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Original Article

Association between multimorbidity and postoperative mortality in patients undergoing major surgery: a prospective study in 29 countries across Europe

STARSurg Collaborative and **EuroSurg Collaborative**[†]

Department of Global Health and Surgery, Institute of Applied Health Research, University of Birmingham.

Summary

Background Multimorbidity poses a global challenge to healthcare delivery. This study aimed to describe the prevalence of multimorbidity, common disease combinations and outcomes in a contemporary cohort of patients undergoing major abdominal surgery.

Methods This was a pre-planned analysis of a prospective, multicentre, international study investigating cardiovascular complications after major abdominal surgery conducted in 446 hospitals in 29 countries across Europe. The primary outcome was 30-day postoperative mortality. The secondary outcome measure was the incidence of complications within 30 days of surgery.

Results Of 24,227 patients, 7006 (28.9%) had one long-term condition and 10,486 (43.9%) had multimorbidity (two or more long-term health conditions). The most common conditions were primary cancer (39.6%); hypertension (37.9%); chronic kidney disease (17.4%); and diabetes (15.4%). Patients with multimorbidity had a higher incidence of frailty compared with patients $\leq$ 1 long-term health condition. Mortality was higher in patients with one long-term health condition (adjusted odds ratio 1.93 (95%CI 1.16–3.23)) and multimorbidity (adjusted odds ratio 2.22 (95%CI 1.35–3.64)). Frailty and ASA physical status 3–5 mediated an estimated 31.7% of the 30-day mortality in patients with one long-term health condition (adjusted odds ratio 1.30 (95%CI 1.12–1.51)) and an estimated 36.9% of the 30-day mortality in patients with multimorbidity (adjusted odds ratio 1.61 (95%CI 1.36–1.91)). There was no improvement in 30-day mortality in patients with multimorbidity who received pre-operative medical assessment.

Conclusions Multimorbidity is common and outcomes are poor among surgical patients across Europe. Addressing multimorbidity in elective and emergency patients requires innovative strategies to account for frailty and disease control. The development of such strategies, that integrate care targeting whole surgical pathways to strengthen current systems, is urgently needed for multimorbid patients. Interventional trials are warranted to determine the effectiveness of targeted management for surgical patients with multimorbidity.

Correspondence to: Sivesh K. Kamarajah
Email: s.k.kamarajah@bham.ac.uk
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[†]Collaborators are listed in online Supporting Information Appendix S1.
Twitter/X: @STARSurgUK; @EuroSurgIntroduction; @Sivesh93

Introduction

Multiple long-term health conditions or multimorbidity are defined by the World Health Organization (WHO) as the ``*co-existence of two or more chronic conditions within the same individual*´´ [1]. Multimorbidity poses unique challenges to the provision of healthcare globally, which has developed over time to address single conditions [2]. In England, an estimated 14 million people currently have multimorbidity, a figure expected to increase two- to threefold by 2040 [3, 4]. Multimorbidity is associated with poor health outcomes, worse quality of life, increased risk of healthcare use and death, and disproportionately affects people from racially minoritised and socio-economically disadvantaged communities [5, 6]. Research in multimorbidity has focused on patients in community settings such as primary care [7]. However, as multimorbidity is increasing across all settings, healthcare professionals need to understand multimorbidity and the implications for their practice.

Each year, 313 million patients undergo surgery globally [8]. With an increasing proportion of surgical patients being older, it is likely that more patients presenting to surgical services will also have coincident multimorbidity [9], affecting peri-operative risk [10]. Despite this, there are few data on the prevalence of multimorbidity and how this affects surgical outcomes in the context of an ageing surgical population. Studies published to date have produced conflicting results on the prevalence of chronic diseases among patients undergoing surgery [11–15]. These may relate to the inherent differences in the surgical patient population or which long-term conditions were included in the study. Furthermore, some of these studies are small, retrospective and over a decade old.

Understanding common long-term health conditions in people with multimorbidity undergoing surgery is important to appreciate peri-operative risk. There is also an opportunity to improve and optimise management of underlying conditions in the peri-operative period. However, strategic planning mandates detailed and accurate information, so that appropriate resources can be allocated and quality improvement prioritised. Demographic and clinical data, together with details of hospital resources, are needed to help refine public health initiatives, treatment strategies and quality improvement interventions. The aim of this study was to describe the prevalence of multimorbidity, common disease combinations and impact of multimorbidity on postoperative mortality in a contemporary cohort of patients undergoing major abdominal surgery across Europe.

Methods

This was a pre-planned secondary analysis of the CArdiovaSCulAr outcomes after major abDominal surgEry (CASCADE) cohort study, conducted according to a published study protocol [16]. CASCADE was a prospective, multicentre, international study investigating cardiovascular complications after major abdominal surgery conducted in 446 hospitals in 29 countries across Europe.The study included all consecutive adult patients (aged ≥ 18 y) undergoing major abdominal surgeries across five surgical disciplines (abdominal and/or pelvic visceral resection; formation or reversal of stoma; open vascular surgery; anterior abdominal wall hernia repair; or transplant surgery) and through any surgical approach. We did not study patients undergoing planned day case procedures or those undergoing non-abdominal surgeries. Local collaborators at each participating hospital identified eligible patients during five data collection periods from 24 January to 3 April 2022.

This cohort study collected routine anonymised data with no change to clinical care pathways. In the UK and Ireland, this study was considered an audit and no formal ethical approval was required. However, in all other countries in Europe, ethical approval was sought. The study required confirmation of appropriate local or national regulatory approval before patient enrolment. This international cohort study was registered according to the appropriate local or national approval pathways in each participating country. This study was conducted in accordance with STROBE guidelines [17].

We selected long-term health conditions based on a previously published national Delphi consensus on the definitions and measurement of multimorbidity in research. This Delphi process included 150 clinicians and 25 public participants across the UK [18]. The main exposure variable was the number of long-term health conditions, defined as none, one, or two or more. Multimorbidity was defined as someone living with two or more long-term health conditions [18]. Since no data on mental health were collected in the study, long-term mental health conditions were not studied.

We used a prespecified case report form to collect data on patient and surgical characteristics and 30-day outcomes for each patient [16]. For this pre-planned secondary analysis we used the following variables from the CASCADE dataset: age (y); sex (male or female); BMI ($kg.m^{-2}$); ASA physical status (1–5); smoking status; surgical indication (benign or malignant); surgical urgency (elective, intervention planned in advance of admission or emergency, intervention planned after admission); and surgical approach (open or minimally invasive). We extracted full data from routinely collected patient health records with no changes to clinical care pathways. We submitted data using a secure Research Electronic Data Capture server [19].

The primary outcome measure for this study was 30-day postoperative mortality. Secondary outcome measures were the incidence of major complications (Clavien–Dindo grade 3–5) and the incidence of any complication (defined by Clavien–Dindo grade 1–5) [20]. We assessed all outcomes 30 days after surgery with follow-up completed in-person, by telephone or by review of medical records, based on local clinical practice.

We reported differences in patient- and surgical-level characteristics by the number of long-term health conditions. For univariable comparisons between groups, we used one-way ANOVA, χ^2 test or Mann–Whitney *U*-test as applicable. Specifically, we used the χ^2 test to compare 30-day mortality in patients with different numbers of long-term health conditions. We constructed multilevel logistic regression to account for the case-mix (patient, disease and surgical characteristics). We included population-level stratification by hospital and country as random intercepts.

We developed models using the following principles: we included covariates strongly associated with the outcome measures from previous studies; population stratification by country and hospital as random effects; we checked and included first-order interactions in final models if found to be influential (reaching statistical significance or resulting in ≥ 10% in the odds ratio (OR) of the explanatory variable of interest); and we selected the final model using a criterion-based approach by minimising the Akaike information criterion and discrimination determined using the C-statistic (area under the receiver operator curve). Effect estimates are presented as OR (95%CI).

We performed mediation analysis by three-way decomposition of total effects into direct, indirect and interactive effects using natural effect models [21]. We examined mediators at the level of the patient, defined as the presence of frailty and ASA physical status 3–5, and incorporated in a joint model. We assumed that there was no causal relationship between these and patient-level covariates. Similarly, we did not specify any mediator-outcome confounders. We determined uncertainty using bootstrap resampling (5000 draws) and constructed confidence intervals using percentiles. We performed all analyses in R version 3.4.2 (R Computing, Vienna, Austria) using the dplyr, finalfit and medflex packages.

Results

Of 24,246 patients from the CASCADE study, this pre-planned analysis included 24,227 undergoing major abdominal surgery from 446 hospitals across 29 European countries (20,548 patients from high-income; 3649 from upper middle-income; and 30 from low-income countries) (Fig. 1). Median (IQR [range]) age of the entire cohort was 61 (28 [48–71]) y, 12,780 (52.8%) were female, 17,362 (71.7%) had elective surgery and 9804 (40.5%) had cancer surgery. A summary of baseline characteristics of patients included in the study is in online Supporting Information Table S1.

Of the 24,227 patients, 7006 (28.9%) and 10,486 (43.3%) had one and two or more long-term health conditions, respectively (Table 1). The four most common long-term health conditions were cancer (39.6%); hypertension (37.9%); chronic kidney disease (17.4%); and diabetes (15.4%). A summary of all the long-term health conditions is in the online Supporting Information (Figure S1 and Table S2). In patients with two long-term health conditions (n = 5101), the most common combinations were cancer and hypertension (1585, 31.1%) and diabetes and hypertension (534, 10.5%) (Table 2).

Increasing age was associated with increasing number of long-term health conditions (online Supporting Information Figure S2). Patients with multimorbidity were more likely to be male compared with female (51.2% vs. 36.2%). Multimorbidity was more common in patients with BMI ≥30 $kg.m^{-2}$ (50.9%) and frailty scores 4–6 and 7–9 (73.9% and 70.8%). Patients undergoing elective surgery (46.2% vs. 33.6%, compared with emergency surgery) and cancer surgery (64.0% vs. 29.2%, compared with benign surgery) had higher rates of multimorbidity. Table 1 gives a summary of patient- and surgical-level characteristics.

In total, 463 (1.9%) patients died within 30 days of surgery. The rates of 30-day mortality were higher in patients with multimorbidity compared with those with either one or no long-term health conditions (3.2% vs. 1.4% vs. 0.4%; $p < 0.001$) (Fig. 2a, online Supporting Information Fig. S3a). People with multiple long-term conditions had higher risk of mortality even when adjusted for age and sex (Fig. 2b). In a model accounting for patient factors and clustering by hospital and country, patients with long-term health conditions (adjusted odds ratio (aOR) 1.93 (95%CI 1.16–3.23)) or multimorbidity (aOR 2.22 (95%CI 1.35–3.64)) had higher rates of 30-day mortality compared with those with no long-term health conditions (Fig. 2c and 2d). Emergency surgery and open surgical approach were strong predictors of 30-day mortality after surgery (online Supporting Information Table S3).

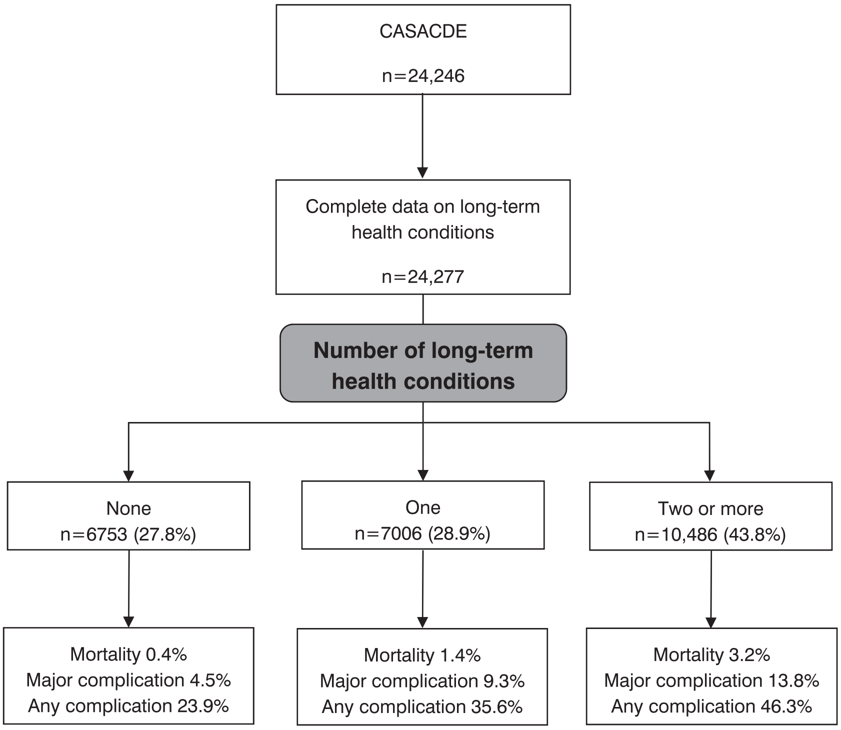

Figure 1 Flow diagram of patients included into the pre-planned secondary analysis of the CASCADE cohort study.

When frailty and ASA physical status were discounted from the multilevel model, there was no significant change in the associations observed except for the number of long-term health conditions, and discrimination remained consistent (online Supporting Information Table S4). No interaction was found between either of these mediators and number of long-term health conditions. The association between number of long-term health conditions and 30-day mortality was examined in a three-way decomposition mediation model of frailty and ASA physical status (Fig. 3, online Supporting Information Table S5).

A significant proportion of excess mortality was mediated by the presence of frailty and ASA physical status 3–5 in patients with one long-term health condition (31.7%, aOR 1.30 (95%CI 1.12–1.51)) and two or more long-term health conditions (36.9%, aOR 1.61 (95%CI 1.36–1.91)). The proportions of patients having pre-operative assessment for elective and emergency surgery are shown in Table 1. The odds of 30-day mortality and incidence of complications (major and overall) for each category of number of long-term health conditions are shown in Figures 4a–c.

The proportion of patients with multimorbidity having major (13.8% vs. 9.3% vs. 4.5%, $p < 0.001$) or any complications (46.3% vs. 35.6% vs. 23.9%, $p < 0.001$) was higher compared with patients with one or no long-term health conditions, respectively (online Supporting Information Fig. S3a). In the multilevel model, patients with multimorbidity had higher 30-day major complications (aOR 1.77 (95%CI 1.48–2.13), online Supporting Information Table S6) or any complications (aOR 1.68 (95% CI 1.51–1.88), online Supporting Information Table S7).

A statistically significant interaction was seen between multimorbidity and urgency of surgery (i.e. elective and emergency surgery) for major and overall complications (Fig. 5a and 5b) but not for 30-day mortality (Fig. 5c). Therefore, stratified analyses were performed based on urgency of surgery. Baseline characteristics of patients undergoing elective and emergency surgery are presented separately in online Supporting Information Tables S8 and S9, respectively. With increasing age and BMI, there was an increasing number of long-term health conditions when stratified by elective and emergency surgery (online Supporting Information Fig. S2). Rates of multimorbidity were higher in male patients in both elective and emergency surgery (online Supporting Information Fig. S4). The most common long-term health conditions observed, stratified by urgency, is shown in online Supporting Information Table S2. The number of co-occurring long-term health conditions observed in patients with specific long-term conditions is presented in online Supporting Information Fig. S5.

Table 1 Clinical characteristics of patients undergoing major abdominal surgery stratified by number of long-term health conditions. Values are number (proportion).

		Number of long-term health conditions		
		0 n = 6735	1 n = 7006	≥ 2 n = 10,486
Patient factors				
Age; y	18–40	2507 (37.2%)	955 (13.6%)	249 (2.4%)
	41–60	3026 (44.9%)	2856 (40.8%)	2391 (22.8%)
	61–80	1112 (16.5%)	2890 (41.3%)	6513 (62.1%)
	≥ 81	90 (1.3%)	305 (4.4%)	1333 (12.7%)
Sex; female		4297 (63.8%)	3861 (55.1%)	4622 (44.1%)
ASA physical status	1	2632 (39.1%)	971 (13.9%)	372 (3.5%)
	2	3304 (49.1%)	4172 (59.5%)	4507 (43.0%)
	3	727 (10.8%)	1693 (24.2%)	4915 (46.9%)
	4/5	69 (1.0%)	167 (2.4%)	688 (6.6%)
	Missing	3 (< 0.1%)	3 (< 0.1%)	4 (< 0.1%)
BMI; $kg.m^{-2}$	< 18.5	127 (1.9%)	205 (2.9%)	234 (2.2%)
	18.5–24.9	2574 (38.2%)	2559 (36.5%)	3028 (28.9%)
	25–29.9	2019 (30.0%)	2252 (32.1%)	3708 (35.4%)
	≥ 30.0	1327 (19.7%)	1473 (21.0%)	2904 (27.7%)
	Missing	688 (10.2%)	517 (7.4%)	612 (5.8%)
Smoker	Current	1491 (22.1%)	1255 (17.9%)	1749 (16.7%)
	Missing	1075 (16.0%)	1043 (14.9%)	1405 (13.4%)
Clinical frailty score	1–3	6470 (96.1%)	6334 (90.4%)	7872 (75.1%)
	4–6	231 (3.4%)	626 (8.9%)	2424 (23.1%)
	7–9	32 (0.5%)	45 (0.6%)	187 (1.8%)
	Missing	2 (< 0.1%)	1 (< 0.1%)	3 (< 0.1%)
Operative factors				
Emergency	Elective	4173 (62.0%)	5271 (75.2%)	7918 (75.5%)
	Emergency	2562 (38.0%)	1733 (24.7%)	2563 (24.4%)
	Missing	0	2 (< 0.1%)	5 (< 0.1%)
Indication	Benign	6278 (93.2%)	3920 (56.0%)	4207 (40.1%)
	Malignant	452 (6.7%)	3078 (43.9%)	6274 (59.8%)
	(Missing)	5 (0.1%)	8 (0.1%)	5 (< 0.1%)
Approach	Minimally invasive	4740 (70.4%)	3978 (56.8%)	5187 (49.5%)
	Open	1994 (29.6%)	3027 (43.2%)	5298 (50.5%)
	(Missing)	1 (< 0.1%)	1 (< 0.1%)	1 (< 0.1%)
Contamination	Clean	3259 (48.4%)	2814 (40.2%)	3936 (37.5%)
	Clean/Contaminated	2941 (43.7%)	3659 (52.2%)	5671 (54.1%)
	Contaminated/Dirty	529 (7.9%)	521 (7.4%)	865 (8.2%)
	(Missing)	6 (0.1%)	12 (0.2%)	14 (0.1%)
Specialty	Upper gastrointestinal	230 (3.4%)	524 (7.5%)	934 (8.9%)
	Hepatobiliary	2241 (33.3%)	1953 (27.9%)	2830 (27.0%)
	Lower gastrointestinal	2597 (38.6%)	2980 (42.5%)	4724 (45.1%)
	Gynaecology	1526 (22.7%)	1006 (14.4%)	887 (8.5%)
	Urology	141 (2.1%)	543 (7.8%)	1111 (10.6%)
Assessment	None	2235 (33.2%)	1868 (26.7%)	2605 (24.8%)
	Pre-operative assessment (Elective)	3206 (47.6%)	4351 (62.1%)	6829 (65.1%)
	Inpatient assessment (Emergency)	1294 (19.2%)	787 (11.2%)	1052 (10.0%)

Table 2 Patients undergoing major abdominal stratified by number of long-term health conditions. Values are proportion (95%CI).

	Number of long-term health conditions		
	1 (n = 7014)	**2 (n = 5109)**	**≥ 3 (n = 5383)**
Atrial fibrillation	1.2% (1.0–1.5)	4.5% (3.9–5.1)	18.2% (17.2–19.2)
Cancer	43.0% (41.8–44.1)	57.1% (55.7–58.4)	68.2% (67.0–69.5)
Chronic kidney disease	10.8% (10.1–11.5)	24.1% (23.0–25.3)	41.4% (40.1–42.7)
Chronic liver disease	1.4% (1.1–1.7)	3.5% (3.0–4.0)	5.8% (5.2–6.4)
Chronic obstructive pulmonary disease	0	3.4% (2.9–3.9)	23.7% (22.5–24.8)
Congestive heart failure	0.3% (0.2–0.4)	1.4% (1.1–1.7)	8.7% (7.9–9.4)
Coronary artery disease	1.3% (1.1–1.6)	5.8% (5.2–6.5)	23.5% (22.3–24.6)
Diabetes mellitus	5.5% (4.9–6.0)	19.4% (18.3–20.5)	43.8% (42.4–45.1)
Hypertension	25.3% (24.2–26.3)	60.8% (59.4–62.1)	80.0% (78.9–81.0)
Inflammatory bowel disease	7.6% (7.0–8.2)	5.1% (4.5–5.7)	4.9% (4.3–5.4)
Other respiratory disease	1.9% (1.6–2.2)	7.8% (7.1–8.6)	34.7% (33.4–36.0)
Cerebrovascular disease	0.7% (0.5–0.9)	2.8% (2.3–3.2)	9.4% (8.6–10.2)
Venous thromboembolic disease	1.1% (0.8–1.3)	3.9% (3.3–4.4)	7.8% (7.1–8.5)

In patients having elective surgery, 30-day mortality (1.3% vs. 0.5% vs. 0.1%, $p < 0.001$) and incidence of major complications (10.2% vs. 7.6% vs. 3.7%, $p < 0.001$) were higher in patients with multimorbidity compared with those with one or no long-term health conditions (online Supporting Information Fig. S3b). Patients with multimorbidity undergoing emergency surgery had higher 30-day mortality (9.2% vs. 4.3% vs. 0.8%, $p < 0.001$) and incidence of major complications (25.0% vs. 14.4% vs. 5.9%, $p < 0.001$) compared with those with one or no long-term health conditions (online Supporting Information Fig. S3b). Outcomes were adjusted in a three-level model accounting for patient and surgical level factors nested within hospitals and country of treatment (online Supporting Information Tables S10–S15).

Discussion

This pre-planned secondary analysis of an international, multicentre prospective cohort study of patients undergoing major surgery has several important findings. First, 50–70% of patients undergoing surgery had pre-existing multimorbidity. Second, although multimorbidity was associated with a twofold increase in mortality, poor control of long-term health conditions (i.e. high ASA physical status) and functional status (i.e. frailty) appeared key.

Findings from this study differ from previously published studies. Multimorbidity in patients undergoing major surgery was higher than that shown in previous studies [12, 22]. A study including > 13 million patients undergoing surgery in England from 2010 to 2015 identified only one in eight patients as having multimorbidity. The higher rates reported in our study may reflect the change in multimorbidity rates over the past decade and inclusion of more chronic conditions. Variation in inclusion of type of long-term health conditions in previous studies limits generalisability of data, especially peri-operative outcomes. For instance, a study from the USA defined lists of disease combinations associated with elevated mortality after general surgery [23]. The study excluded patients with cancer and dementia and found that one-third of patients had a high-risk combination; these patients experienced a threefold increase in death [15, 24]. Finally, none of the published studies have examined the relationship between multimorbidity, frailty [25] and ASA physical status, where the latter is often a surrogate for control of long-term health conditions.

Understanding how multimorbidity interacts with urgency of surgery is important. The majority of studies have only focused on emergency surgery [12, 23, 26, 27], apart from one recent study that showed rates of multimorbidity were higher in patients undergoing emergency compared with those undergoing elective surgery [22]. This contrasts with the present study where rates of multimorbidity were higher in elective surgery. Despite this, peri-operative morbidity and mortality were disproportionately higher in patients undergoing

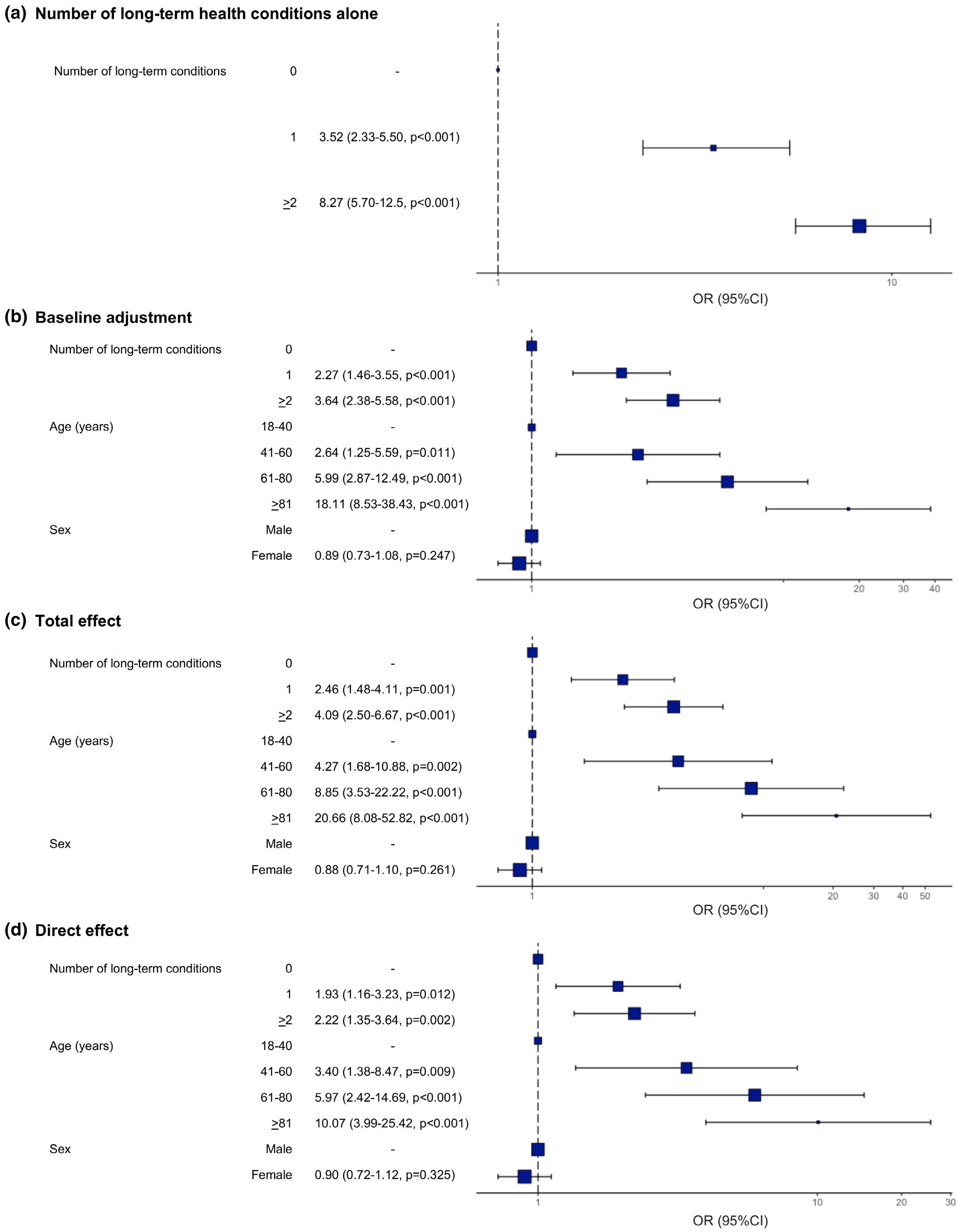

Figure 2 Thirty-day mortality after major abdominal surgery. (a) Unadjusted for number of long-term health conditions; (b) adjusted for age, sex, hospital and country; (c) adjusted for age, sex, confounders (BMI, surgical urgency, approach, contamination, assessment), hospital and country; (d) adjusted for age, sex, confounders (BMI, surgical urgency, approach, contamination, assessment), hospital, country and potential mediators (ASA physical status, frailty).

emergency surgery in patients with multimorbidity. These staggering differences warrant a closer focus to improving outcomes.

No difference in mortality or complications was identified between patients with multimorbidity who received pre-operative assessment and those who did not.

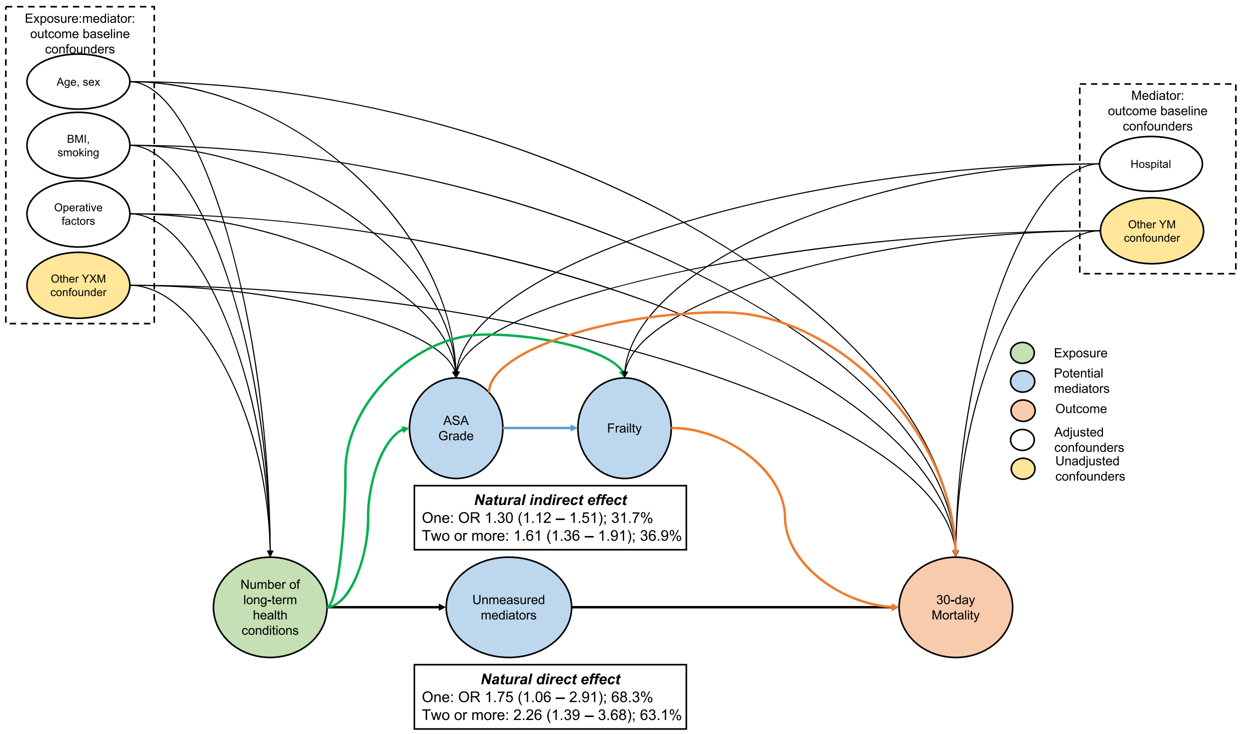

Figure 3 Three-way decomposition mediation model of the proportion of the effect of number of long-term health conditions on 30-day mortality mediated by ASA physical status and presence of frailty. OR, odds ratio (95%CI).

It is difficult to know with any certainty what can be interpreted from this. It does not necessarily suggest that pre-operative assessment has no impact. For example, this could represent effective selection of patients, based on important factors other than multimorbidity, who would benefit from pre-operative assessment and whose outcomes would otherwise have been significantly worse. However, our study does show an association between worse outcomes and multimorbidity and it would seem sensible that, when possible, these patients are assessed pre-operatively. It is concerning, therefore, that 26.5% of patients with multimorbidity did not receive pre-operative assessment before elective surgery. These findings highlight an urgent need to improve systems to identify these patients and/or improve healthcare system pre-operative assessment capacity. Further research into the impact of pre-operative assessment in patients with multimorbidity is warranted.

A major strength of this study is the large study size and the prospective, multinational design. CASCADE included patients undergoing major surgery from 446 hospitals in 29 countries across Europe, providing national granularity. Although patients were identified on admission for elective or emergency abdominal surgery, these findings are consistent with other reports and should be applicable to a more general population undergoing surgery. There are, however, important limitations to be addressed. First, this study does not include an exhaustive list of all long-term health conditions that can be included. For instance, pre-existing important mental health conditions, such as depression and anxiety, were not captured. In addition, we assumed that all long-term health conditions were equally weighted in the context of multimorbidity, regardless of severity. However, the latter is important as patients with uncontrolled or severe long-term health conditions may likely have poorer outcomes. Second, we did not perform follow-up beyond 30 days after surgery. Therefore, the long-term impact of pre-existing multimorbidity in patients undergoing surgery remains unclear, especially with respect to return to normal activities of daily living. This is especially important in the global context where dedicated rehabilitation programs may be needed.

With the need for surgical care rising rapidly globally in parallel with multimorbidity, there is a need to act urgently to address this. This contemporary cohort study offers new insight into the intersection between surgery and multimorbidity. This study has important implications for clinical practice and policy. It highlights that pre-existing

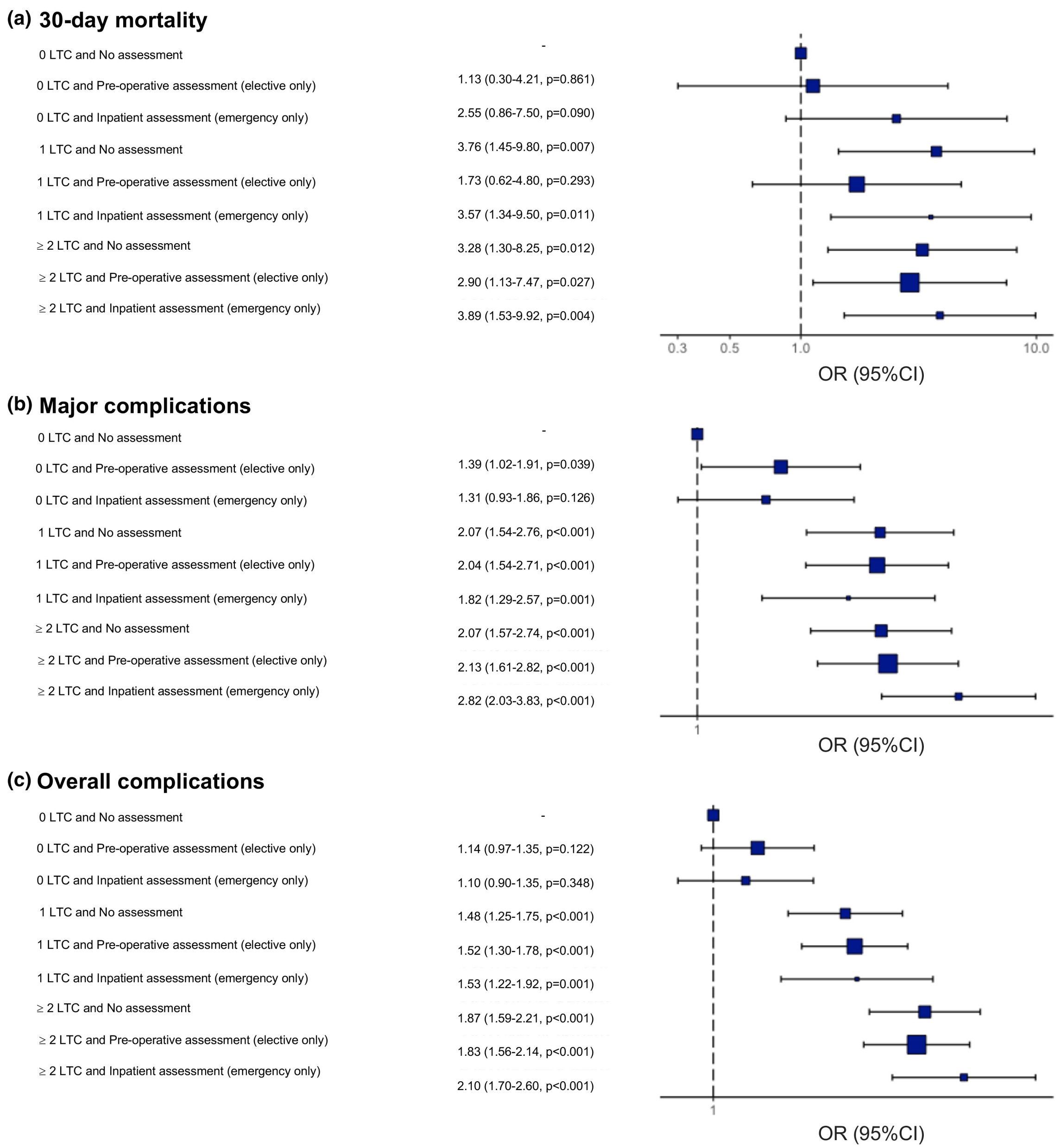

Figure 4 Adjusted analysis of the interaction between number of long-term health conditions (LTC) and the receipt of pre-operative assessment for: (a) 30-day mortality; (b) major complications; and (c) overall complications.

multimorbidity is an important surrogate for peri-operative risk that clinicians need to consider. Patients presenting through surgical pathways with multimorbidity offer a window of opportunity to address some of these common conditions to provide holistic care. This is important as exemplified by the recent reports on the ageing population requiring healthcare [4, 28]. The need to address multimorbidity in healthcare should be a responsibility of every clinician, including secondary care, to move towards integrated care.

In summary, multimorbidity is common among surgical patients across Europe and outcomes are poor in these patients, particularly following emergency surgery. Further research is warranted to determine the effectiveness of targeted management of surgical patients with multimorbidity.

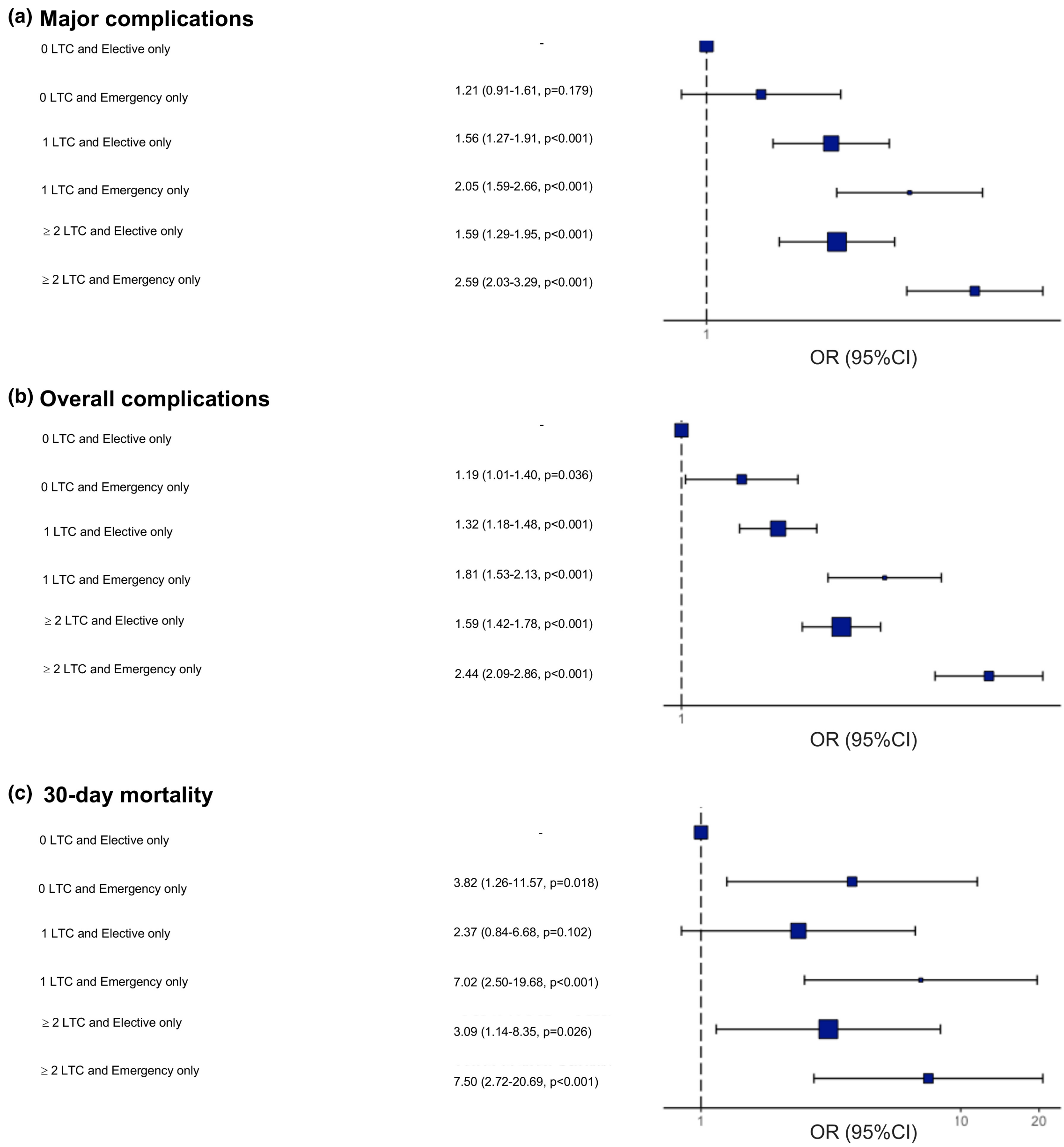

Figure 5 Adjusted analysis of the interaction between number of long-term health conditions (LTC) and the urgency of surgery for: (a) 30-day mortality; (b) major complications; and (c) overall complications.

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protection issues but the correspondence author is happy to be contacted. No statistical code is available. No competing interests declared.

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Supporting Information

Additional supporting information may be found online via the journal website.

Appendix S1. STARSurg and EuroSurg collaborators.

Figure S1. Distribution of multimorbidity by the type of long-term health conditions in all patients undergoing major abdominal surgery by proportion of patients with co-occurring long-term health conditions.

Figure S2. Distribution of long-term health conditions by urgency of surgery stratified by age and BMI in patients undergoing major abdominal surgery stratified by urgency.

Figure S3. Postoperative complications and mortality in patients undergoing major abdominal surgery by the number of long-term health conditions.

Figure S4. Distribution of long-term health conditions by urgency of surgery stratified by age and sex in patients undergoing major abdominal surgery stratified by urgency.

Figure S5. Distribution of type of long-term health conditions in patients undergoing major abdominal surgery stratified by urgency.

Table S1. Baseline characteristics of all patients undergoing major abdominal surgery.

Table S2. Summary of long-term health conditions in patients undergoing major abdominal surgery stratified by urgency.

Table S3. Univariable and adjusted multivariable and multilevel logistic regression model for the 30-day mortality in patients undergoing major abdominal surgery.

Table S4. Multilevel adjusted logistic regression model for the 30-day mortality in patients undergoing major abdominal surgery excluding potential mediators.

Table S5. Mediation models examining effects of potential mediators on 30-day postoperative mortality.

Table S6. Full adjusted logistic regression model for the presence of major complications in patients undergoing major abdominal surgery.

Table S7. Full adjusted logistic regression model for the presence of any complications in patients undergoing major abdominal surgery.

Table S8. Clinical characteristics of patients undergoing elective major abdominal surgery stratified by number of long-term health conditions.

Table S9. Clinical characteristics of patients undergoing emergency major abdominal surgery stratified by number of long-term health conditions.

Table S10. Full adjusted logistic regression model for the 30-day mortality in patients undergoing elective major abdominal surgery.

Table S11. Full adjusted logistic regression model for the presence of major complications in patients undergoing elective major abdominal surgery.

Table S12. Full adjusted logistic regression model for the presence of any complications in patients undergoing elective major abdominal surgery.

Table S13. Full adjusted logistic regression model for the 30-day mortality in patients undergoing emergency major abdominal surgery.

Table S14. Full adjusted logistic regression model for the presence of major complications in patients undergoing emergency major abdominal surgery.

Table S15. Full adjusted logistic regression model for the presence of any complications in patients undergoing emergency major abdominal surgery.