, which has been linked to a less favourable prognosis.[3]

We declare no competing interests.

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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Pearse RM, Moreno RP, Bauer P, et al, for the European Surgical Outcomes Study (EuSOS) group for the Trials groups of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology. Mortality after surgery in Europe: a 7 day cohort study. *Lancet* 2012; **380:** 1059–65.

Variations in mortality for surgical patients across 28 European nations: An international seven day cohort study

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***see appendix**

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Supplementary table 1. Percentage of patients presenting with co-existent diseases and proportions of procedures categorized as minor, intermediate or major per country. COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; IDDM, diabetes mellitus taking insulin; NIDDM, diabetes mellitus not taking insulin.

	Co-morbid factors (% of patients)									Hospital factors			Grade of Surgery (% of patients)		
	Smoker	Cirrhosis	Heart failure	COPD	CAD	IDDM	NIDDM	Cancer	Stroke	n	Patients per hospital	University hospitals n (%)	Minor	Inter-mediate	Major
Belgium	21·4	1·5	5·9	12·4	13·2	5·0	7·9	7·1	4·2	16	93	7 (44%)	32·1	42·3	25·7
Croatia	22·4	1·6	4·7	6·6	13·4	3·8	8·6	4·9	3·8	16	110	8 (50%)	23·7	56·5	19·8
Cyprus	17·8	2·2	8·9	8·9	17·8	4·4	11·1	4·4	2·2	1	45	0 (0%)	68·9	26·7	4·4
Czech Republic	21·0	0·7	0·7	8·1	12·2	2·5	9·2	1·8	4·6	2	217	2 (100%)	42·9	47·7	9·4
Denmark	23·3	1·0	4·2	13·6	12·4	3·7	7·1	3·1	5·3	15	67	6 (40%)	28·5	47·2	24·3
Estonia	23·4	0·6	6·3	6·9	19·8	2·9	5·8	6·3	2·9	4	182	2 (50%)	11·0	50·1	38·9
Finland	18·8	1·1	5·4	12·7	16·2	6·7	9·5	5·2	6·0	12	89	3 (25%)	20·6	49·7	29·7
France	25·4	1·4	4·7	10·7	8·3	4·0	6·8	3·7	3·4	23	99	16 (70%)	40·4	42·7	16·8
Germany	23·2	1·4	10·5	11·3	14·5	6·6	7·6	6·5	4·6	37	143	19 (51%)	42·0	42·9	15·1
Greece	29·1	0·6	3·1	7·8	16·0	2·8	9·4	2·6	3·4	29	62	11 (38%)	21·9	55·7	22·5
Hungary	23·2	2·4	5·6	12·2	21·3	5·6	10·3	4·3	5·8	9	69	3 (33%)	20·1	61·0	18·8
Iceland	11·7	0·0	6·2	11·1	17·3	1·9	6·2	1·2	6·8	4	41	3 (75%)	11·7	56·8	31·5
Ireland	24·5	0·7	3·9	13·8	11·2	4·2	6·1	4·0	2·2	18	48	15 (83%)	20·4	54·3	25·2
Italy	20·5	1·6	2·3	10·9	8·3	3·5	7·4	5·8	4·2	35	76	15 (43%)	28·7	43·3	28·1
Latvia	26·5	0·7	4·0	7·6	27·8	4·3	4·0	3·3	4·0	3	101	2 (67%)	7·3	51·3	41·4
Lithuania	12·5	0·5	7·7	4·3	32·0	2·4	4·5	4·0	6·4	3	125	2 (67%)	28·0	62·1	9·9
Netherlands	21·0	0·8	6·2	9·2	11·2	5·4	4·7	7·2	4·9	18	90	6 (33%)	17·9	44·2	37·9
Norway	19·9	0·3	5·2	8·4	13·8	4·4	4·6	4·8	4·1	10	69	4 (40%)	16·1	47·8	36·1
Poland	27·2	0·5	3·3	11·8	30·2	6·5	5·8	3·0	3·5	6	66	1 (17%)	45·1	42·1	12·8
Portugal	19·7	1·4	5·7	9·9	8·3	4·4	10·4	5·6	4·4	19	78	9 (47%)	27·9	47·5	24·6
Romania	24·4	1·5	8·8	6·6	32·1	2·6	8·5	4·4	3·5	22	59	11 (50%)	20·9	61·6	17·6
Serbia	34·1	0·0	3·5	4·8	16·5	3·5	10·6	2·4	2·4	2	43	2 (100%)	18·8	37·6	43·5
Slovakia	22·4	1·0	1·9	8·0	27·2	5·4	8·5	5·8	4·2	10	116	5 (50%)	34·9	50·0	15·1
Slovenia	19·1	0·6	5·2	6·8	10·2	3·5	6·4	2·9	3·7	5	104	2 (40%)	41·3	45·4	13·3
Spain	21·9	1·5	3·1	11·3	7·7	4·7	10·1	4·2	4·5	61	89	43 (70%)	17·5	49·7	32·8
Sweden	16·5	1·3	4·9	10·0	12·7	6·2	4·8	5·6	5·7	10	131	7 (70%)	30·1	46·6	23·3
Switzerland	21·1	0·9	3·5	7·9	9·9	3·6	5·2	3·7	2·3	5	204	2 (40%)	23·1	56·1	20·8
United Kingdom	18·1	0·5	2·5	14·5	13·4	4·0	6·5	3·8	4·5	103	103	52 (50%)	20·1	45·9	33·9

Supplementary table 2. Sensitivity analysis for univariate logistic regression model utilising three random (disjoint) sub-samples of countries (models one to three) and a fourth model containing the whole set excluding the United Kingdom. OR, odds ratio; ASA, American Society of Anesthesiologist's score; COPD, chronic obstructive pulmonary disease, IDDM, diabetes mellitus taking insulin; NIDDM, diabetes mellitus not taking insulin.

	Random model 1 (n=22488)		Random model 2 (n=13899)		Random model 3 (n=10037)		Without UK (n=35873)		Simulation Results		Analysis of whole dataset	
	Country n= 10		Country n= 9		Country n= 9						n= 46073	
	OR	p-value	OR	p-value	OR	p-value	OR	p-value	OR		OR	p-value
									Lowest	Highest		
Age (per year)	1·02	<0·0001	1·01	<0·0001	1·02	<0·0001	1·01	<0·0001	1·01	1·02	1·01	<0·0001
Male sex	1·10	0·17	1·17	0·05	1·26	0·04	1·17	0·003	1·10	1·26	1·15	0·003
Smoker (yes/no)	0·84	0·06	0·94	0·52	0·96	0·75	0·91	0·13	0·75	0·91	0·90	0·07
ASA score												
1	-	-	-	-	-	-	-	-	-	-	-	-
2	0·96	0·66	0·95	0·61	0·91	0·56	0·88	0·08	0·88	0·96	0·94	0·36
3	1·53	<0·0001	1·47	0·001	1·62	0·004	1·36	<0·0001	1·36	1·62	1·51	<0·0001
4	6·48	<0·0001	6·33	<0·0001	9·32	<0·0001	6·15	<0·0001	6·15	9·32	6·75	<0·0001
5	41·30	<0·0001	16·94	<0·0001	128·06	<0·0001	31·32	<0·0001	16·94	128·06	35·61	<0·0001
Grade of Surgery												
Minor	-	-	-	-	-	-	-	-	-	-	-	-
Intermediate	0·78	0·009	0·96	0·66	1·30	0·08	0·97	0·68	0·78	1·30	0·93	0·22
Major	1·40	<0·0001	1·31	0·012	3·07	<0·0001	1·63	<0·0001	1·31	3·07	1·59	<0·0001
Urgency of surgery												
Elective	-	-	-	--	-	-	-	-	-	-	-	-
Urgent	1·64	<0·0001	1·51	<0·0001	2·56	<0·0001	1·81	<0·0001	1·51	2·56	1·71	<0·0001
Emergency	3·47	<0·0001	2·42	<0·0001	4·35	<0·0001	3·36	<0·0001	2·42	4·35	3·20	<0·0001
Surgical specialty												
Orthopaedics	1·07	0·65	0·88	0·47	1·16	0·50	0·89	0·29	0·88	1·16	1·02	0·85
Breast	0·60	0·08	0·86	0·57	0·86	0·75	0·87	0·46	0·60	0·87	0·76	0·12
Gynaecology	0·85	0·38	0·89	0·56	0·31	0·004	0·81	0·14	0·31	0·85	0·76	0·04
Vascular	1·72	0·003	1·58	0·03	1·31	0·39	1·49	0·004	1·31	1·72	1·61	0·0001
Upper gastro-intestinal	1·79	0·002	1·41	0·10	3·35	<0·0001	1·91	<0·0001	1·41	3·35	1·88	0·0001
Lower gastro-intestinal	1·32	0·09	1·59	0·008	2·22	0·001	1·65	<0·0001	1·32	2·22	1·54	0·0001
Hepato-biliary	1·23	0·31	1·48	0·06	1·35	0·32	1·41	0·01	1·23	1·48	1·35	0·025
Plastic / cutaneous	0·93	0·73	0·66	0·10	0·73	0·38	0·71	0·04	0·66	0·93	0·79	0·12
Urology	0·72	0·07	0·88	0·52	0·80	0·42	0·82	0·15	0·72	0·88	0·78	0·042
Kidney	0·23	0·04	0·33	0·13	1·80	0·24	0·59	0·15	0·23	1·80	0·51	0·05
Head and neck	0·66	0·03	1·07	0·71	0·61	0·07	0·81	0·10	0·61	1·07	0·82	0·09
Other	-	-	-	-	-	-	-	-	-	-	-	-
Laparoscopic surgery	0·64	<0·0001	0·86	0·25	0·52	0·004	0·75	0·002	0·52	0·75	0·69	<0·0001
Co-morbid disease												
Cirrhosis	3·28	<0·0001	3·09	<0·0001	3·91	<0·0001	3·67	<0·0001	3·09	3·91	3·64	<0·0001
Heart failure	2·86	<0·0001	1·51	0·014	2·16	<0·0001	1·90	<0·0001	1·51	2·86	2·10	<0·0001
COPD	1·13	0·24	1·35	0·015	1·23	0·23	1·15	0·09	1·13	1·35	1·21	0·0008

Coronary artery disease	1·67	<0·0001	1·64	<0·0001	2·14	<0·0001	1·71	<0·0001	1·64	2·14	1·73	<0·0001
IDDM	1·73	<0·0001	1·80	<0·0001	1·64	0·016	1·78	<0·0001	1·64	1·80	1·73	<0·0001
NIDDM	1·02	0·89	1·03	0·83	1·14	0·51	1·05	0·59	1·02	1·14	1·05	0·61
Metastatic cancer	1·80	<0·0001	1·96	<0·0001	2·04	<0·0001	1·98	<0·0001	1·80	2·04	1·91	<0·0001
Stroke	1·57	0·001	1·68	0·001	1·33	0·25	1·53	<0·0001	1·33	1·68	1·57	<0·0001

Supplementary table 3. Binary logistic regression analysis (single level) (n=46073/46539) assessing pre- or intra-operative factors relating to hospital mortality.

	n	Odds ratio	95% confidence intervals	p-value
Country				<0·0001
Belgium	1478/1486	1·07	0·78 - 1·46	0·69
Croatia	1755/1767	2·77	2·23 - 3·44	<0·0001
Cyprus	45/45	0·70	0·10 - 4·92	0·72
Czech Republic	427/434	0·89	0·46 - 1·71	0·73
Denmark	994/1000	0·94	0·65 - 1·37	0·76
Estonia	726/727	0·45	0·25 - 0·80	0·007
Finland	1070/1071	0·40	0·26 - 0·61	<0·0001
France	2264/2278	1·05	0·81 - 1·37	0·71
Germany	5243/5284	0·76	0·62 - 0·94	0·01
Greece	1795/1803	1·13	0·86 - 1·49	0·37
Hungary	619/621	1·09	0·70 - 1·70	0·69
Iceland	162/162	0·38	0·09 - 1·56	0·18
Ireland	854/856	2·02	1·48 - 2·75	<0·0001
Italy	2622/2673	1·85	1·50 - 2·29	<0·0001
Latvia	300/302	8·53	6·13 - 11·87	<0·0001
Lithuania	373/375	1·07	0·58 - 1·97	0·84
Netherlands	1566/1627	0·61	0·42 - 0·89	0·01
Norway	686/689	0·41	0·22 - 0·78	0·006
Poland	391/397	7·73	5·71 - 10·48	<0·0001
Portugal	1477/1489	1·18	0·90 - 1·56	0·23
Romania	1290/1298	2·32	1·80 - 2·99	<0·0001
Serbia	85/85	0·89	0·21 - 3·74	0·88
Slovakia	1150/1156	4·52	3·58 - 5·69	<0·0001
Slovenia	514/518	1·01	0·60 - 1·71	0·97
Spain	5412/5433	1·17	0·98 - 1·40	0·09
Sweden	1304/1314	0·49	0·32 - 0·75	0·001
Switzerland	1019/1019	0·66	0·42 - 1·04	0·07
United Kingdom (reference)	10452/10630	1·00	-	-
Urgency of surgery				<0·0001
Elective (reference)	34734/35049	1·00	-	-
Urgent	8810/8923	1·44	1·28 - 1·63	<0·0001
Emergency	2529/2557	2·23	1·89 - 2·64	<0·0001
Grade of surgery				<0·0001
Minor (reference)	11932/12041	1·00	-	-
Intermediate	22070/22231	0·83	0·73 - 0·94	0·004
Major	12071/12170	1·15	0·99 - 1·32	0·06
Surgical specialty				<0·0001
Orthopaedics	12123/12214	1·08	0·87 - 1·33	0·50
Breast	1496/1500	0·91	0·63 - 1·30	0·59
Gynaecology	3952/3972	0·96	0·73 - 1·26	0·76
Vascular	2354/2376	1·10	0·84 - 1·43	0·49

Upper gastro-intestinal	2214/2228	1·57	1·21 - 2·04	0·001
Lower gastro-intestinal	4937/4972	1·24	0·99 - 1·56	0·07
Hepato-biliary	2237/2247	1·14	0·86 - 1·51	0·36
Plastic / cutaneous	2404/2247	0·91	0·67 - 1·23	0·53
Urology	4846/4881	0·85	0·66 - 1·11	0·23
Kidney	456/463	0·47	0·24 - 0·95	0·035
Head and neck	5614/5640	1·04	0·82 - 1·33	0·74
Other (Reference)	3440/3463	1·00	-	-
Age (per year)	46073/46539	1·01	1·01 - 1·01	<0·0001
ASA				<0·0001
1 (reference)	11540/11642	1·00	-	-
2	21418/21582	0·77	0·66 - 0·89	0·001
3	11482/11574	1·06	0·89 - 1·25	0·54
4	1545/1559	3·85	3·13 - 4·75	<0·0001
5	88/90	13·51	8·07 - 22·60	<0·0001
Metastatic cancer	46073/46539	1·36	1·12 - 1·64	0·002
Cirrhosis	46073/46539	2·01	1·49 - 2·72	<0·0001
Intercept		0·02	0·01 - 0·00	<0·0001

Supplementary table 4. Hierarchical binary logistic regression model (n= 46073/46539) assessing pre- or intra-operative factors relating to in-hospital mortality using a two level model (patient / hospital) with hospital as a random factor. ASA, American Society of Anesthesiologist's score.

Variable	n	Odds ratio	95% confidence intervals	p-value
Country				<0·0001
Belgium	1478/1486	1·65	0·81 – 3·40	0·17
Croatia	1755/1767	1·89	0·94 – 3·80	0·07
Cyprus	45/45	0·82	0·04 – 16·70	0·90
Czech Republic	427/434	1·30	0·23 – 7·46	0·77
Denmark	994/1000	1·16	0·52 – 2·61	0·72
Estonia	726/727	0·60	0·16 – 2·28	0·45
Finland	1070/1071	0·44	0·19 – 1·05	0·06
France	2264/2278	1·36	0·73 – 2·56	0·34
Germany	5243/5284	0·85	0·50 – 1·43	0·54
Greece	1795/1803	1·20	0·67 – 2·16	0·55
Hungary	619/621	1·23	0·43 – 3·50	0·69
Iceland	162/162	0·47	0·07 – 3·41	0·46
Ireland	854/856	2·61	1·30 – 5·27	0·007
Italy	2622/2673	1·70	0·98 – 2·97	0·06
Latvia	300/302	4·98	1·22 – 20·29	0·025
Lithuania	373/375	1·21	0·21 – 6·95	0·83
Netherlands	1566/1627	0·63	0·28 – 1·41	0·26
Norway	686/689	0·51	0·17 – 1·49	0·22
Poland	391/397	6·92	2·37 – 20·27	<0·0001
Portugal	1477/1489	1·43	0·72 – 2·83	0·30
Romania	1290/1298	3·19	1·61 – 6·29	<0·0001
Serbia	85/85	1·06	0·11 – 10·05	0·96
Slovakia	1150/1156	2·15	0·91 – 5·07	0·08
Slovenia	514/518	1·12	0·30 – 4·22	0·86
Spain	5412/5433	1·39	0·89 – 2·18	0·15
Sweden	1304/1314	0·58	0·23 – 1·49	0·26
Switzerland	1019/1019	0·86	0·25 – 2·97	0·81
United Kingdom (reference)	10452/10630	1·00	-	-
Urgency of surgery				<0·001
Elective (reference)	34734/35049	1·00	-	-
Urgent	8810/8923	1·78	1·56 – 2·04	<0·0001
Emergency	2529/2557	3·23	2·66 – 2·64	<0·0001
Grade of surgery				<0·0001
Minor (reference)	11932/12041	1·00	-	-
Intermediate	22070/22231	0·79	0·68 – 0·91	0·001
Major	12071/12170	1·12	0·96 – 1·32	0·16
Surgical specialty				<0·0001
Orthopaedics	12123/12214	0·79	0·62 – 1·01	0·06
Breast	1496/1500	1·08	0·72 – 1·60	0·72
Gynaecology	3952/3972	0·92	0·68 – 1·25	0·60
Vascular	2354/2376	0·95	0·72 – 1·27	0·75
Upper gastro-intestinal	2214/2228	1·57	1·18 – 2·07	0·002

Lower gastro-intestinal	4937/4972	1·13	0·88 – 1·45	0·36
Hepato-biliary	2237/2247	1·10	0·81 – 1·49	0·53
Plastic / cutaneous	2404/2247	0·83	0·59 – 1·15	0·26
Urology	4846/4881	0·74	0·56 – 0·98	0·03
Kidney	456/463	0·38	0·18 – 0·82	0·01
Head and neck	5614/5640	1·15	0·88 – 1·49	0·32
Other (Reference)	3440/3463	1·00	-	-
Age (per year)	46073/46539	1·00	1·00 - 1·01	<0·0001
ASA				<0·0001
1 (reference)	11540/11642	1·00	-	-
2	21418/21582	0·76	0·64 – 0·90	0·002
3	11482/11574	1·20	0·98 – 1·46	0·07
4	1545/1559	4·75	3·74 – 6·04	<0·0001
5	88/90	18·03	10·73– 30·31	<0·0001
Metastatic cancer	46073/46539	1·39	1·14 – 1·71	0·002
Cirrhosis	46073/46539	2·13	1·54 – 2·95	<0·0001
Intercept	-	0·01	0·01 – 0·01	<0·0001

Supplementary table 5. Sensitivity analysis for two level model utilising three random (disjoint) sub-samples of countries (models one to three) of the dataset and a fourth model containing the whole set excluding the United Kingdom. OR, odds ratios; ASA, American Society of Anesthesiologist's score.

	Random model 1 (n=22337)		Random model 2 (n=13751)		Random model 3 (n=9985)		Without UK		Simulation Results		Analysis of whole dataset	
	Countries = 10		Countries = 9		Countries = 9		n= 35261				n= 46073	
	OR	p-value	OR	p-value	OR	p-value	OR	p-value	OR		OR	p-value
									Lowest	Highest		
Age (per year)	1·01	<0·0001	1·01	0·003	1·01	0·046	1·01	<0·0001	1·01	1·01	1·00	0·0001
Co-morbid disease												
Metastatic disease	1·20	0·25	1·56	0·01	1·52	0·06	1·55	0·0001	1·20	1·56	1·39	0·002
Cirrhosis	1·35	0·31	2·41	0·001	3·44	<0·0001	2·20	<0·0001	1·35	3·44	2·13	<0·0001
Urgency of surgery												
Elective (reference)	1·00	-	1·00	-	1·00	-	1·00	-	-	-	-	-
Urgent	1·80	<0·0001	1·70	<0·0001	1·90	<0·0001	1·77	<0·0001	1·70	1·90	1·78	<0·0001
Emergency	3·27	<0·0001	2·36	<0·0001	3·01	<0·0001	3·25	<0·0001	2·36	3·27	3·23	<0·0001
Grade of surgery												
Minor (reference)	1·00	-	1·00	-	1·00	-	1·00	-	-	-	-	-
Intermediate	0·72	0·002	0·81	0·08	0·94	0·73	0·81	0·008	0·72	0·94	0·79	0·001
Major	1·00	0·97	1·25	0·13	1·23	0·29	1·17	0·10	1·00	1·25	1·12	0·16
ASA score												
1 (reference)	1·00	-	1·00	-	1·00	-	1·00	-	-	-	-	-
2	0·75	0·02	0·81	0·17	0·78	0·22	0·73	0·001	0·73	0·81	0·76	0·002
3	1·23	0·15	1·25	0·21	1·18	0·48	1·09	0·45	1·09	1·25	1·20	0·07
4	4·47	<0·0001	6·19	<0·0001	4·66	<0·0001	4·45	<0·0001	4·45	6·19	4·75	<0·0001
5	24·05	<0·0001	7·75	<0·0001	54·16	<0·0001	16·05	<0·0001	7·75	54·16	18·03	<0·0001
Surgical procedure												
Orthopaedics	0·78	0·95	0·80	0·32	0·77	0·34	0·77	0·05	0·77	0·80	0·79	0·06
Breast	0·98	0·15	1·23	0·53	0·87	0·80	1·26	0·29	0·87	1·26	1·08	0·72
Gynaecology	1·18	0·58	0·77	0·33	0·48	0·08	0·94	0·71	0·48	1·18	0·92	0·60
Vascular	0·91	0·81	0·91	0·74	1·01	0·98	0·94	0·73	0·91	1·01	0·95	0·75
Upper gastro-intestinal	1·58	0·06	1·06	0·82	2·54	0·002	1·60	0·003	1·06	2·54	1·57	0·002
Lower gastro-intestinal	1·03	0·12	1·01	0·96	1·52	0·13	1·18	0·25	1·01	1·52	1·13	0·36
Hepato-biliary	1·13	0·12	1·15	0·59	0·90	0·76	1·14	0·42	0·90	1·15	1·10	0·53
Plastic / cutaneous	0·90	0·50	0·65	0·17	0·86	0·68	0·78	0·20	0·78	0·90	0·83	0·26
Urology	0·82	0·90	0·67	0·11	0·64	0·16	0·77	0·09	0·64	0·82	0·74	0·04
Kidney	0·17	0·09	0·11	0·02	1·95	0·22	0·46	0·07	0·11	1·95	0·38	0·014
Head and neck	0·90	0·64	1·54	0·50	0·93	0·81	1·22	0·18	0·90	1·54	1·14	0·32
Other (reference)	1·00	-	1·00	-	1·00	-	1·00	-	-	-	-	-

Supplementary table 6. Country estimates from two level model (hospital and patient) assessing in hospital death as the dependent variable together with the following independent variables: age, surgical procedure category, American Society of Anesthesiologist's (ASA) score, urgency and grading of surgery, presence of metastatic disease or cirrhosis. In addition the following interaction factors were included in the model: ASA*urgency (p<0·0001), Age*urgency (p=0·017), Age*grade of surgery (p=0·007) and country*age (p<0·0001).

	Odds Ratio	95% confidence intervals	p-value
Belgium	1·65	0·80 – 3·40	0·17
Croatia	1·87	0·93 – 3·77	0·08
Cyprus	0·82	0·04 – 16·65	0·90
Czech Republic	1·25	0·22 – 7·17	0·80
Denmark	1·14	0·51 – 2·57	0·75
Estonia	0·57	0·15 – 2·18	0·41
Finland	0·42	0·18 – 1·01	0·05
France	1·38	0·73 – 2·60	0·32
Germany	0·82	0·49 – 1·39	0·46
Greece	1·18	0·65 – 2·12	0·59
Hungary	1·16	0·41 – 3·29	0·79
Iceland	0·52	0·07 – 3·70	0·51
Ireland	2·97	1·47 – 5·99	0·002
Italy	1·70	0·98 – 2·97	0·06
Latvia	5·21	1·28 – 21·25	0·02
Lithuania	1·14	0·20 – 6·56	0·88
Netherlands	0·62	0·27 – 1·39	0·24
Norway	0·48	0·16 – 1·42	0·19
Poland	6·66	2·28 – 19·49	0·001
Portugal	1·42	0·72 – 2·81	0·31
Romania	3·11	1·57 – 6·16	0·001
Serbia	0·98	0·10 – 9·23	0·99
Slovakia	2·07	0·88 – 4·87	0·10
Slovenia	1·12	0·30 – 4·18	0·86
Spain	1·41	0·90 – 2·21	0·13
Sweden	0·56	0·22 – 1·44	0·23
Switzerland	0·87	0·25 – 2·99	0·82
United Kingdom	1·00	-	-

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