Post-operative serious adverse events in a mixed surgical population – a retrospective register study

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Background: The number of surgical procedures is increasing, and knowledge of surgical risk factors, post-operative mortality and serious adverse events (SAE) is essential. The aim with our study was to determine the risk of a composite outcome of post-operative: death; myocardial infarction; pulmonary embolism; stroke; gastrointestinal bleeding; dialysis or reoperation.

Methods: Data of surgical procedures in the period from January 1, 2012 to June 30, 2012 were retrieved from the Danish Anaesthesia Database (DAD). Follow-up of all patients undergoing hip or knee replacement, abdominal or gynaecological surgery was conducted retrieving data from The Danish Civil Registration System and the National Patient Register. Total observation time was from January 1, 2012 to June 6, 2013.

Results: A total 7449 adult patients were included in the final analysis. The risk of the composite outcome during a follow-up until 342 days after inclusion of the last patient was estimated to 8.3%, 95% Confidence Intervals (CI) (7.8–9.0), with a median observation time of 437 days (IQR 387–485, range 0–522). The risk of the composite outcome within 90- and 180-day follow-up of each patient was 4.8% (4.4–5.3) and 5.9% (5.4–6.5), respectively. Mortality within longest follow-up as well as 90 and 180 days post-operatively was 3.6% (3.1–4.0), 1.7% (1.4–2.0), and 2.2% (1.9–2.6), respectively.

Conclusion: We found a risk of one or more events in the composite outcome within 342 days after inclusion of the last patients of 8.3% (7.8–9.0). The results are applicable in estimations of adequate sample sizes in future clinical trials investigating effects of interventions on SAEs.

Editorial Comment
Based on the national Danish Anaesthesia Database, this analysis reports the rates of serious adverse events, including reoperations and mortality after different major surgical procedures. The findings confirm that age, abdominal, and emergency surgery strongly increase the risk. This knowledge is needed for planning future and more detailed studies on serious adverse perioperative events.
The number of surgical procedures is increasing, and globally more than 312 million procedures are performed each year. With the large and increasing number of surgical procedures, knowledge of surgical risk factors, post-operative mortality, as well as risks of complications and serious adverse events is essential.

Several studies have investigated the mortality and post-operative complications in a wide variety of surgical populations, but in the majority of studies, observation time is short and appears to vary between in-hospital, 30-day, and 90-day mortality.

Moreover, very few studies have investigated the risk of serious adverse events following non-cardiac surgery, and to our knowledge, no studies have investigated the long-term risk of known serious adverse events (SAEs), such as major cardiovascular events, bleeding, dialysis, or reoperations in a diverse surgical population. Studies investigating the risk of SAE’s following pharmacological or surgical interventions are warranted to provide optimal treatment recommendations for relevant patients; thus, the safety, short as well as long term, of an intervention should be established prior to the use of the intervention based on other outcomes; however, this is rarely the case.

The current evidence on the use of Non-steroidal Anti-inflammatory Drugs (NSAIDs) is an example, where the analgesic and opioid sparing effects have been demonstrated. However, several studies have indicated that use of NSAIDs may increase the risk of post-operative thrombo-embolic events, haemorrhage, renal failure, anastomotic leakage, and delayed bone healing or non-union. However, no large randomised trials have investigated the long-term risk of SAE’s following NSAID administration. This has resulted in concerns involving the present use of NSAIDs post-operatively, and large randomised trials investigating potential harmful effects may be necessary to bring answers to the many questions concerning NSAIDs.

To plan and conduct prospective randomised trials of the effect of peri- and post-operative interventions on SAE’s, adequate risk stratifications and reliable sample size estimations are essential, and for this, evidence on long-term risk of SAE’s following surgery is needed.

Based on the discussions involving the use of NSAIDs, we aimed to investigate the risk of known post-operative SAE’s to provide results that could be instrumental in the planning of clinical randomised trials investigating the effect of peri- and post-operative interventions on SAEs in a surgical population.

Our aim with this study was to determine the risk up to 1 year after inclusion of the last patient, as well as the risk of a composite outcome of SAE’s after 90 and 180 days follow-up of each patient. We chose a composite outcome including major cardiovascular events as well as reoperation, dialysis and gastrointestinal bleeding potentially due to complications following knee or hip surgery, abdominal surgery, or gynaecological surgery in a Danish adult population.

Methods

Data of all surgical procedures requiring anaesthesia in the period from January 1, 2012 to June 30, 2012, performed on patients with an age of 18 years or above, and with an American Society of Anaesthesiologists classification (ASA) score of ≤ 4 were retrospectively retrieved from the Danish Anaesthesia Database (DAD) (Fig. 1). Follow-up of all included patients until 1 year from the last included patient was retrieved from The Danish Civil Registration System (DCPR), and the National Patient Register (NPR) in the period from January 1, 2012 to end of follow-up on June 6, 2013.

A full description of methods and data extraction models is in Appendix S1. Below follows a brief description of the applied methods.

Outcomes

Primary outcome

To investigate the risk of one or more events in the composite outcome of: post-operative death, myocardial infarction, pulmonary embolism, cerebral thrombosis or cerebral haemorrhage, gastrointestinal haemorrhage, dialysis, or reoperation whatever comes first within a follow-up period until 342 days for the last registered patient, reaching 522 days for the first registered patient.
### Secondary outcomes

1. The risk of having one or more components of the composite outcome 90 and 180 days post-operatively for each patient.
2. The risk of death within the follow-up period of 1 year from the last included patient, and the mortality 90 and 180 days post-operatively for each patient.
3. The risk of having one or more components of the composite outcome and mortality following stratification for ASA score, unscheduled vs. elective index surgery, and type of index surgery.
4. The risk of each of the non-fatal events in the primary composite outcome within the follow-up period of 1 year from the last included patient, and 90 and 180 days post-operatively for each patient.

### Databases

The DAD contains baseline information of patients and procedures in relation to surgery and anaesthesia. Data entry is conducted electronically and in real time (during or immediately after surgery) by the anaesthetist. Data are collected and saved at a central server and are available for review upon formal request.

The Danish Civil Person Register (DCPR) is controlled by the Danish government and has since 1968 assigned a unique 10-digit identification number to each Danish citizen. The DCPR contains information on the date of birth, date of death, and gender of all Danish citizens. The Civil Registration Number (DCPR number) is a unique identifier of the individual, and can be applied in linking of data across different public registers.

The National Patient Register (NPR) was established in 1976, and is a national register of all patients receiving treatment in Danish hospitals. NPR contains individual patient data, including date of admission and discharge, diagnoses, as well as conducted surgeries and procedures. All surgical procedures logged in the NPR are recorded in accordance to the Nordic Classification of Surgical Procedures (NCSP). The classification used in NPR can be found in the web-based healthcare classification system (SKS) and are allotted by the surgeon performing the surgical procedure.

### Inclusion criteria

All adult patients (age ≥ 18 years), ASA ≤ 4, undergoing hip replacement surgery, knee replacement surgery, abdominal surgery (performed on the small intestines, colon, and rectum, with the involvement of anastomoses), or gynaecological surgery (surgery performed on female genitals) (for the specific SKS codes, see Appendix S1) in the period from January 1, 2012 to June 30, 2012 were included.

### Extraction of Data

Records of all surgical procedures requiring anaesthesia in the inclusion period were included.
extracted from the DAD. For patients registered with more than one surgical procedure, the procedures were sorted according to the first registered surgical procedure. The first relevant surgical procedure extracted from DAD was categorised as the index surgery.

Based on the included patients from the DAD, data from the DCPR and NPR were retrieved. Data from the DCPR contained information on the status of the patient: diseased or not diseased, and if diseased, the date of death.

Data from the NPR contained information on medical diagnoses assigned to the patients as well as reoperations and dialyses therapy. Data also contained information about admission and discharge, as well as dates on which the reoperations and dialyses were performed.

The data from NPR contained the following information:

1. Diagnoses ICD-10: acute myocardial infarction, pulmonary embolism, cerebral thrombosis or cerebral haemorrhage, and gastrointestinal haemorrhage.
2. Reoperations/surgical procedures SKS codes: hip or knee replacement surgery, classified as reoperations or same-side surgery, abdominal surgery, and gynaecological surgery.
3. Dialysis SKS procedure.

Only events that occurred after the index surgery were included; thus, if a patient had undergone, e.g. dialyses prior to the index surgery, dialyses after the index surgery was not included as an event in the analysis.

We stipulated specific criteria in the data analysis plan for including a surgical procedure as a reoperation (see Appendix S1).

Data extraction models

To improve the accuracy of the results, data were extracted from the NPR in two versions: In version 1 (automated), we aimed to minimise the risk of observer bias, and conducted a predefined automated data extraction with no manual review of included records. In version 2 (manual), all included events were manually reviewed to minimise a possible over/underestimation of the findings. We chose to report the results primarily obtained from the automated data extraction model Version 1. For detailed description, please see Appendix S1.

Post hoc analyses

During data extraction for Version 1 and Version 2, a discrepancy between DAD and NPR was encountered. The index surgeries found in DAD could not all be identified in the data set retrieved from NPR. Reasons for the missing records could not be identified, but probably encompass date and code discrepancies between registrations in DAD and NPR. To account for this a third data extraction version (Version 3) was conducted. In Version 3, we only included records where DCPR number, date of index surgery, and SKS code of index surgery were identical in DAD and NPR. Data analysis identical with the one performed in Version 1 and 2 was performed.

Statistics

The percentage of the patients with one or more events of the composite outcome was calculated with a 95% confidence interval (CI). The risk of the composite outcome was estimated for the entire population, and also after stratification for ASA 1-4, unscheduled vs. elective index surgery, and for the three types of index surgery.

The risk of each of the non-fatal events in the composite outcome was estimated with a 95% CI.

The risk of death until 1-year follow-up of the last included patient and the risk of death, at 90- and 180-day follow-up for every patient, post-operatively were estimated with a 95% CI. Kaplan–Meier curves were constructed to investigate the time to death in the follow-up period until 1 year after inclusion of the last patient, stratified for ASA score, unscheduled vs. elective index surgery, and type of index surgery.

Log rank test was applied to test for statistically significant differences between the stratified groups.

In evaluation of the risk of the composite outcome and mortality, Cox regression was conducted and the following covariates were applied: age, unscheduled surgery (reference: elective surgery), type of index surgery (reference: gynaecological index surgery), and ASA score (dichotomised to ASA 1+2 and ASA 3+4) (reference ASA 1+2). Hazard ratios (HR) with 95% CI’s in a multivariate model are reported. P-values < 0.05 are considered statistically significant.
The proportionality assumption for all covariates was checked and the cumulative hazard functions as well as the log minus log plots were very close to parallel and did not suggest violation of the assumption of proportional hazards.

All analyses were made using the software IBM Statistical Package for the Social Sciences (SPSS) version 22 for Windows.

Registration and approvals

Because of the strictly observational design of the study, the National Committee on Health Research Ethics waived approval and informed consent from individual patients. Based on an elaborate protocol, the study was approved by the Danish Data Protection Agency (Ref. no.: 2013-41-1878) and the National Board of Health (Ref. no.: FSEID-00000724) and the Steering Committee of the DAD (Ref. No.: 2013-331-0410).

Results

Data from 113,068 patients (158,869 records) were retrieved from the DAD. Following data cleansing and extraction, 7449 patients were eligible for inclusion (Fig. 1) (for the specific SKS codes, see Appendix S1). Of the 7449 included patients, 4081, 1158, and 2210 patients had undergone orthopaedic, abdominal, and gynecological index surgery, respectively. The median observation time was 437 days (IQR 387–485) with a range 0–522 days, and the median age was 66 years (IQR 53–74) (Table 1).

By applying Version 1 of the data extraction model, we found that of the 7449 patients, 6222 could be identified in NPR. Of the 6222 patients, a total of 621 patients had a registration of one or more events in the composite outcome, resulting in a total of 705 registered events (Table 2). Patients were followed for 8679 person years, of which 8343 where event free. When comparing the two data extraction models (Versions 1 and 2) similar results were found (Appendix S2).

Primary outcome

The risk of one or more events of the composite outcome was 8.3%, 95% CI (7.8–9.0).

Secondary outcomes

The risk of one or more events of the composite outcome at 90 and 180 days after inclusion of each patient was 4.8% (4.4–5.3) and 5.9% (5.4–6.5), respectively.

The risk of death until 342 days after inclusion of the last patient was 3.6% (3.1–4.0) and the risk of death at 90 and 180 days after inclusion of each patient was 1.7% (1.4–2.0) and 2.2% (1.9–2.6), respectively. The risk of having an event at 90 and 180 days and the risk for each of the events in the composite outcome are displayed in Table 2.

Table 1 Demographics of included patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Orthopaedic</th>
<th>Abdominal</th>
<th>Gynaecological</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median, IQR (years)</td>
<td>69.7 (63–76)</td>
<td>68.5 (59–77)</td>
<td>48.8 (42–60)</td>
<td>65.8 (53–74)</td>
</tr>
<tr>
<td>Observational time, median IQR (years)</td>
<td>442 (388–485)</td>
<td>421 (367–478)</td>
<td>440 (388–485)</td>
<td>437 (387–485)</td>
</tr>
<tr>
<td>Number of patients</td>
<td>4081</td>
<td>1158</td>
<td>2210</td>
<td>7449</td>
</tr>
<tr>
<td>Number of patients with unscheduled index surgery</td>
<td>123 (3.01%)*</td>
<td>230 (19.88%)*</td>
<td>89 (4.03%)*</td>
<td>442</td>
</tr>
<tr>
<td>Number of patients with elective index surgery</td>
<td>3958 (96.99%)*</td>
<td>927 (80.05%)*</td>
<td>2121 (95.97%)*</td>
<td>7006</td>
</tr>
<tr>
<td>Number of patients with ASA score = 1</td>
<td>796 (19.5%)*</td>
<td>202 (17.44%)*</td>
<td>1105 (50.0%)*</td>
<td>2103</td>
</tr>
<tr>
<td>Number of patients with ASA score = 2</td>
<td>2687 (65.84%)*</td>
<td>668 (57.69%)*</td>
<td>1009 (45.66%)*</td>
<td>4364</td>
</tr>
<tr>
<td>Number of patients with ASA score = 3</td>
<td>557 (13.65%)*</td>
<td>257 (22.19%)*</td>
<td>84 (3.8%)*</td>
<td>898</td>
</tr>
<tr>
<td>Number of patients with ASA score = 4</td>
<td>12 (0.29%)*</td>
<td>30 (2.59%)*</td>
<td>2 (0.9%)*</td>
<td>44</td>
</tr>
</tbody>
</table>

IQR, Interquartile range. All results are from the data extraction Version 1. *percentage of the total number of patients within surgical classification. Abbreviations: ASA, American Society of Anaesthesiologists.
Stratification for ASA classification

Significant differences in the risk of the composite outcome as well as death were found when stratifying for ASA classification. The risk of an event of the composite outcome in ASA group 1, 2, 3, and 4 was 3.9% (3.1–4.8), 7.0% (6.3–7.8), 19.6% (17.0–22.2), and 57.8% (43.3–72.2), respectively, and the risk of death in the four ASA groups was estimated to 0.6% (0.2–0.9), 2.7% (2.2–3.1), 13.3% (11.0–15.5), and 42.2% (27.8–56.7), respectively (Figs 1A and 2A, and Appendix S3).

Stratification for unscheduled vs. elective index surgery

The risk of one or more events of the composite outcome differed significantly when comparing the patients undergoing unscheduled and elective index surgery, illustrated by a risk of 29.0% (24.7–33.2) and 7.0% (6.4–7.6) in the unscheduled and elective index surgery groups, respectively. Likewise, there was a significant difference in the risk of death between the two groups with a mortality of 20.1% (16.4–23.8) in the unscheduled and 2.5% (2.2–2.9) in the elective index surgery group (Figs 1B and 2B, and Appendix S3).

Stratification for type of index surgery

When stratifying for type of index surgery, significant differences in the risk of having one or more events of the composite outcome were illustrated, with a risk of 6.2% (5.5–7.0), 23.2% (20.8–25.6), and 4.5% (3.7–5.4) in the orthopaedic, abdominal, and gynaecological groups, respectively.

When investigating the risk of death within the follow-up until 342 days after inclusion of the last patient, significant differences were demonstrated when comparing the group undergoing abdominal index surgery, 12.7% (10.8–14.6), with the orthopaedic, 2.7% (1.8–2.7), and gynaecological, 1.2% (0.7–1.6), index surgery groups (Figs 1C and 2C, and Appendix S3).

Following Cox regression, ASA score of 3 or 4, unscheduled surgery, abdominal surgery, and increasing age were significantly associated with an increased mortality and an increased risk of having an event in the composite outcome (Table 3).

Post hoc analyses

Following data extraction model Version 3 we found that of the 7449 patients, a total number of 5034 patients had identical date of index surgery and index surgery SKS code in DAD and NPR. Thus, 5034 patients were included in the analysis.

The risk of one or more events of the composite outcome was 6.7% (6.0–7.3), and the risk of one or more events of the composite outcome at 90 and 180 days after inclusion of each patient was 3.8% (3.3–4.3) and 4.5% (3.9–5.1), respectively.

<table>
<thead>
<tr>
<th>Event</th>
<th>Absolute number of events</th>
<th>Relative percentage of patients</th>
<th>90 days</th>
<th>180 days</th>
<th>Full observation period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>126</td>
<td>1.7% (1.4–2.0)</td>
<td>166</td>
<td>2.2% (1.9–2.6)</td>
<td>266</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>4</td>
<td>0.1% (0.0–0.1)</td>
<td>7</td>
<td>0.1% (0.0–0.1)</td>
<td>10</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>8</td>
<td>0.1% (0.0–0.2)</td>
<td>8</td>
<td>0.1% (0.0–0.1)</td>
<td>11</td>
</tr>
<tr>
<td>Cerebral thrombosis/haemorrhage</td>
<td>11</td>
<td>0.1% (0.0–0.2)</td>
<td>13</td>
<td>0.2% (0.1–0.4)</td>
<td>18</td>
</tr>
<tr>
<td>Gastrointestinal haemorrhage</td>
<td>15</td>
<td>0.2% (0.1–0.4)</td>
<td>22</td>
<td>0.3% (0.2–0.4)</td>
<td>39</td>
</tr>
<tr>
<td>Dialysis</td>
<td>9</td>
<td>0.1% (0.0–0.2)</td>
<td>11</td>
<td>0.1% (0.0–0.2)</td>
<td>29</td>
</tr>
<tr>
<td>Reoperation</td>
<td>179</td>
<td>2.4% (2.1–2.8)</td>
<td>226</td>
<td>3.0% (2.7–3.4)</td>
<td>332</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>7449</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ninety and 180 days risk and risk up to 342 days after inclusion of the last patient (patients observed in the entire observation period from January 1, 2012 to June 6, 2013) of the components in the composite outcome. All results are from the data extraction Version 1. Numbers in parentheses are 95% Confidence Intervals (CI).
The risk of death was estimated to 3.2% (2.7–3.6), and the 90- and 180-day mortality were 1.4% (1.0–1.7) and 1.8% (1.4–2.2), respectively (Appendix S2).

**Discussion**

We have conducted a retrospective study of all patients undergoing hip and knee surgery (orthopaedic surgery), gynaecological surgery, or abdominal surgery in the period from January 1, 2012 to June 30, 2012 with a follow-up until June 6, 2013. We included 7449 patients and found a risk of one or more events within the composite outcome of 8.3% (7.8–9.0), and a risk of death until 342 days of follow-up of the last included patient of 3.6% (3.1–4.0).

To our knowledge, no study has previously estimated the long-term risk of the composite outcome and its components following surgery in a diverse surgical population.

The aim of our study was to investigate the risk of a composite outcome of SAE’s following orthopaedic, abdominal, or gynaecological...
surgery. When constructing a composite outcome used to evaluate interventions, all components in the outcome should ideally be equal in terms of seriousness.44 However, we chose to base the composite outcome on known SAE’s, well aware that the components in the composite outcome were not equally serious (e.g. death vs. gastrointestinal haemorrhage). The different components were selected based on known SAE’s and, to compensate for the difference in seriousness, we reported the risk of the individual outcome components in the composite outcome as well.20

The stratification variables were chosen as known risk factors for death and post-operative complications that were readily definable, easy comprehensible, registered in DAD, and often used in daily clinical practice in a wide variety of surgical specialities. Increasing ASA score and unscheduled surgery has been demonstrated to be associated with increasing mortality,45,46 and the stratification in surgical subgroups was necessary to differentiate between the three main surgical groups (orthopaedic, abdominal, and gynaecological).

Our results demonstrate that increasing age, unscheduled index surgery, increasing ASA score, and abdominal index surgery were associated with a significantly higher mortality and a higher risk of experiencing an event in the composite outcome.

However, the predictive value of some components in the multivariate model may be imprecise. The proportion of patients undergoing unscheduled index surgery was unevenly distributed between the three surgical groups. Thus, a higher proportion of the patients undergoing abdominal index surgery underwent unscheduled index surgery when compared to the two remaining groups (Table 1). Likewise, a higher proportion of abdominal patients had ASA scores of 3 and 4 when compared to the two remaining groups (Table 1).

Consequently, due to residual confounding the predictive value of the multivariate model described above may be inaccurate.

Death and reoperation were the two most frequent events in the composite outcome with a risk of 3.6% and 4.5%, respectively, during maximal follow-up. When investigating the risks of the remaining five components taken together all were 0.5% or less. The 30-day incidences of myocardial infarction, stroke, dialysis, and pulmonary embolism, reported in the POISE-120 and POISE-2 trials,47,48 were all higher than the 90-day risk in our study. The rather high differences in risks, in particular the risk of acute myocardial infarction, may result from the inclusion criteria applied in the POISE trials that focused primarily on a history of cardiovascular disease, also that all patients underwent extensive cardiovascular risk monitoring, and that an adjudication committee was applied in classifying myocardial infarction. In our study, we included patients solely based on the type of the surgical procedure, and excluded patients with age below 18 and ASA score above 4.

Long-term mortality has previously been investigated in well-defined surgical populations, with reports of a 90-day mortality of 0.29% in staged total hip arthroplasty,49 180-day mortality of 23.4% in hip fracture patients,45 and 1-year mortality of 29.8%45 and 27%50 in hip fracture patients.

Our results demonstrate a 90-day mortality of 0.9%, and a cumulated mortality of 2.7% in a mixed orthopaedic group, including both unscheduled and elective surgery, with no stratification for type of orthopaedic surgery (i.e. hip vs. knee surgery); only patients with ASA score of 1–4 were included.

<table>
<thead>
<tr>
<th>Table 3 Hazard ratios of composite outcome and mortality.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covariate</td>
</tr>
<tr>
<td>Unscheduled index surgery†</td>
</tr>
<tr>
<td>ASA score, 3 and 4‡</td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Abdominal index surgery§</td>
</tr>
<tr>
<td>Orthopaedic index surgery§</td>
</tr>
</tbody>
</table>

The hazard ratios of relevant covariates on the risk of experiencing an event in the composite outcome and the mortality. All results are from the data extraction Version 1. Numbers in parentheses are 95% Confidence Intervals. *P-value below 9.0*10−6. †Reference group: elective index surgery. ‡Reference group: ASA scores 1 and 2. §Reference group: gynaecological index surgery. Abbreviations: ASA, American Society of Anaesthesiologists; CI, confidence interval.
The median observation period in our study is 14.6 months (437 days) and therefore longer than any study previously published. Current clinical interventional studies investigating mortality or other adverse events often report outcomes such as time until discharge, 24 h, in-hospital, or 30-day mortality/incidence. At present there exists no consensus on observation time following an intervention, and no clear evidence-based recommendations have been provided when evaluating harmful effects of an intervention. It is important to consider that patient comorbidity, and other patient-related factors may influence the long-term risk of the investigated outcomes, and the link between surgery and outcome may weaken as time progress. However, to which degree the effect of time and other factors have on the investigated outcomes remains unknown. For example may an index operation followed by a reoperation due to interventions during the course of the index admission lead to further complications or even death several months afterwards. From the Kaplan–Meier curves (Figs 1 and 2), it is clear that the highest rate of events occurs during the first 10 days. However, the curve flattens and becomes linear after approximately 90 days. A 30-day event rate may therefore result in an underestimation of the risk of harm, and we recommend at least 90-day follow-up when investigating mortality and SAE’s. Our retrospective study may be instrumental to conduct a prospective randomised trial of the effect of a peri- or post-operative interventions on SAE’s in a surgical population. Thus, adequate risk stratifications and proper sample size estimations may be obtained by applying our results.

Our study has limitations, and a register-based study is naturally limited by the information contained in the included register. We identified 7449 patients with a relevant index surgery in the DAD. Of the 7449 patients identified in DAD, only 6222 could be identified in NPR, and of the 6222 patients, only 5034 had an index surgery registered where the date of the index surgery and the SKS code were identical in DAD and NPR. This result was remarkable and we therefore chose to conduct a post hoc analysis only including 5034 patients. The result of the post hoc analysis demonstrated a slightly lower risk of the composite outcome and mortality compared to our primary analysis (Appendix S2). We also identified patients with relevant reoperation codes and diagnoses, but without registration of an index surgery in the NPR. Therefore, we are confident that relevant reoperation SKS codes and diagnoses were registered in NPR following an index surgery registered in DAD, and chose to extract all index surgeries from DAD and all other relevant surgical procedures and diagnoses from the NPR. We conducted a thorough pre-defined data extraction from the three registers (DAD, NPR, and DCPR) and have described the details in full (Appendix S1); however, the reason for the 1227 patients not registered with an index surgery in NPR remains unknown.

Finally, it was not possible to examine the use of pharmaceuticals in the included patients, which may have influenced mortality and the composite outcome.

In conclusion, our retrospective register-based study found a risk of one or more events of the composite outcome of 8.3% and a mortality within the maximal follow-up of 3.6% in a cohort of 7449 orthopaedic, abdominal, or gynaecological surgical patients. Important differences were detected among strata of ASA classification, elective/unscheduled surgery, and types of surgery.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher’s web-site:

Appendix S1. Extraction of data from Danish Anaesthesia Database (DAD), the Danish Central Person Register (DCPR), and the National Patient Register (NPR)

Appendix S2. Important outcomes from the three different data extraction models

Appendix S3. Additional results

Table S1: Risk of composite outcome stratified for ASA classification

Table S2: Mortality stratified for ASA classification

Table S3: Risk of composite outcome stratified for unscheduled vs. elective surgery

Table S4: Mortality for unscheduled vs. elective surgery

Table S5: Risk of composite outcome stratified for type of index surgery

Table S6: Mortality stratified for type of index surgery