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Using data to understand outcomes for cancer surgery in low- and middle-income countries

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I, Stephen Knight, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis. Parts of this work have been published in The British Journal of Surgery, BMJ Open, The Lancet, and Lancet Global Health.

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Abstract

Background

Of the 15.2 million individuals diagnosed with cancer worldwide in 2015, 80% had a need for surgery. Yet little comparative data globally exist on early outcomes, particularly within low-income and middle-income countries (LMICs). I designed and delivered an international, prospective cohort study to provide comprehensive data across income settings on early outcomes in patients undergoing surgery for three common cancers.

Methods

I determined the early outcomes following cancer surgery through standardised and prospective methodology to gather contemporaneous and comprehensive data across multiple countries. Next, I validated this data to ensure accuracy and high case ascertainment. Finally, I determined the patient- and hospital-level factors which influence early outcomes following cancer surgery, to identify potential interventions which may improve surgical cancer care worldwide.

Results

In an international cohort of 15 958 patients from 428 hospitals and 82 countries undergoing surgery for breast, colorectal, or gastric cancer, case ascertainment and data accuracy were high. Higher postoperative mortality was seen in patients receiving surgery in LMICs, despite equivalent complication rates. The capacity to rescue patients from death after the development of common postoperative complications explains some of the disproportionate mortality burden experienced in LMICs. I demonstrated improvements in hospital facilities, which correlate with a hospital's ability to perform safe, high-quality operations and aid the early identification and treatment of postoperative complications,

are likely to prevent up to three early surgical deaths for every 100 patients undergoing cancer surgery worldwide.

Conclusions

Perioperative mortality is disproportionately greater in LMICs, which contributes to worse cancer survival in these settings. Excess early mortality following cancer surgery is avoidable, but improving access to surgical care alone is unlikely to significantly reduce cancer-associated mortality. Urgent assessment of pragmatic perioperative interventions led by investigators in LMICs is needed to avert avoidable mortality after the development of common complications after cancer surgery.

Lay summary

The main aim of my thesis was to understand how well patients recover in the initial period after cancer surgery worldwide.

More than 15 million people develop cancer each year. Despite 80% of people needing surgery to help manage their cancer, less than one fifth will have access to safe surgical care across the world. We already know that patients generally have poorer outcomes following surgery in countries with weaker healthcare systems, but little is known about how these outcomes vary following surgery for cancer worldwide. If we can describe and understand why the outcomes are different across the world, we hope this information will help to identify changes which will improve care for a significant number of people undergoing surgery for cancer in future.

Other researchers have identified patients have worse outcomes after cancer surgery in low- and middle-income countries, but the data is not very accurate or generalisable to the majority of countries. We have a global network of surgeons across more than 80 countries who are able to collect data on patients undergoing surgery for cancer, which makes it easier to describe early outcomes after surgery and where improvements could be made for the benefit of patients.

In this thesis, I demonstrate that early outcomes after cancer surgery are significantly worse in the majority of countries worldwide. By collecting better data across multiple countries, I have been able to understand the reasons why more early deaths occur in these settings after surgery for cancer. Furthermore, my work has identified what improvements in hospital infrastructure and treatment could save a large number of lives worldwide following cancer surgery in future.

Contents

Acknowledgements....3

Abstract....4

Lay summary....6

Contents....7

List of Figures....11

List of Tables....15

List of Abbreviations....23

Chapter 1 Introduction....26

1.1 The origins of 'Global Surgery'....26

1.2 Burden of global disease amenable to surgical treatment....27

1.3 The cost-effectiveness of surgery....36

1.4 Developing surgical systems....38

1.5 Measuring the effectiveness and quality of surgical care....39

1.6 Global surgical cancer care....43

1.7 Summary of motivation for thesis....53

1.8 Research Gaps....54

1.9 Aim and objectives....54

Chapter 2 Use of data to improve surgery in low- and middle-income countries....56

2.1 Introduction....56

2.2 Methods....58

2.3 Results....61
2.4 Discussion....81
2.5 Contribution statement....84
2.6 Outputs relating to this chapter....85
Chapter 3 Measuring early postoperative outcomes in global cancer surgery: the GlobalSurg 3 study....86
3.1 Introduction....86
3.2 Methods....87
3.3 Discussion....99
3.4 Contribution statement....101
3.5 Outputs relating to this chapter....101
Chapter 4 Patients undergoing surgery for cancer worldwide....102
4.1 Introduction....102
4.2 Methods....102
4.3 Results....104
4.4 Discussion....130
4.6 Outputs relating to this chapter....133
Chapter 5 Global variation in postoperative mortality and complications after cancer surgery....135
5.1 Introduction....135
5.2 Methods....136

5.3 Results....137
5.4 Discussion....161
5.5 Contribution statement....166
5.6 Outputs relating to this chapter....166
Chapter 6 Effects of hospital facilities on patient outcomes after cancer surgery....167
6.1 Introduction....167
6.2 Methods....167
6.3 Results....169
6.4 Discussion....193
6.5 Contribution statement....198
6.6 Outputs relating to this chapter....199
Chapter 7 The impact of malnutrition on early outcomes after cancer surgery....200
7.1 Introduction....200
7.2 Methods....201
7.3 Results....202
7.4 Discussion....224
7.5 Contribution statement....228
7.6 Outputs relating to this chapter....228
Chapter 8 Discussion....230
8.1 Summary of key findings in context of wider literature....230
8.2 Future research priorities....234

8.3 Wider relevance and applications of methodology used in this thesis 237

8.4 Conclusion 240

8.5 Outputs relating to this chapter 240

Chapter 9 References 242

Chapter 10 Appendix: Supplementary material 275

10.1 Supplementary material for Chapter 2 275

10.2 Supplementary material for Chapter 3 277

10.3 Supplementary material for Chapter 5 306

10.4 Supplementary material for Chapter 6 364

10.5 Supplementary material for Chapter 7 390

List of Figures

Figure 1-1. The multiple facets of global surgery. 28

Figure 1-2. Estimated minimum need for surgical procedures each year worldwide. 32

Figure 1-3. Estimated unmet need for surgical procedures each year worldwide. 33

Figure 1-4. United Nations Sustainable Development Goals. 34

Figure 1-5. Proportion of population without access to safe, affordable surgery and anaesthesia. 35

Figure 1-6. Annual value of lost economic output due to surgical conditions expressed as percentage loss of gross domestic product (GDP). 37

Figure 1-7. Number of global deaths by cause between 1990 to 2018. 45

Figure 1-8. Number of global deaths stratified by World Bank income group by cause between 1990 to 2018. 46

Figure 1-9. Global deaths attributed to cancer type. 47

Figure 1-10. Disease burden rates from cancers in 2018. 48

Figure 1-11. Disease burden rates by cancer type. 49

Figure 1-12. Conceptual framework for scaling up surgical cancer services in resource-limited settings. 51

Figure 2-1. Conceptualising big data in healthcare. 57

Figure 2-2. Systematic literature search PRISMA flowchart. 65

Figure 2-3. Distribution of patient number across included studies. 78

Figure 2-4. Global distribution of patients across low- and middle-income countries for included articles. 79

Figure 2-5. Subject area of large volume studies of surgery in low- and middle-income countries. 80

Figure 3-1. Breast cancer Essential TNM classification 91

Figure 3-2. Hierarchical scale for basis of cancer diagnosis 92
Figure 4-1. Patient flow chart. 105
Figure 4-2. Distribution of patients within the GlobalSurg 3 cohort. 106
Figure 4-3. Comparison between preoperative clinical and postoperative final pathological staging. 114
Figure 4-4. Patient follow-up and method of diagnosis. 116
Figure 4-5. Proportion of all patients who sustained specific complications, stratified by cancer-type and country income group. 117
Figure 4-6. Hospital type and facilities for centres treating cancer, stratified by country income group. 118
Figure 4-7. Map of missing values. 125
Figure 4-8. Case ascertainment. 126
Figure 4-9. Distribution of patients enrolled per hospital stratified by validation. 126
Figure 4-10. Correlation of patient age in validation compared to primary datasets. 128
Figure 5-1. Patients and outcomes by cancer-type and country income group. 138
Figure 5-2. Stage of presentation, 30-day mortality, and 30-day complications by cancer and country income group. 139
Figure 5-3. Multilevel logistic regression adjusted outcomes by country income group. 154
Figure 5-4. Early outcomes following surgery for cancer by cancer and country income group 156
Figure 5-5. Stage of presentation, 30-day mortality, and 30-day complications by cancer and country income group. 157
Figure 5-6. Capacity to rescue from major complication. 158

Figure 5-7. Capacity to rescue from major complication mediated by postoperative care infrastructure.. 159
Figure 5-8. Absolute risk difference for 30-day mortality after major complication in the presence of consistently available postoperative care infrastructure. 160
Figure 6-1. Study flowchart for hospital facility analysis. 171
Figure 6-2. Relationship between hospital facilities and country income group..... 173
Figure 6-3. Distribution of outcomes across total number of hospital facility characteristics. 174
Figure 6-4. Distribution of facility characteristics worldwide. 178
Figure 6-5. Absolute risk for 30-day mortality associated with four or more hospital facility characteristics within each income group stratified by cancer type and sex. 191
Figure 6-6. Absolute risk for 30-day mortality associated with four or more hospital facilities within each income group stratified by cancer type and sex for higher risk surgical patients. 192
Figure 7-1. Patient flowchart for malnutrition analysis 203
Figure 7-2. Multivariable regression model for factors associated with presence of severe malnutrition. 206
Figure 7-3. Distribution of complications by nutritional state and country income group. 207
Figure 7-4. Distribution of 30-day complications by nutritional state and country income group for colorectal cancer. 210
Figure 7-5. Distribution of 30-day complications by nutritional state and country income group for gastric cancer. 211
Figure 7-6. Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status..... 212

Figure 7-7. Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status.....219
Figure 7-8. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status.....220
Figure 7-9. Three-way decomposition mediation model of the effect of country income group on 30-day mortality mediated by nutritional state.....221
Figure 7-10. Three-way decomposition mediation model of the effect of country income group on 30-day surgical site infection rates mediated by nutritional state. 222
Figure 10-1. Stage of presentation, 30-day mortality, and 30-day complications by cancer and country income group. 308
Figure 10-2. Adjusted rates of 30-day complication rates after surgery for cancer 309
Figure 10-3. Capacity to rescue from major complication: sensitivity analysis using postoperative final pathological staging. 319
Figure 10-4. Relationship between hospital facilities and country income group.....372
Figure 10-5. Distribution of outcomes across number of available hospital facilities. ...373
Figure 10-6. Absolute risk for 30-day mortality in hospitals with more than three facilities within each income group stratified by cancer type and gender.....385
Figure 10-7. Absolute risk for 30-day mortality associated with four or more hospital facilities within each income group stratified by cancer type and gender for higher risk surgical patients. 388

List of Tables

Table 1-1. Proportion of patients requiring surgical management and estimated disease burden for five major surgical disease categories. 29

Table 1-2. Total value of gross domestic product losses secondary to surgical diseases. . 37

Table 1-3. Core indicators for monitoring of universal access to safe, affordable surgical and anaesthesia care. 40

Table 1-4. Surgical quality indicators in low-resource settings 42

Table 1-5. New cases and deaths for ten most common global cancers. 44

Table 2-1. Medline search strategy for systematic review to evaluate the current use of data to measure and improve surgical outcomes in LMICs. 59

Table 2-2. Eligibility criteria for systematic review. 60

Table 2-3. Studies included within the systematic review 66

Table 2-4. Aims of included studies grouped by primary outcome measure and surgical specialty. 71

Table 3-1. Patient inclusion and exclusion criteria. 89

Table 3-2. Clavien-Dindo classification of major postoperative complications 94

Table 4-1. Patient characteristics by country income group. 107

Table 4-2. Method of presentation: all patients. 110

Table 4-3. Method of presentation: colorectal and gastric cancer only. 111

Table 4-4. Stage of presentation by region. 113

Table 4-5. Summary of hospital care services for centres treating cancer stratified by country income group. 119

Table 4-6. Patient and operative characteristics by country income group stratified by cancer type, including missing data. 122

Table 4-7. Availability of sampled variables to validators by country income group 127

Table 4-8. Validation study for categorical variables. Data are counts. 129
Table 5-1. Cancer stage by other predictors (breast). 140
Table 5-2. Cancer stage by other predictors (colon). 144
Table 5-3. Cancer stage by other predictors (gastric). 149
Table 6-1. Distribution of hospital-level infrastructure and resources by country income group. 172
Table 6-2. Adjusted mortality rates stratified by hospital inclusion. 175
Table 6-3. Hospital facility selection using backward elimination. 176
Table 6-4. Hospital facility selection sensitivity analysis 177
Table 6-5. Patient characteristics by hospital facility characteristic level. 180
Table 6-6. Relationship between hospital facility level and patient safety and quality of cancer care metrics. 182
Table 6-7. Proportion of hospitals performing elective operations for each cancer across hospital facility level. 184
Table 6-8. Adjusted mortality rate across hospital facility characteristic count. 185
Table 6-9. Sensitivity analysis using imputed dataset for adjusted mortality. 186
Table 6-10. Adjusted major complication rates across hospital facility characteristic count. 187
Table 6-11. Capacity to rescue patients following major complication following case-mix adjustment. 188
Table 6-12. Sensitivity analysis using imputed dataset for capacity to rescue. 189
Table 7-1. Patient Characteristics by country income level. 204
Table 7-2. Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status in patients undergoing surgery for colorectal cancer. 213

Table 7-3. Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status in patients undergoing surgery for gastric cancer. .215
Table 7-4. Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status after multiple imputation for missing data. 217
Table 7-5. Three-way decomposition mediation model of the effect of country income group on 30-day mortality mediated by nutritional state after multiple imputation for missing data. 223
Table 7-6. Three-way decomposition mediation model of the effect of country income group on surgical site infection mediated by nutritional state after multiple imputation for missing data. 223
Table 10-1. Patient and operative characteristics by country income group stratified by cancer type, including missing data. 306
Table 10-2. Cancer stage by other predictors (breast). 310
Table 10-3. Cancer stage by other predictors (colon). 313
Table 10-4. Cancer stage by other predictors (gastric). 316
Table 10-5. Surgical procedure (breast). 320
Table 10-6. Surgical procedure (colorectal). 322
Table 10-7. Surgical procedure (gastric). 324
Table 10-8. Detailed outcomes stratified by cancer and country income level. 326
Table 10-9. Breast cancer logistic regression analyses: 30-day mortality. 329
Table 10-10. Breast cancer logistic regression analyses: major complication. 331
Table 10-11. Breast cancer logistic regression analyses: all complications. 333
Table 10-12. Colorectal cancer logistic regression analyses: mortality. 335
Table 10-13. Colorectal cancer logistic regression analyses: major complication. 338
Table 10-14. Colorectal cancer logistic regression analyses: all complications. 341

Table 10-15. Gastric cancer logistic regression analyses: mortality. 344
Table 10-16. Gastric cancer logistic regression analyses: major complication. 347
Table 10-17. Gastric cancer logistic regression analyses: all complications. 350
Table 10-18. Complications in patients who died. 353
Table 10-19. Summary of hospital care services for centres treating gastric and colon cancer stratified by country income group. 357
Table 10-20. 30-day mortality in patients who sustained a major complication - capacity to rescue models. 359
Table 10-21. Three-way mediation decomposition of proportion of effect of country income group on 30-day mortality mediated by the absence of postoperative care infrastructure. 361
Table 10-22. Absolute risk difference for 30-day mortality after major complication in the presence of consistently available postoperative care infrastructure. 362
Table 10-23. Proportion of hospitals performing elective operations for each cancer by income group. 370
Table 10-24. Proportion of hospitals performing elective operations for each cancer stratified by included cancers in GlobalSurg 3. 371
Table 10-25. Case volume stratified by hospital inclusion. 374
Table 10-26. Adjusted mortality rates stratified by hospital inclusion. 375
Table 10-27. Relationship between hospital facility level and postoperative complication rates. 376
Table 10-28. Relationship between hospital facility level and patient safety and quality of cancer care metrics. 377
Table 10-29. Adjusted mortality rate for colorectal and gastric cancer across hospital facility level. 378

Table 10-30. Sensitivity analysis using imputed dataset. 379
Table 10-31. Sensitivity analysis for adjusted outcome rates across all eleven hospital facilities.....381
Table 10-32. Adjusted major complication rates across hospital facility level. 382
Table 10-33. Capacity to rescue patients following major complication following case-mix adjustment. 383
Table 10-34. Absolute risk for 30-day mortality associated with four or more hospital facilities within each income group stratified by cancer type and gender. 384
Table 10-35. Absolute risk for 30-day mortality in hospitals with more than three facilities within each income group stratified by cancer type and gender.....386
Table 10-36. Absolute risk for 30-day mortality associated with four or more hospital facilities within each income group stratified by cancer type and gender for higher risk surgical patients undergoing elective surgery.....389
Table 10-37. Summary of missing data for 30-day mortality.....390
Table 10-38. Summary of missing data for 30-day major complication. 391
Table 10-39. Missing data for nutritional status stratified by World Bank tertile. 392
Table 10-40. Distribution of individual major complications by nutritional state. 393
Table 10-41. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for 30-day mortality. 394
Table 10-42. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for 30-day major complication. 395
Table 10-43. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for 30-day major complication in patients with colorectal cancer. 396

Table 10-44. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for 30-day major complication in patients with gastric cancer. 397
Table 10-45. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for all complications. 398
Table 10-46. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for all complications in patients with colorectal cancer. 399
Table 10-47. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for all complications in patients with gastric cancer. 400
Table 10-48. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for anastomotic leak. 401
Table 10-49. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for anastomotic leak in patients with colorectal cancer. 402
Table 10-50. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for anastomotic leak in patients with gastric cancer. 403
Table 10-51. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for surgical site infection. 404
Table 10-52. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for surgical site infection in patients with colorectal cancer. 405

Table 10-53. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for surgical site infection in patients with gastric cancer. 406
Table 10-54. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for major complication after multiple imputation for missing data. 407
Table 10-55. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for all complications after multiple imputation for missing data. 408
Table 10-56. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for surgical site infection after multiple imputation for missing data. 409
Table 10-57. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for 30-day mortality after imputation of missing GLIM criteria. 410
Table 10-58. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for major complication after imputation of missing GLIM criteria. 412
Table 10-59. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for all complications after imputation of missing GLIM criteria. 414
Table 10-60. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for surgical site infection after imputation of missing GLIM criteria. 416

Table 10-61. Three-way decomposition mediation model of the effect of country income group on 30-day mortality mediated by nutritional state after imputation of missing GLIM criteria. 418
Table 10-62. Three-way decomposition mediation model of the effect of country income group on 30-day mortality mediated by nutritional state after imputation of missing GLIM criteria. 419

List of Abbreviations

aOR	Adjusted Odds Ratio
ASA	American Society of Anaesthesiologists Score
BCG	Bacille Calmette-Guérin
BMI	Body Mass Index
CD	Clavien-Dindo
CI	Confidence Intervals
COVID-19	Coronavirus disease
CT	Computerised Tomography
DALYs	Disability-Adjusted Life-Years
DCIS	Ductal Carcinoma In Citu
ECOG	Eastern Cooperative Oncology Group Performance Status
EPR	Electronic Patient Record
GBD	Global Burden of Disease
GDP	Gross Domestic Product
GEE	Generalised Estimating Equations
GLIM	Global Leadership Initiative on Malnutrition
HDI	Human Development Index

HDU	High Dependency Unit
HIC	High Income Countries
HIV	Human Immunodeficiency Virus
IQR	Interquartile Range
ITU	Intensive Care Unit
LMICs	Low- and Middle-Income Countries
MDT	Multidisciplinary Team
NELA	National Emergency Laparotomy Audit
NICE	National Institute for Health and Care Excellence
NNT	Number Needed to Treat
OSI	Organ Space Infection
POMR	Perioperative Mortality Rates
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
REDCap	Research Electronic Data Capture
SAMPL	Statistical Analyses and Methods in the Published Literature
SD	Standard Deviation
SDG	Sustainable Development Goals

SNLB	Sentinel Lymph Node Biopsy
SSI	Surgical Site Infection
STROBE	STrengthening the Reporting of OBservational studies in Epidemiology
eTNM	Essential TNM Classification of Malignant Tumours
UICC	Union for International Cancer Control
WB	World Bank
WHO	World Health Organization
YLD	Years Lost to Disability
YLL	Years of Life Lost

Chapter 1 Introduction

1.1 The origins of 'Global Surgery'

1.1.1 Defining 'Global Surgery'

Global Surgery has been defined as the "*Enterprise of providing improved and equitable surgical care to the World's population, with its core tenets as the issues of needs, access, and quality*"[1] (Figure 1-1). It not only encompasses the treatment of surgical disease, but also its equitable provision across health systems globally. Often this results in an explicit focus on low- and middle-income countries (LMICs) due to these areas having the greatest burden of surgical disease, but often with the least capacity to manage it.

The scale of the problem was recently highlighted by the World Health Organisation (WHO), which estimated 95% of medical equipment in LMICs is imported, with 80% funded by international donors or foreign governments[2]. Furthermore, even when medical devices are available less than one third becomes operational[3].

1.1.2 Surgery in the global context

In 1980 Dr Halfdan Mahler, the then WHO Director-General, highlighted that the vast majority of the world's population dd not have access to adequate surgical care[4]. Typically, surgical care was considered too complex, expensive and had limited impact upon the global burden of disease[5]. Subsequently, the Millennium Development Goals (MDGs)[6] have drawn attention to key health issues in LMICs, generating resources and providing targets for policy makers. However, those that were not included within the agenda, including the majority of non-communicable diseases, were left behind[7].

Long neglected compared to other global public health topics, such as the prevention and treatment of childhood malnutrition, obstetric disorders, and communicable disease[8], the

Lancet Commission on Global Surgery in 2015 increased awareness of extreme disparities internationally and encouraged collaboration between surgeons, healthcare professionals, epidemiologists, and policy makers[9]. Meanwhile, data highlighted the volume of global disease amenable to surgical intervention, together with profound differences in the access, delivery, and cost-effectiveness of surgical treatments worldwide[10]. This resulted in the acknowledgement that every individual should have affordable access to timely, safe, and high-quality surgical care.

1.2 Burden of global disease amenable to surgical treatment

1.2.1 The global burden of surgical disease

Findings from the Global Burden of Disease 2010 study demonstrated that disease amenable to surgical intervention is substantial and growing[11]. It is estimated that surgery is required for around 30% of diseases worldwide[12], with an almost 17 million lives lost each year from conditions needing surgical care[13].

Major surgical diseases, which contribute more than 85% of all surgical deaths, cause significant mortality and disability worldwide (Table 1-1). However, the disability associated with conditions needing surgical care in LMICs has received little attention. For example, road-traffic injuries account for 75.5 million disability-adjusted life-years (DALYs), which has increased by one third over a 20-year period[14].

Figure 1-1. The multiple facets of global surgery.

Reproduced from Bath *et al*[1] by permission of BMJ Publishing Group Ltd. What is 'global surgery'? Defining the multidisciplinary interface between surgery, anaesthesia and public health, BMJ Global Health 4: e001808. Licence: CC BY-NC 4.0. http://dx.doi.org/10.1136/bmjgh-2019-001808

Meanwhile, as life expectancy increases worldwide[15,16], continued exposure to leading risk factors for disease are expected to translate into adult chronic disease, particularly solid malignant tumours[11]. This has already begun, with cancer causing 76% more disability globally between 1990 and 2010[17]. With the current trend in epidemiological transition across LMICs, it is expected that non-communicable diseases will surpass previous communicable disease challenges by 2035[10].

1.2.2 Worldwide availability of surgical intervention

However, surgical management in the majority of diseases remains out of reach for most of the world's population. Whilst an estimated 266 million operations are performed globally in 2008[18], these were largely restricted to high-income countries, with only 3.5% performed in the poorest third of the world's population[19] (Figure 1-2).

Table 1-1. Proportion of patients requiring surgical management and estimated disease burden for five major surgical disease categories.

Estimated worldwide means for five major surgical diseases using data from [13]. YLL, non-discounted years of life lost (mortality) using Institute for Health Metrics and Evaluation standardised life-expectancy[20]; YLD, years lost to disability (morbidity). Adapted from [21].

	Proportion of patients (%)	Deaths	YLL	YLD
Digestive disorders	30.3	337 000	8 246 000	1 658 000
Injury	60.8	3 085 000	141 283 000	30 144 000
Maternal disorders	36.7	93 000	5 251 000	657 000
Neonatal disorders	27.3	611 000	52 594 000	2 586 000
Cancer	62.0	4 943 000	113 995 000	2 777 000

Subsequent analysis demonstrated the number of surgical operations performed globally increased by a third over an eight year period[22], yet 143 million additional surgical procedures are needed each year to save lives and prevent disability[10] (Figure 1-3). These figures are likely to underestimate the actual surgical need, due to methodological assumptions and calculated estimates based on a healthcare system where population coverage was very good. Therefore, the actual need for surgical intervention may be much higher in weaker health systems.

1.2.3 Disparity in global surgical outcomes

Even when surgical procedures are available, outcomes are often suboptimal in lower resourced settings. For example, caesarean delivery comprised 30% (5.8 million operations) of the total surgical volume in countries with lower healthcare resource[22], yet maternal deaths following caesarean sections in LMICs remain 100 times higher and unfortunately around one third of babies do not survive[23].

An estimated 4.2 million people die annually worldwide within 30 days of surgery, more than human immunodeficiency virus (HIV), tuberculosis and malaria combined, with half of these deaths occurring in LMICs[24]. Previous large international cohort studies have identified that perioperative mortality and morbidity are up to seven times higher in LMICs[25–27], with further work suggesting the quality of surgical care is a key driver of overall outcomes[28].

1.2.4 The Lancet Commission on Global Surgery

In response to the challenges posed by diseases amenable to surgical intervention, the *Lancet* Commission on Global Surgery was launched in January 2014[9]. Aligned with a renewed global commitment to universal health coverage, which included representation within the updated Sustainable Development Goals (SDGs; Figure 1-4), the Commission aimed to examine the case for surgery as an integral component of health care. While the need for safe, affordable and high-quality surgical care extends across all countries, LMICs were the main focus due to the largest area of unmet need.

Estimates demonstrate five billion people do not have access to safe, affordable, and timely surgical and anaesthesia care[10]. This equates to 94% of the population in low-income and lower-middle-income countries, compared with 15% in high-income countries (Figure 1-

5). As a result, untreated surgical conditions exert a substantial but largely unrecognised negative effect on human health, welfare, and economic development within LMICs.

1.2.5 Limitations of global surgical research

Despite this, substantial deficits in global surgery research were identified by the *Lancet* Commission on Global Surgery. Historically, global health research efforts have not focused on diseases with a high burden or the greatest clinical need across LMICs[29]. Understanding the patient population and subsequent management of surgical disease have been further restricted by an absence of high quality local research, contributed by a shortage of funding, training, and capacity building[10,30].

Surgical research volume is slowly increasing within LMICs[10], but low-income country activity and multicountry collaborations remain very limited. This issue is not isolated to surgical specialities, however research capacity for surgery should be a priority[29]; including South-South collaboration with support and skills provided from high-income country groups.

1.2.6 Priorities in global surgical research

Supporting this move, several groups have identified key topics which should be prioritised for research in LMICs[10,31]. These include determinants of quality in surgical care; impact of improved hospital facilities on patient outcomes; surgical management of cancer; and sustainable, low-cost perioperative interventions. Meanwhile, current literature is heavily reliant on simulated models based on limited data sources[21,32,33]. Prospective, observational data collection on high burden surgical diseases will help to quantify global inequalities, highlight differences in patient presentation, treatment practices and early outcomes following surgery.

Figure 1-2. Estimated minimum need for surgical procedures each year worldwide.

Adapted from [10].

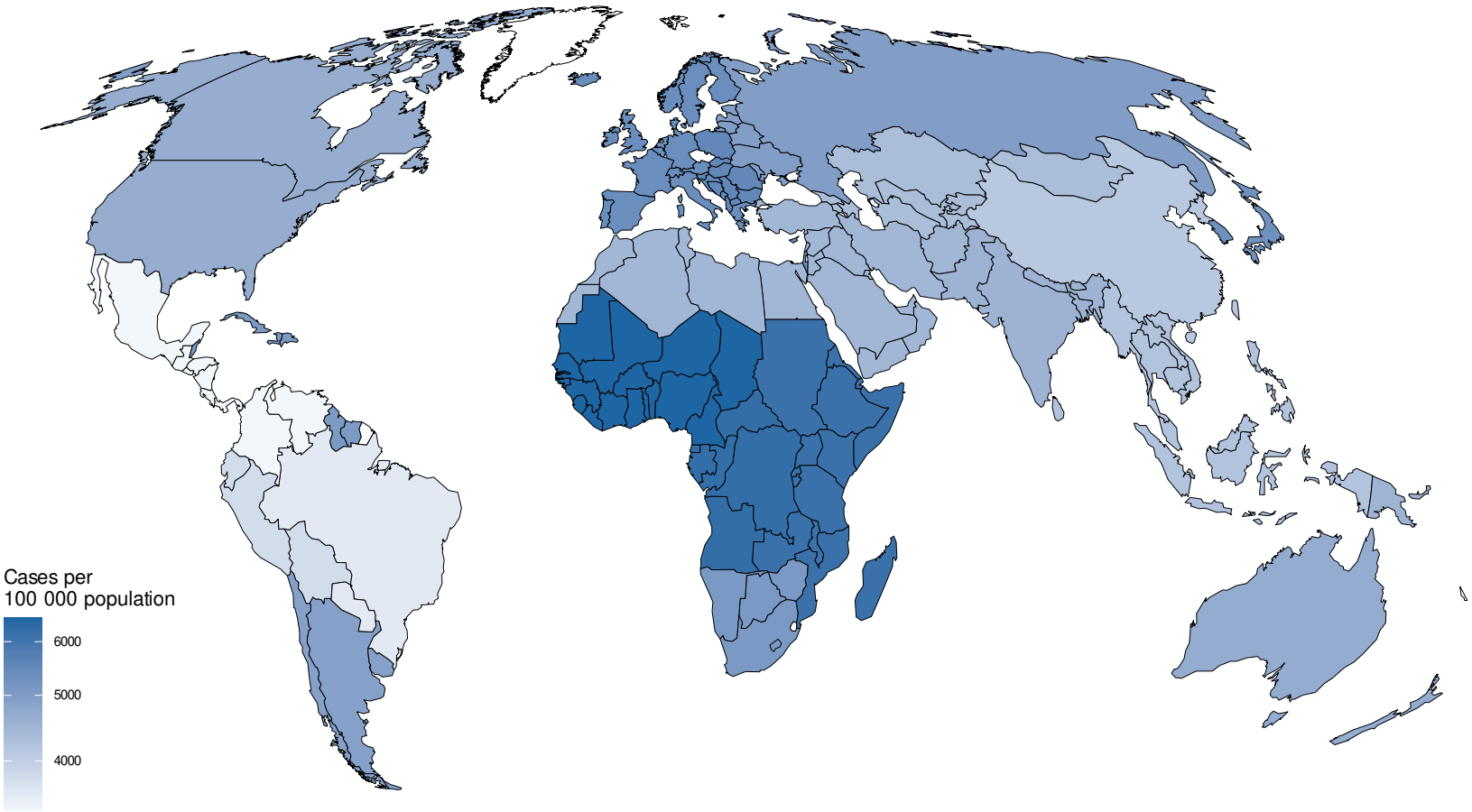


Figure 1-3. Estimated unmet need for surgical procedures each year worldwide.

Adapted from [10].

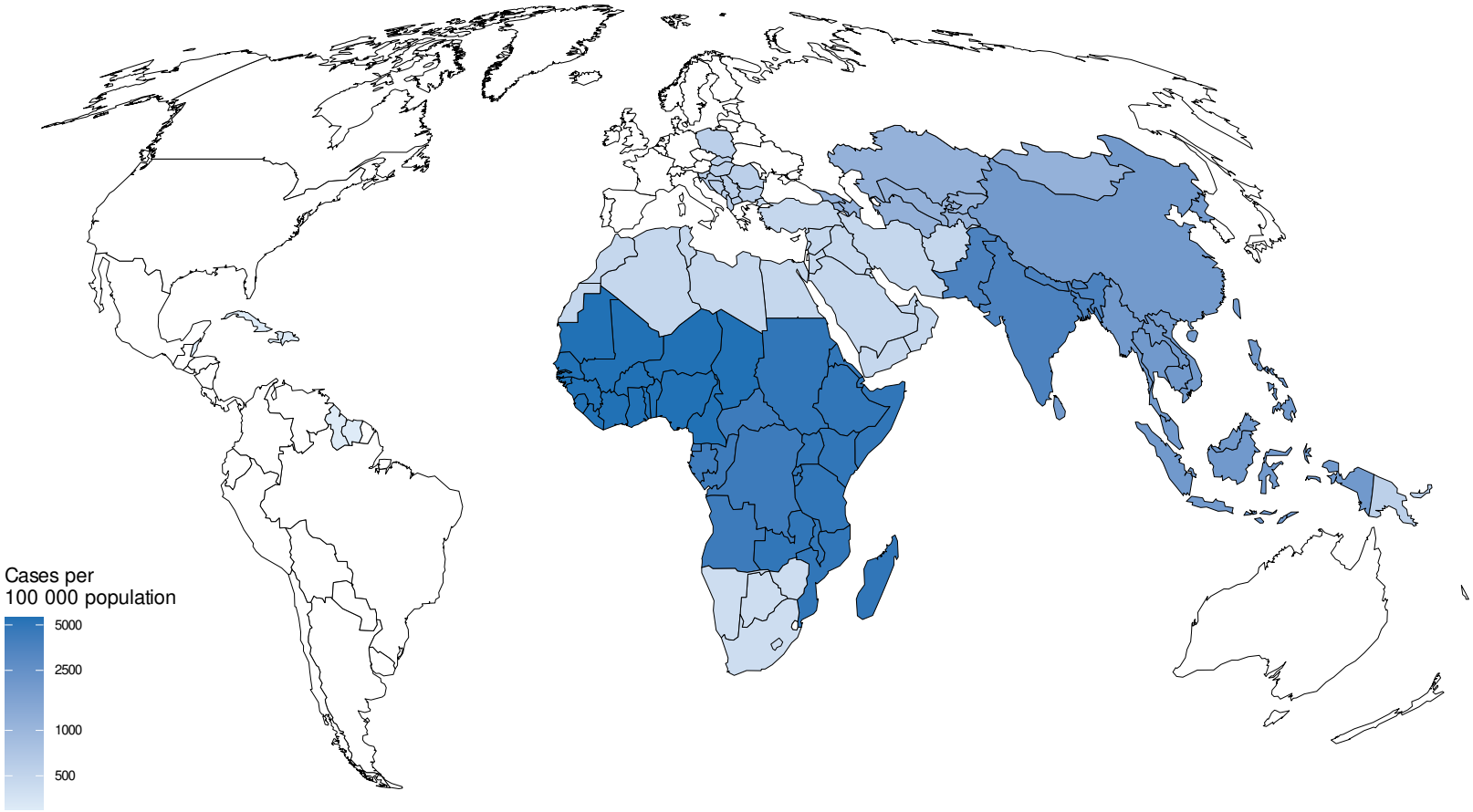


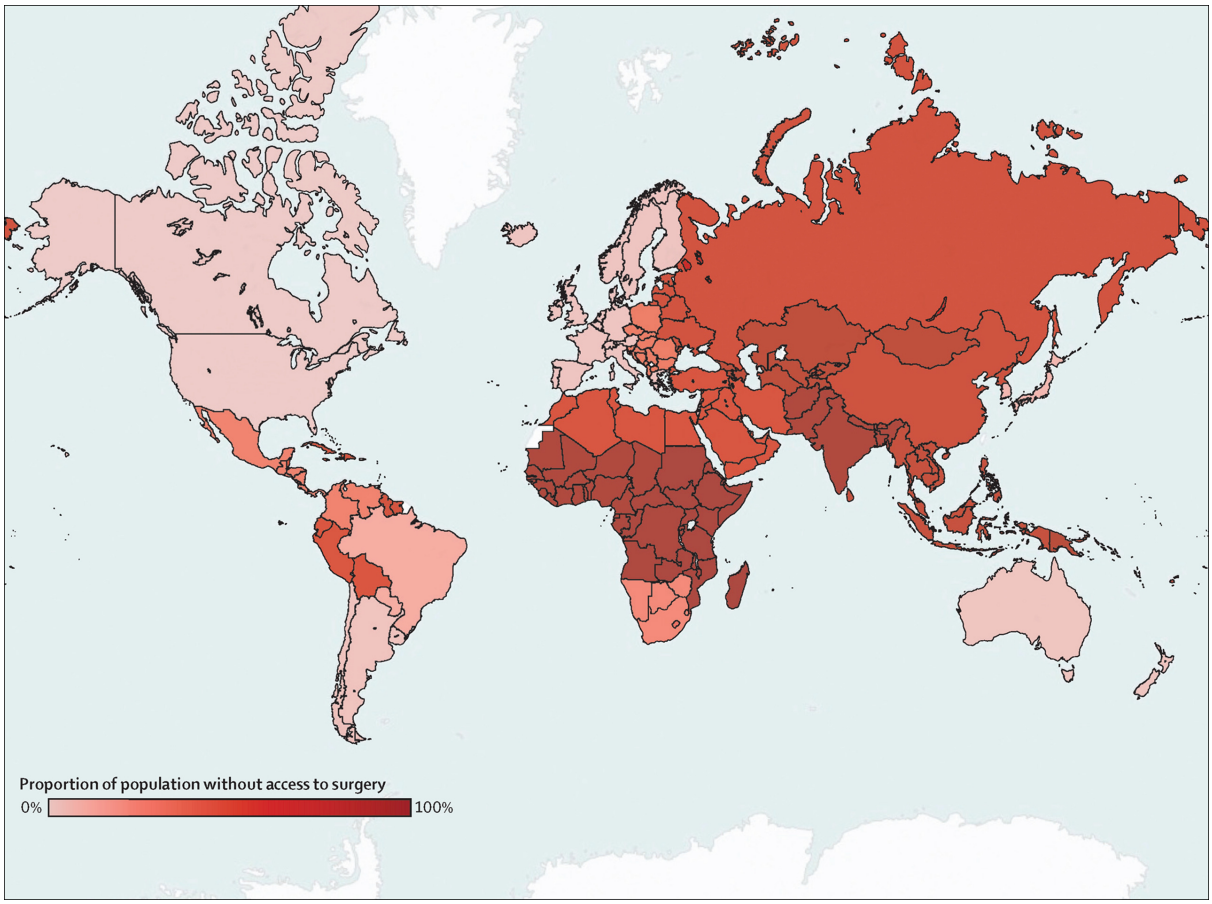
Figure 1-4. United Nations Sustainable Development Goals.

Sustainable Development Goals linked to safe, affordable and high-quality surgical care worldwide highlighted. Reproduction of Sustainable Development Goals by permission of United Nations [34].

Figure 1-5. Proportion of population without access to safe, affordable surgery and anaesthesia.

Reproduced from Meara *et al* (2015)[10] by permission of Elsevier. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development, Lancet 86(9993): 569-624. Licence: CC BY-NC 4.0.

https://doi.org/10.1016/S0140-6736(15)60160-X



1.3 The cost-effectiveness of surgery

1.3.1 The economic benefit of surgery

Surgery can often be perceived as an expensive intervention when compared to other public health measures, which limits its acceptance as a key player in achieving global health goals[8,35]. However, scaling up basic surgical care is a necessary step in improving global health[10]. Chao *et al* found that many essential surgical interventions are cost-effective in resource poor settings[17]. All seven categories of surgical interventions compared favourably to medical treatment for ischaemic heart disease and HIV treatment, with general surgery procedures demonstrating similar economic benefit to that of the BCG vaccine. In addition, the majority of interventions were deemed to be very cost effective according to WHO cost effectiveness thresholds[36].

The economic consequences of untreated surgical conditions are catastrophic. Estimates suggest that the total value of lost economic output secondary to commonly treated surgical conditions across 128 countries between 2015 and 2030 is $20.7 trillion, or 1.3% of projected global economic output[21] (Table 1-2). More than half of all losses to the global economy would occur within LMICs, with surgical conditions in middle-income countries projected to consume up to 2% of these countries' annual GDP growth[21] (Figure 1-6). However, a $420 billion investment required to scale up surgical services to treat these conditions compares favourably[10].

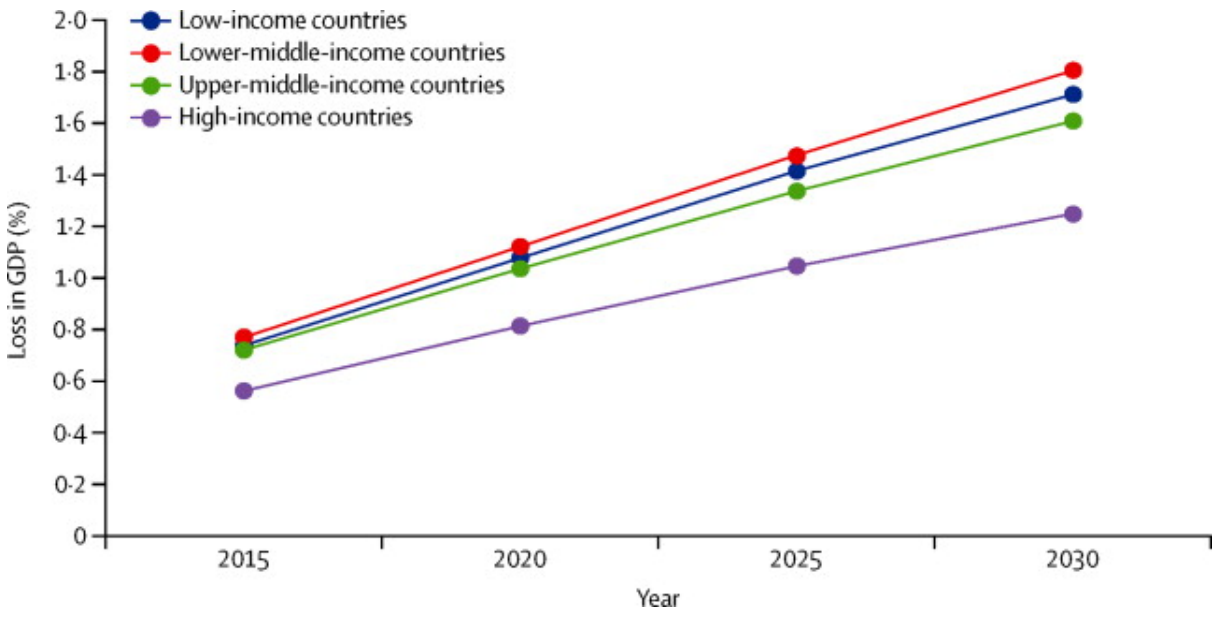
Table 1-2. Total value of gross domestic product losses secondary to surgical diseases.

Estimates for five major diseases requiring surgical treatment between 2015 and 2030. GDP: Gross Domestic Product. Values in billions of US$. Adapted from [21].

	Cumulative GDP loss	Lower uncertainty bound	Upper uncertainty bound
Digestive disorders	470	220	1010
Injury	7860	4330	13 240
Maternal disorders	80	20	220
Neonatal disorders	190	70	360
Cancer	12 120	7450	18 360
Total	20 720	12 090	33 190

Figure 1-6. Annual value of lost economic output due to surgical conditions expressed as percentage loss of gross domestic product (GDP).

Reproduced from Alkire *et al* (2015)[21] by permission of Elsevier. Global economic consequences of selected surgical diseases: a modelling study, Lancet 3: S21-27. Licence: CC BY-NC 4.0. https://doi.org/10.1016/S2214-109X(15)70088-4



1.3.2 Implementation challenges

However, it should be acknowledged that surgery in LMICs faces implementation challenges. For example, simple interventions, such as the WHO Surgical Safety Checklist[37], have been found to reduce 30-day mortality following emergency laparotomy to a greater extent in LMICs[38]. However, use of the WHO checklist is greatly reduced in lower resourced settings[27].

Despite a powerful argument for improving surgical provision as part of global health improvement programmes, surgery requires more resources and infrastructure compared to vaccination programmes and antiretroviral treatment. Therefore, further defining the burden of surgical disease, the patient population receiving operative intervention, and current variation in outcomes worldwide can help to prioritise areas of improvement and bolster the political prioritisation of global surgery[1].

1.4 Developing surgical systems

1.4.1 Surgical capacity

Basic infrastructure and resources necessary for safe, effective surgery are often in short supply, limiting the provision of basic surgical care within healthcare systems. Workforce capacity is also greatly limited, with an estimated 800 000 more surgeons, obstetricians and anaesthetists required by 2030 to achieve minimal workforce densities in LMICs[39]. With a median of 34 000 person years required to achieve this increase, the implementation of task shifting has been proposed to decrease costs and training times[39,40].

Workforce deficits are also intensified by the unequal distribution of surgical providers, with a greater density of surgical healthcare providers in urban regions[41]. Whilst partnerships exist between high-income institutions and LMIC surgical colleges, to support

the standardisation of surgical care, the dual challenge of training and retaining surgical providers where they are most needed remains[42].

Collaboration remains an important principle when developing, maintaining, and monitoring surgical capacity within LMICs. Multiple successful, long-term partnerships between high-income and LMIC institutions exist[42], together with significant interest from medical students and junior surgeons regarding training in global health.

1.5 Measuring the effectiveness and quality of surgical care

1.5.1 Key performance metrics

Improving the quality of healthcare requires the ability to measure quality, however the definition of 'surgical quality' is heterogenous and often difficult to capture[43,44]. In addition, few quality metrics have been designed specifically for surgery within LMICs. Many high-income country quality improvement programmes demand resource-intensive data collection and prolonged patient follow-up[45,46], which can be particularly challenging in low-resource settings.

LMIC-based studies frequently measure early outcome measures, including post-operative mortality and morbidity rate, surgical site infection, and length of hospital stay. However, reporting quality is often variable and heterogenous in nature. The *Lancet* Commission developed six core surgical indicators (Table 1-3), recommending they should be tracked and reported by all countries and global health organisations[10]. Rather than collected and analysed separately, they suggested indicators would provide the most information and provide adequate representation of the current state of surgical health systems when interpreted together. Some have been included within the WHO 100 Core Global Health

and the World Bank's World Development Indictors, however none are currently routinely collected and reported to the WHO[1].

Table 1-3. Core indicators for monitoring of universal access to safe, affordable surgical and anaesthesia care.

Adapted from Meara *et al*[10].

	Definition	Target (by 2030)
Access to timely essential surgery	Proportion of the population that can access, within two hours, a facility that can perform caesarean section, laparotomy, and treatment of open fracture (the Bellwether Procedures)	Minimum of 80% coverage per country
Specialist surgical workforce density	Number of specialist surgical, anaesthetic, and obstetric physicians per 100 000 population	100% countries with at least 20 per 100 000 population
Surgical volume	Procedures performed in an operating theatre per 100 000 population per year	100% countries tracking surgical volume and a minimum of 5000 procedures per 100 000 population
Perioperative mortality	All-cause death rate before discharge in patients who have undergone a procedure in an operating theatre	100% countries tracking perioperative mortality
Protection against impoverishing expenditure	Proportion of households protected against impoverishment from direct out-of-pocket payments for surgical and anaesthesia care	100% protection against impoverishment from out-of-pocket payments for surgical and anaesthesia care
Protection against catastrophic expenditure	Proportion of households protected against catastrophic expenditure from direct out-of-pocket payments for surgical and anaesthesia care	100% protection against catastrophic expenditure from out-of-pocket payments for surgical and anaesthesia care

1.5.2 Quality indicators of surgical care

In addition, Citron *et al* created a minimum set of evidence-based indicators to measure the quality of surgical care in LMICs (Table 1-4). Their criterion included clinical importance, real-world usability, capability to measure in resource-limited environments, clinical validity, and ability to risk-adjust across different settings. These metrics require few resources to collect and are designed to be accumulated prospectively, in environments potentially without electronic medical records and unique patient identifiers available.

Unfortunately, these metrics have a low level of evidence demonstrating their impact on patient outcomes and are predominantly supported by expert opinion in high-income countries. Furthermore, the adoption of quality-of-care tools are likely to be limited due to staffing levels, data collection platforms and research experience. The minimum collection of 15 co-dependent indicators to determine the quality of surgical care is also highly restrictive to their translation into routine clinical practice.

1.5.3 Variation in reporting of surgical indicators

Variation in surgical indicator reporting commonly occurs in studies originating within LMICs. Take perioperative mortality rates (POMR) as an example. POMR are widely championed as a standardised surgical safety indictor, providing procedure-specific and risk-adjusted rates across income settings[47–49]. A recent systematic review identified 985 studies across 83 LMICs reporting POMR, covering 1 020 869 patients undergoing 191 different procedures in 13 surgical specialities[47]. More than half of included studies did not provide a clear POMR definition, such as the time frame during which death occurred, or varied in their denominator to calculate POMR.

The utility of POMR is clear, with an ability to quantify surgical risk, benchmark current surgical quality at an institution or geographical level, and an aid to improve patient safety. Thirty-day POMR can provide a robust indicator and is less sensitive to variations in discharge practices[47]. However, clear outcome definitions and robust analyses are required before POMR can represent a global indictor of surgical quality and safety[50,51].

Table 1-4. Surgical quality indicators in low-resource settings.

Adapted from Citron *et al*[44].

Quality indicator	Descriptor
Safe structure	Morbidity and mortality conference
Safe process	Use of the safe surgery checklist
Safe outcomes	Perioperative mortality rate
	Proportion of cases with complications graded >2 on the Clavien-Dindo scale
Effective structure	Provider density
Effective process	Procedure rate
Effective outcome	Rate of caesarean sections
Patient-centred process	Use of informed consent
Patient-centred outcome	Patient hospital satisfaction questionnaire
Timely structure	Travel time to hospital
Timely process	Time from emergency department presentation to non-elective abdominal surgery
Timely outcome	Patient follow-up plan
Efficient process	Daily operating room usage
Equitable outcome	Comparative income of patients compared with population
	Proportion of patients facing catastrophic expenditure because of surgical care

1.5.4 Future utility of surgical indicators

With the development of National Surgical, Obstetric and Anaesthesia plans, the recording of surgical indicators to assess progress and identify areas to improve quality of care will become increasingly important. However, since the identification of six core indicators by the *Lancet* Commission on Global Surgery major hurdles still exist to maximise their

utility. Data availability for all six indictors is currently poor, with only one indictor found to have data from more than half of the WHO member states[18]. Therefore, further work standardising definitions and data collection is required to ensure surgical indicators can improve access to safe, affordable, and timely surgical care.

1.6 Global surgical cancer care

1.6.1 Worldwide prevalence of cancer amenable to surgical intervention

Of the 15.2 million individuals diagnosed with cancer in 2015, 80% required surgery[52]. Meanwhile, cancer is projected to contribute to a $12 trillion loss in global GDP by 2030, more than half the estimated loss of all major disease managed by surgery[21]. In tumours amenable to treatment, surgery often offers the best chance of cure, particularly in early-stage disease. Surgery also represents a key pillar across the cancer care pathway providing preventative, diagnostic, and supportive options.

A recent LMIC-led three-stage research prioritisation exercise identified cancer surgery as a major research priority. Yet, most studies that examine the global distribution and outcomes of solid cancers use simulated methods due to the absence of robust prospective data, including country-specific information on cancer epidemiology, stage distribution, and treatment approaches[52].

1.6.2 Global cancer mortality

Every six death in the world is due to cancer[33]. Deaths attributed to cancer have increased across all income groups since 1990 (Figure 1-7 and 1-8), becoming the second leading cause of death behind cardiovascular disease across high, upper middle and lower middle-income countries over this period. Overall, the total number of global cancer deaths has increased by 20% over the last ten years[33], with lung, bowel, stomach, breast, and

pancreatic cancer responsible for the largest number of cancer deaths globally (Figure 1-9, Table 1-5). While death rates from cancer are decreasing in high-income countries, the opposite has been demonstrated in low- and middle-income countries (LMICs)[33], reflecting disparities in cancer prevention, care, and control[52].

Death rates only capture mortality from cancer, without quantifying its impact on patients' quality of life following diagnosis. Many can live with cancer for long periods and suffer significant morbidity over this time. In 2018, more than 3000 years of healthy life were lost from cancers per 100 000 individuals, equating to 250 million worldwide[33]. The impact of cancer on people's lives was distributed evenly across the majority of countries (Figure 1-10). At a global level, the largest disease burden resulted from lung, breast, stomach, and bowel cancer[53] (Figure 1-11).

Table 1-5. New cases and deaths for ten most common global cancers.

Estimates for ten most common global cancers in 2018. Adapted from [54].

Cancer site	Number of new cases (% of all sites)	Number of deaths (% of all sites)
Lung	2 093 876 (11.6)	1 761 007 (18.4)
Breast	2 088 849 (11.6)	626 679 (6.6)
Prostate	1 276 106 (7.1)	358 989 (3.8)
Colon	1 096 601 (6.1)	551 269 (5.8)
Nonmelanoma of skin	1 042 056 (5.8)	65 155 (0.7)
Stomach	1 033 701 (5.7)	782 685 (8.2)
Liver	841 080 (4.7)	781 631 (8.2)
Rectum	704 376 (3.9)	310 394 (3.2)
Oesophagus	572 034 (3.2)	508 585 (5.3)
Cervix uteri	569 847 (3.2)	311 365 (3.3)

Figure 1-7. Number of global deaths by cause between 1990 to 2018.

Adapted from [53].

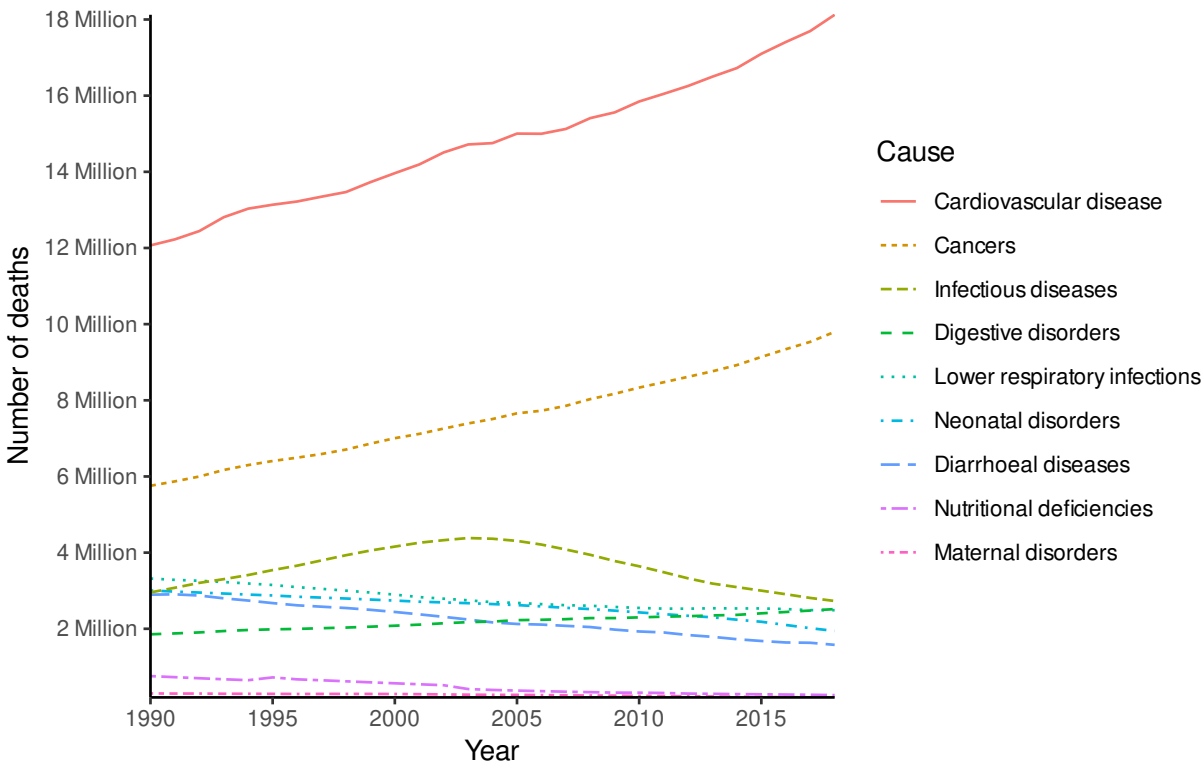


Figure 1-8. Number of global deaths stratified by World Bank income group by cause between 1990 to 2018.

Adapted from [53].

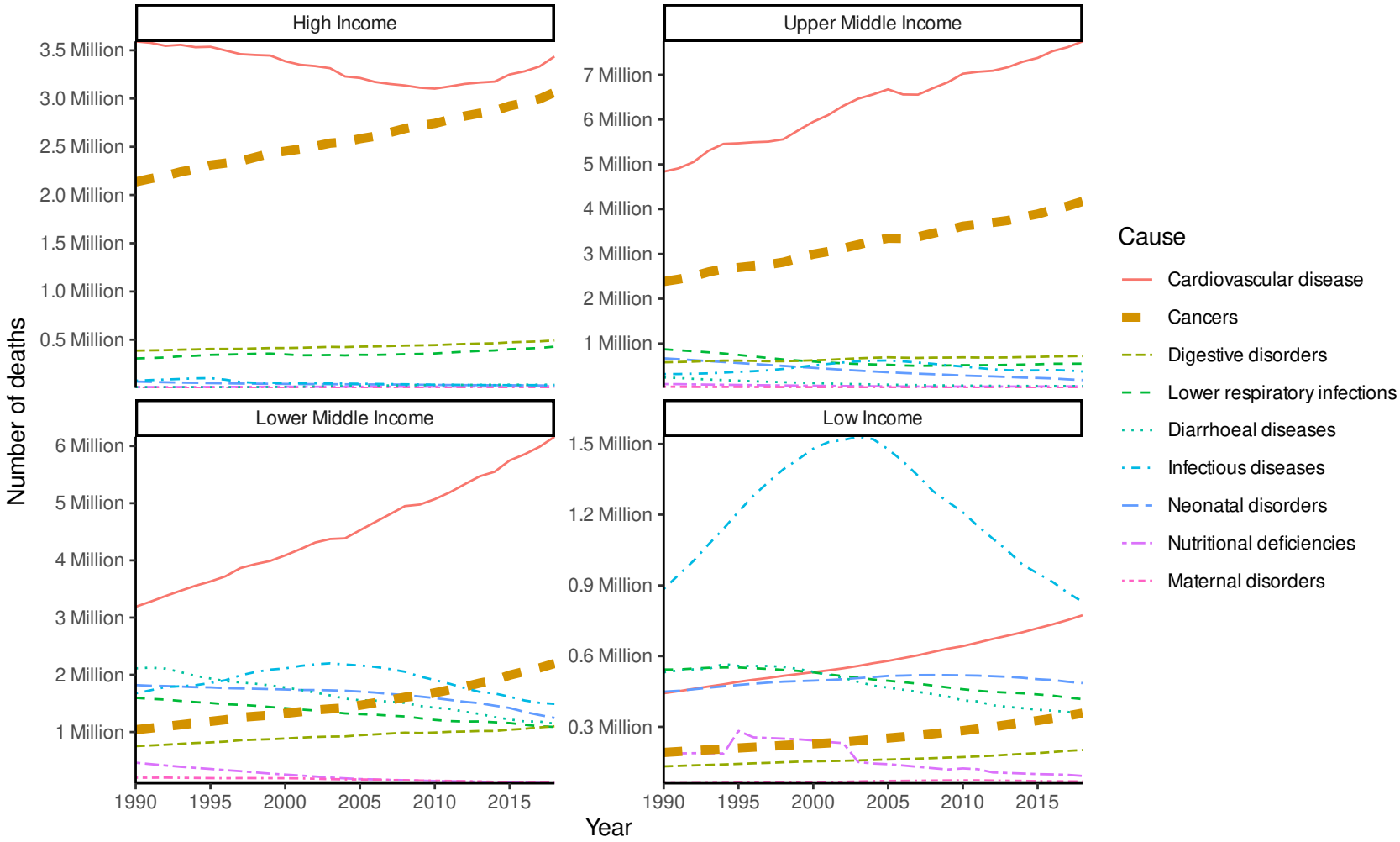


Figure 1-9. Global deaths attributed to cancer type.

Ten cancers causing the highest estimated number of deaths in 2018. Adapted from [53].

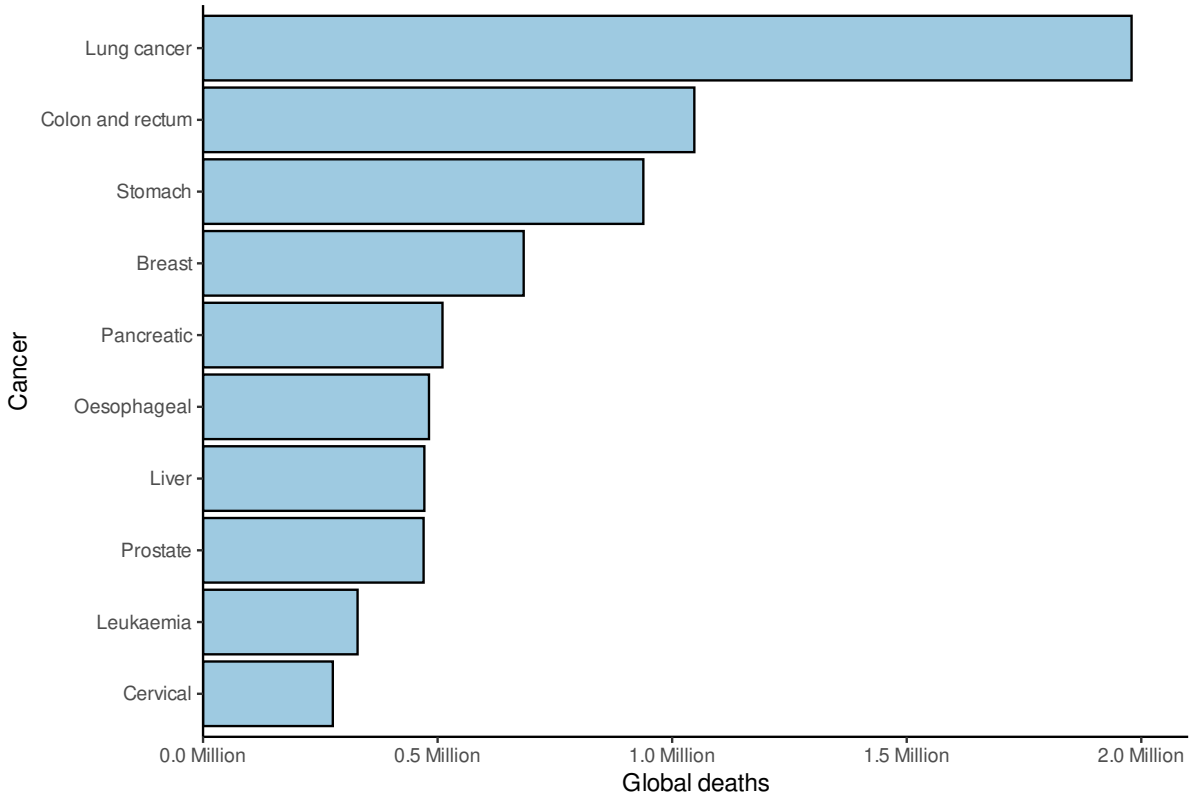


Figure 1-10. Disease burden rates from cancers in 2018.

Disability-adjusted life years (DALYs) per 100 000 individuals from all cancer types. DALYs measure the total burden of disease, both from years of life lost due to premature death and years lived with a disability. One DALY equals one lost year of healthy life. Adapted from [53].

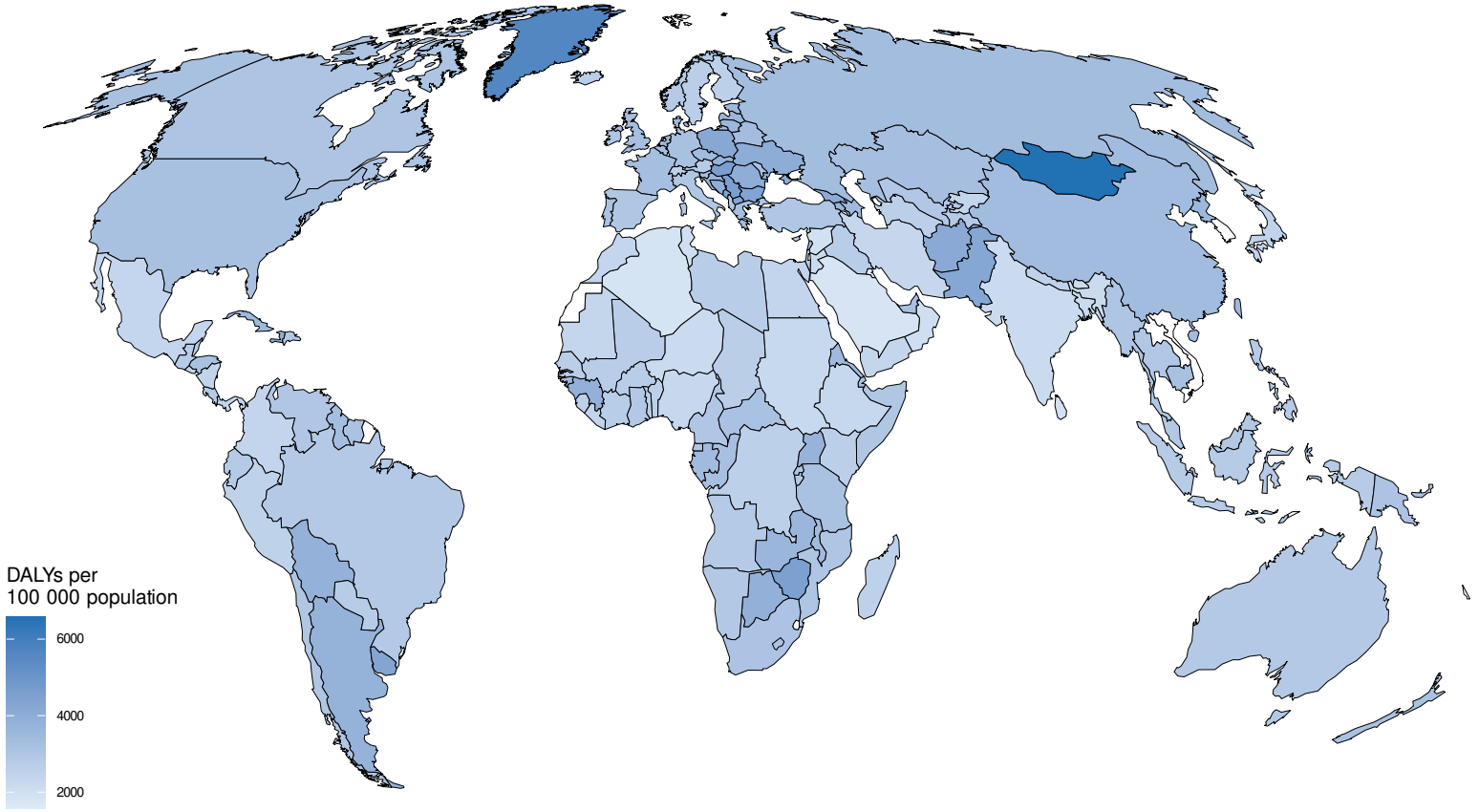
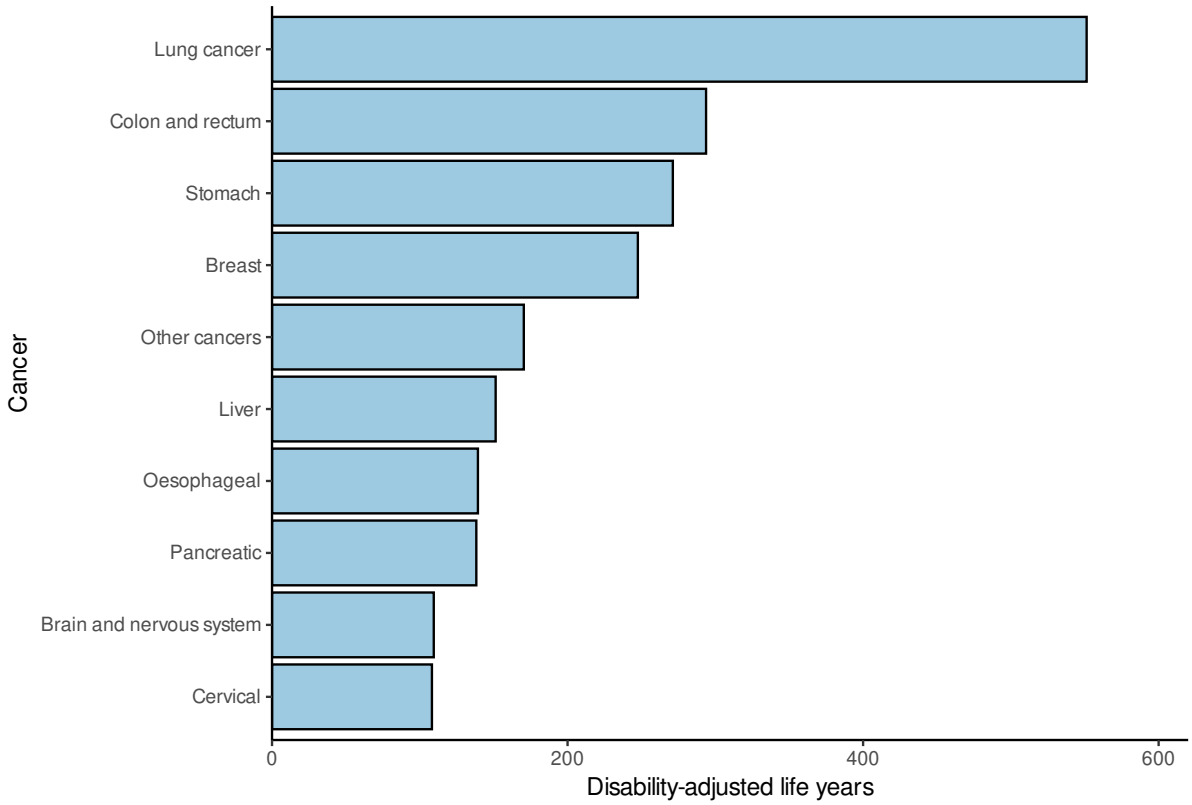


Figure 1-11. Disease burden rates by cancer type.

Ten cancers causing the highest estimated number of healthy life years lost (DALYs) per 100 000 individuals in 2018. DALYs measure the total burden of disease, both from years of life lost due to premature death and years lived with a disability. One DALY equals one lost year of healthy life. Adapted from [53].



1.6.3 Surgical cancer care facilities

Cancer surgery has become increasingly specialised in high-income countries, yet many of the key adjunct treatments supporting surgical cancer care in LMICs, such as pathology and imaging, are inadequate[52]. For example, India only has one licensed Computerised Tomography (CT) scanner per 500 000 of the population[55]. Competing health priorities and financial constraints in LMICs result in surgical services being given a low priority within national cancer plans, translating to little funding and few resources provided for surgical

cancer care. Currently less than one quarter of patients with cancer in LMICs have access to safe, affordable, and timely cancer surgery[52].

1.6.4 Developing national cancer control plans

To strengthen LMIC surgical cancer systems, the *Lancet Oncology* Commission on global cancer surgery developed a conceptual framework of the factors national cancer control plans need to address to provide sustainable cancer care (Figure 1-12). Enhanced training and education was a consistent theme within the Commission, from building surgical capacity, training surgeons in basic cancer procedures, and sharing of knowledge between high-volume and low-volume centres to improve outcomes across the community[52].

This Commission built on Global Surgery 2030, which identified a large gap in basic surgical provision worldwide, particularly in sub-Saharan Africa and southeast Asia. Models demonstrated 82% of countries globally had inadequate numbers of trained cancer surgeons[10]. They argue that planning and building capacity for cancer surgery must commence immediately, with high-quality data guiding education, healthcare professional training, hospital facility improvement and quality improvement initiatives: "*A prerequisite to the scaling up cancer surgical services is an assessment of the specific country's cancer burden and state of cancer care*"[52].

For example, the quantity, quality and functionality of equipment within the cancer care pathway, including postoperative facilities and oncological therapy needs to be captured worldwide[56]. Ultimately, the *Lancet Oncology* Commission on global cancer surgery call for a data-driven map of problems, gaps, and specific needs of each country or region to direct the planning, implementation, and assessment of surgical intervention for cancer.

Figure 1-12. Conceptual framework for scaling up surgical cancer services in resource-limited settings.

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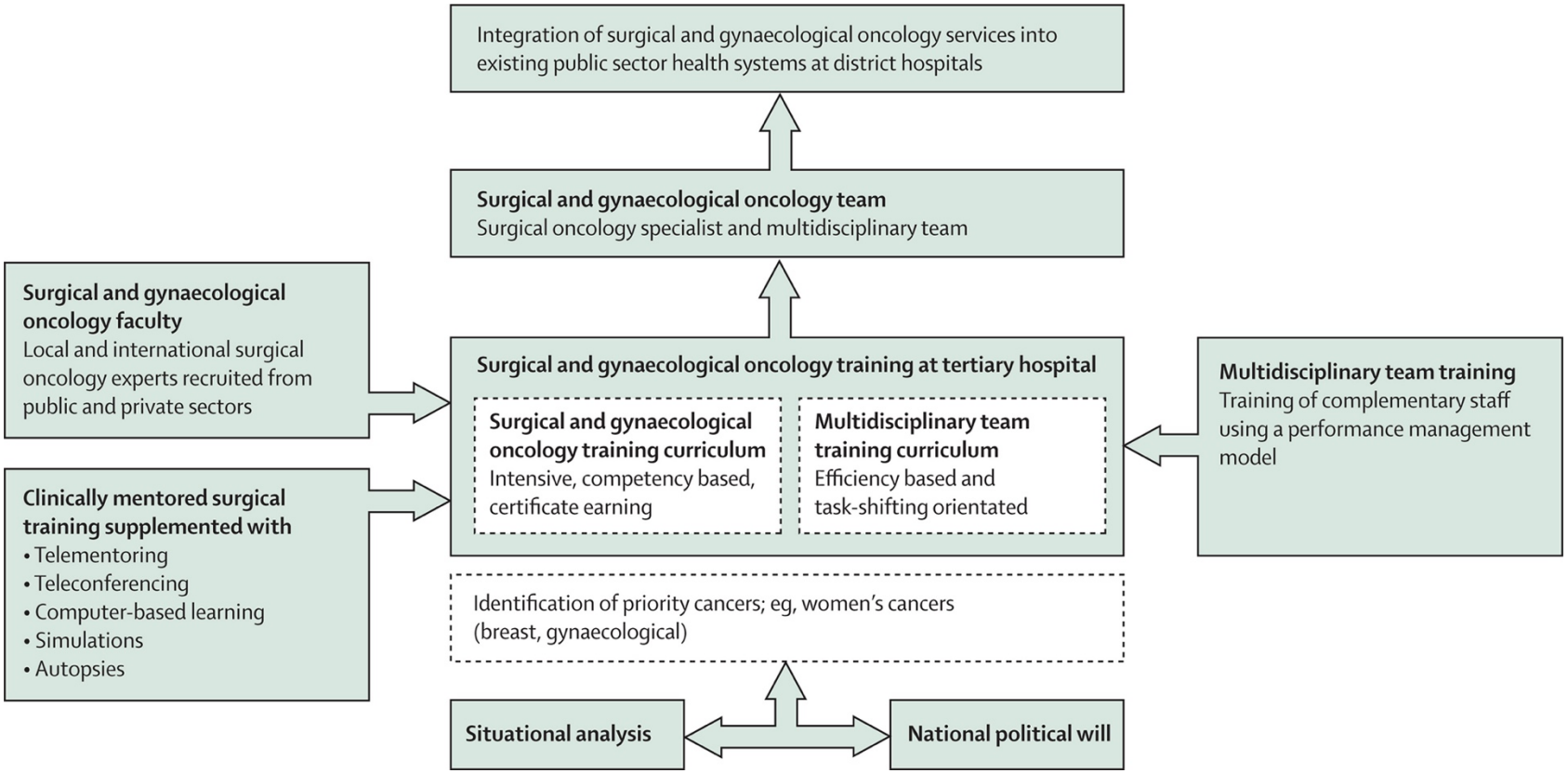
https://doi.org/10.1016/S1470-2045(15)00223-5



1.6.5 Quality of global surgical cancer care

Quality control is an essential part of strengthening surgical systems[57,58]. High quality data in high-income settings exists supporting current pathways for the delivery of safe and effective cancer surgery[59–61]. Cancer registries, peer-reviewed research and audit in LMICs are useful methods to assess and improve quality, yet their scarcity at population level remain one of the biggest barriers to enhancing surgical cancer care[52,62,63].

The indicators used to measure the quality of surgical cancer care are controversial and subject to on-going debate. The implementation of accepted standards of care are estimated to improve cancer outcomes by as much as 30%[64]. However, little evidence exists on the appropriateness of high-income orientated surgical guidelines in LMICs, or what specific pathways and models may indicate the quality of cancer surgery provided in resource-poor settings.

Forecasts of cancer incidence and mortality demonstrate a growing burden in resource-limited settings, with predictions suggesting over two-thirds of the world's cancers will occur in LMICs[65,66]. Therefore, an increasing cancer burden is likely to exacerbate existing disparities in healthcare without significant intervention. Efforts to improve access to cancer care, strengthen infrastructure, and provide comprehensive treatment are now critical.

1.6.6 Improving cancer care pathways in LMICs

The key interventions to improve cancer care pathways are currently unknown. Granular data describing patient populations, associated risk factors, hospital facilities and treatment

outcomes are unavailable, with heavy reliance on simulated estimates that are inherently limited by the absence of high-quality data in many locations. Without local knowledge, the development of national cancer control plans to identify and evaluate potential cost-effective and sustainable interventions will be delayed[67].

1.7 Summary of motivation for thesis

Cancer causes significant morbidity and mortality worldwide. For many common, high-burden cancers, such as breast, colorectal and gastric, surgery often offers the only chance of cure, particularly in early-stage disease. Effective surgical care plays a crucial role in the prevention of death from cancer[52], and requires systems of the highest quality throughout the pre- and postoperative periods[68].

Yet fewer than 25% of patients with cancer have access to safe, affordable, and timely surgery[12]. To address the growing cancer burden in LMICs, investment is needed across the entire cancer care continuum. The *Lancet Oncology* Commission on Global Cancer Surgery has highlighted the absence of high-quality data on the state of surgical cancer care. Little is known about the type or quality of surgical care patients receive for common, high-burden cancers around the world, nor its impact on survival outcomes. This makes it difficult for countries to identify areas of need and make informed investments within their healthcare systems in order to maximise health gains.

1.8 Research Gaps

This thesis will address a number of research gaps.

First, collecting high-quality data on early outcomes following cancer surgery will guide planning, implementation, and assessment of surgical interventions within cancer care pathways worldwide. This also includes the development, in parallel, of national cancer control plans to identify and evaluate potential cost-effective and feasible interventions.

Second, no studies have quantified the impact of improving hospital facilities on early outcomes following cancer surgery. The returns on investment in infrastructure and resources in LMICs for cancer surgical care is therefore unclear.

Finally, there is major interest in developing investigator-led, pragmatic, international multicountry randomised trials to assess simple interventions which may reduce postoperative morbidity and/or mortality. However, while a number of such trials have already been delivered to reduce surgical site infection in LMICs[69,70], no such study focused purely on patients undergoing surgery for cancer has been performed.

1.9 Aim and objectives

1.9.1 Aim

I aim to enable improvement in the diagnosis, investigation, and treatment of cancers amenable to surgical management worldwide.

1.9.2 Objectives

1. Design and deliver an international, multicentre, prospective cohort study capturing early outcomes after surgery for breast, colorectal, and gastric cancer.

2. Determine the variation in mortality and complication rates for these cancers in low-, middle-, and high-income country settings.

3. Examine the relationship between hospital infrastructure and resources on early outcomes after surgery for cancer worldwide.

4. Identify potential perioperative strategies which may improve outcomes for patients in LMICs undergoing surgery for cancer.

Chapter 2 Use of data to improve surgery in low- and middle-income countries

2.1 Introduction

The concept of 'big data' describes the use of unstructured digital information, usually from multiple sources, that is often collected with no clearly defined purpose for its future use[71]. The volume of data already being produced is vast, with frequent increases in complexity, variety and speed[72]. Big data in surgery can be defined as the amalgamation and integration of various data sources along the patient pathway to produce a rich matched dataset[73] (Figure 2-1).

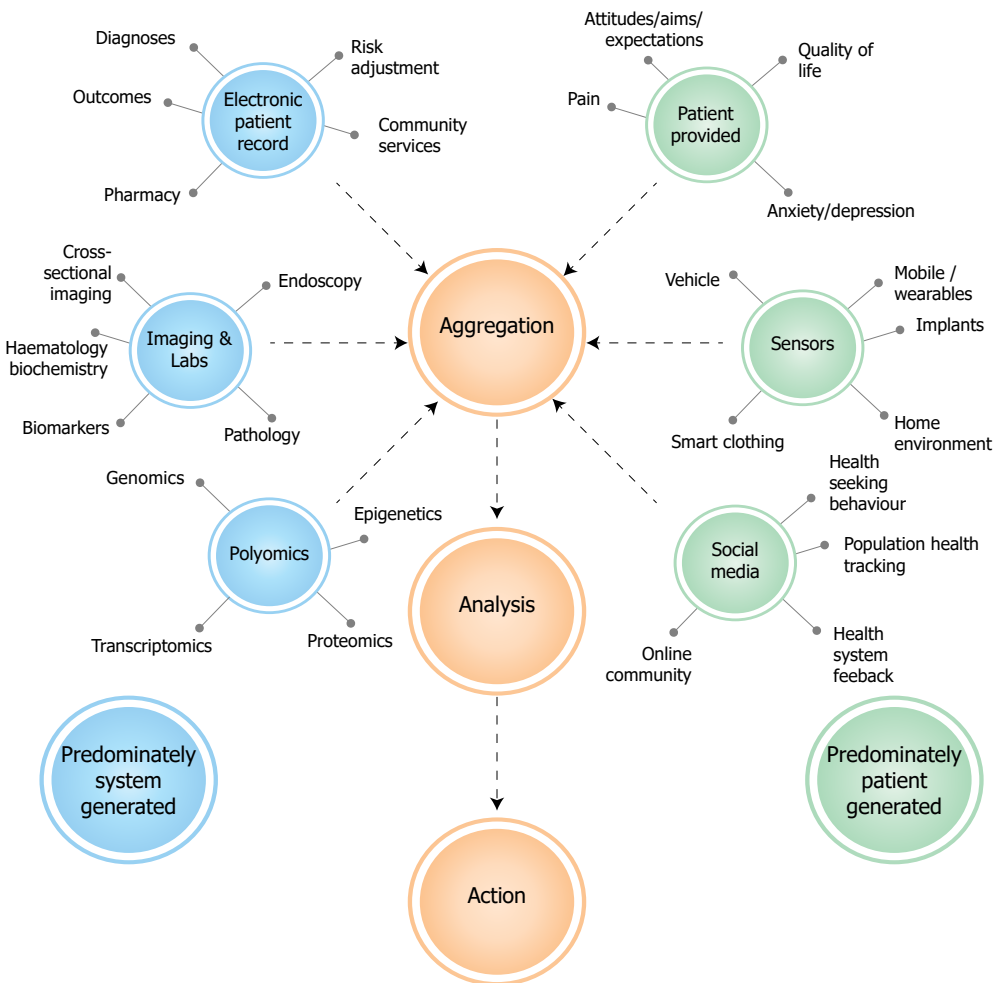
The analysis and translation of big data to maximise quality and improve patient care is a priority for healthcare systems[74]. It is envisaged that measurement and modelling of patient health states and outcomes will quickly become the biggest driver of best practice and healthcare policy[75]. Continual analysis of patient-level outcomes has already been demonstrated to significantly reduce morbidity and mortality in high-income countries (HIC)[76].

However, discussions around large volume patient data frequently place little emphasis on its application in low- and middle-income countries (LMICs), despite the potential for vast gains in patient outcomes and surgical service quality[77]. Currently in LMICs the ability to gather reliable data can be missing[76], with an expectation that this situation is unlikely to change in the near future[78,79]. Ensuring LMICs can keep up to date with technological advances will help to prevent future global health inequalities worsening[80].

We aim to evaluate the current applications of large volume patient-level data in surgery within LMICs, together with highlighting where further focus is required to improve outcomes, define quality indicators and achieve universally available safe surgical care.

Figure 2-1. Conceptualising big data in healthcare.

Health system data are aggregated with data generated by the individual and their environment. Data are transformed and analysed to generate actionable output. Material from [81].



2.2 Methods

An electronic systematic search of the PubMed, EMBASE and Google Scholar databases in accordance with the PRISMA guidelines was performed, involving all published literature up to the last search on 23 August 2018. The PROSPERO international systematic review registry[82] was searched to ensure a similar review had not previously been performed and the protocol was registered accordingly (CRD42018108203).

A thorough search using EMBASE and PubMed was performed using the following keywords (Chapter 10.1): "surgery or surg*", "big data", "large data", "informatics", "database", "cohort" and "registry", combined with LMIC filters as specified by the Cochrane library[83]. A further supplementary search of Google scholar was also undertaken. Search limits applied were English language, full-text, humans and articles published from 2008 onwards to provide contemporary studies which were likely reflective of current approaches to data capture (Table 2-1).

The inclusion criteria were as follows: prospectively collected data (or retrospective analysis of such data) on patients undergoing surgery with care being provided, at least in part, in a low- or middle-income country, using the World Bank classification[84]. Studies were excluded if they contained fewer than 100 patients, were based on retrospective-assembled datasets, or were randomised controlled trials. Conference abstracts were screened to assist in identifying related full-text articles. In cases where more than one article was published from a single dataset, the article analysing the largest cohort of patients was included (Table 2-2).

Table 2-1. Medline search strategy for systematic review to evaluate the current use of data to measure and improve surgical outcomes in LMICs.

1. Developing Countries.sh,kf.
2. (Africa or Asia or Caribbean or West Indies or South America or Latin America or Central America).hw,kf,ti,ab,cp.
3. (Afghanistan or Albania or Algeria or Angola or Armenia or Armenian or Azerbaijan or Bangladesh or Benin or Byelarus or Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or Herzegovina or Hercegovina or Botswana or Brasil or Brazil or Bulgaria or Burkina Faso or Burkina Fasso or Upper Volta or Burundi or Urundi or Cambodia or Khmer Republic or Kampuchea or Cameroon or Cameroons or Cameron or Camerons or Cape Verde or Central African Republic or Chad or China or Colombia or Comoros or Comoro Islands or Comores or Mayotte or Congo or Zaire or Costa Rica or Cote d'Ivoire or Ivory Coast or Croatia or Cuba or Cyprus or Djibouti or French Somaliland or Dominica or Dominican Republic or East Timor or East Timur or Timor Leste or Ecuador or Egypt or United Arab Republic or El Salvador or Eritrea or Ethiopia or Fiji or Gabon or Gabonese Republic or Gambia or Gaza or Georgia Republic or Georgian Republic or Ghana or Gold Coast or Greece or Grenada or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti or Honduras or India or Maldives or Indonesia or Iran or Iraq or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Kosovo or Kyrgyzstan or Kirghizia or Kyrgyz Republic or Kirghiz or Kirgizstan or Lao PDR or Laos or Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania or Macedonia or Madagascar or Malagasy Republic or Sabah or Sarawak or Malawi or Nyasaland or Mali or Marshall Islands or Mauritania or Mauritius or Agalega Islands or Mexico or Micronesia or Middle East or Moldova or Moldovia or Moldovian or Mongolia or Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal or Netherlands Antilles or New Caledonia or Nicaragua or Niger or Nigeria or Northern Mariana Islands or Oman or Muscat or Pakistan or Palau or Palestine or Paraguay or Peru or Philippines or Philipines or Phillipines or Phillippines or Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or Saint Kitts or St Kitts or Nevis or Saint Lucia or St Lucia or Saint Vincent or St Vincent or Grenadines or Samoa or Samoan Islands or Navigator Island or Navigator Islands or Sao Tome or Senegal or Serbia or Montenegro or Seychelles or Sierra Leone or Slovenia or Sri Lanka or Ceylon or Solomon Islands or Somalia or South Africa or Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadzhikistan or Tadjikistan or Tadzhik or Tanzania or Thailand or Togo or Togolese Republic or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or USSR or Soviet Union or Union of Soviet Socialist Republics or Uzbekistan or Uzbek or Vanuatu or New Hebrides or Venezuela or

Vietnam or Viet Nam or West Bank or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia).hw,ti,ab,cp.
4. ((developing or less* developed or under developed or underdeveloped or middle income or low* income or underserved or under served or deprived or poor*) adj (countr* or nation? or population? or world)).ti,ab.
5. ((developing or less* developed or under developed or underdeveloped or middle income or low* income) adj (economy or economies)).ti,ab.
6. (low* adj (gdp or gnp or gross domestic or gross national)).ti,ab.
7. (low adj3 middle adj3 countr*).ti,ab.
8. (lmic or lmics or third world or lami countr*).ti,ab.
9. transitional countr*.ti,ab.
10. or/1-9
11. surgery or surg* not precision medicine
12. big data or large data or informatics or database or cohort or registry
13. Limits: Full text, English language, Humans, 2008 – present

Table 2-2. Eligibility criteria for systematic review.

Inclusion criteria
1. Prospectively collected data
2. Study performed in LMIC (according to World Bank classification system at time of publication)
3. ≥100 patients included within study
Exclusion criteria
1. Retrospective or randomised control trial design
2. Conference abstracts, comments or review articles
3. Studies without associated full-text publications
4. Duplicated studies

Following the literature search, article titles were screened by four investigators, with those meeting the inclusion criteria screened further by abstract and then full-text as appropriate. Any disagreements were resolved by consensus within the group. Bibliographies from included articles were hand searched to identify any further relevant articles.

Data were extracted independently using a standardised proforma and included year of publication, countries involved in the study, patient number for each LMIC country, patient-level data type (cohort, database or registry), surgical specialty and measured outcome(s). In multinational studies where the patient number for individual countries was not reported, the total patient number within the study was recorded. These studies were excluded from analysis mapping global distribution of patients across included studies to avoid data skewing. Individual LMICs where patient numbers were less than 100 in multinational studies were also excluded from analysis mapping. However, studies that did not report patient numbers for individual LMICs and all data from multinational studies were included in all other analyses performed.

I defined the data types as: '*Cohort'* - collection of patient level data over a defined, short period; '*Database'* - concerted and long-term collection of patient-level data of consecutive patients over a small geographical area; '*Registry'* - studies meeting database classification but performed over wide geographical area (e.g. national registries).

Definitions were discussed and consensus reached within the group where dubiety existed for particular studies. Due to the narrative nature of the review, a qualitative analysis was performed using the R statistical programming language[85] and the tidyverse packages[86].

2.3 Results

2.3.1 Systematic literature search

The literature search identified 3805 articles, of which 218 full-texts were assessed for eligibility (Figure 2-2). Following assessment, 68 articles[25–27,87–151] (Table 2-3), involving 708 032 patients across 71 LMIC countries were included within the review. Country-

specific patient numbers were reported in 60 studies but were absent in six[26,27,121–123,132] and two provided total LMIC patient numbers only[104,126].

2.3.2 Patients and studies

Studies utilising big data were well represented across the ten-year analysis period, however, a dramatic increase in study and patient numbers was seen from 2015 onwards (Figure 3-3). Relatively few studies were found for the period 2012 to 2014 despite no decrease in the total number of studies returned in the initial literature search (2012 to 2014, 339, 358 and 469 studies respectively, compared to other years, median 222, range 129 to 487).

The number of patients included in studies ranged from 335 to 428 346, with a median of 2483 patients per study. Over 3000 patients were included in 25 (37%) studies, with the biggest studies being published in the period 2015 to 2018. Studies based on database and registry data were most common and represented 43 (63%) of included studies. The majority of datasets identified arose from prospective cohorts of patients. Several of these were performed in single centres[114,135] or single nations[149,151] with comparisons made to high-income countries. The largest cohort of patients originated from the DATASUS registry in Brazil (428 346 patients), exploring outcomes following hysterectomy[150]. Five multinational observational cohort studies were performed in the last five years[25–27,121,122,132], with the majority conducted over a seven day period.

2.3.3 Geographical distribution

Studies originated across a wide geographical distribution (Figure 4-4). The majority of studies, however, were from Brazil (12), China (11), India (5) and Thailand (4). Patient-

level data were collected from 71 LMICs in total, but overall patient representation was particularly low in Africa and Latin America (Figure 2-4).

2.3.4 Subject of studies

The focus of study varied across included articles (Figure 2-5). Short-term outcomes from surgery were most commonly captured (33 studies), and of these studies, eight included over 10 000 patients each. Outcomes following cancer surgery were common topics, with breast[90,102,109,116–118,147], gastric[87,93,94,131], colorectal[95,129,146,151], prostate[89,101] and hepatocellular carcinoma[127,130] cancer predominant. Cardiac surgery[92,105,114,135,140], caesarean section[115,120,139] and genitourinary fistula[98,104,144] were also well represented within included articles, while clinical presentations included burn management[126], trauma[136], appendicitis[141], groin herniae[106] and orthopaedic fracture management[119,143] (Table 2-4).

However, the overall journey of a patient through the surgical care process was poorly represented, with only a single study examining access to surgical care and the cost of surgical care to the patient. No study assessed whether the results of big data analyses have resulted in meaningful changes to healthcare systems or impacted significantly on patient outcomes in LMIC settings.

A number of studies successfully demonstrated the ability to assemble large prospective datasets on patients across multiple nations. The International Surgical Outcomes Study (ISOS) Group[122] included 15 806 patients in eight LMIC countries, and the African Surgical Outcomes Study (ASOS)[25] included 11 422 patients across 25 African countries. These studies captured mortality and complication rates, but as importantly, were able to

capture patient risk profiles and patterns of surgical practice. Highlighting differences in surgical outcome by country-income level, a lack of critical care provision in LMICs was postulated to significantly impact on the ability to rescue patients from complications, with implications for resource planning at a governmental level[25,111,122].

Multinational studies also targeted specific disease areas (GlobalSurg 1: Emergency abdominal surgery) or specific complications of surgery (GlobalSurg 2: Surgical site infection). These two studies gathered prospective data on 23 284 patients and demonstrated low-income countries carry a disproportionately higher burden of surgical site infection and three-fold higher mortality rates[26,27].

Figure 2-2. Systematic literature search PRISMA flowchart.

Two studies provided total LMIC patient number, identified in figure by *. Material from [81].

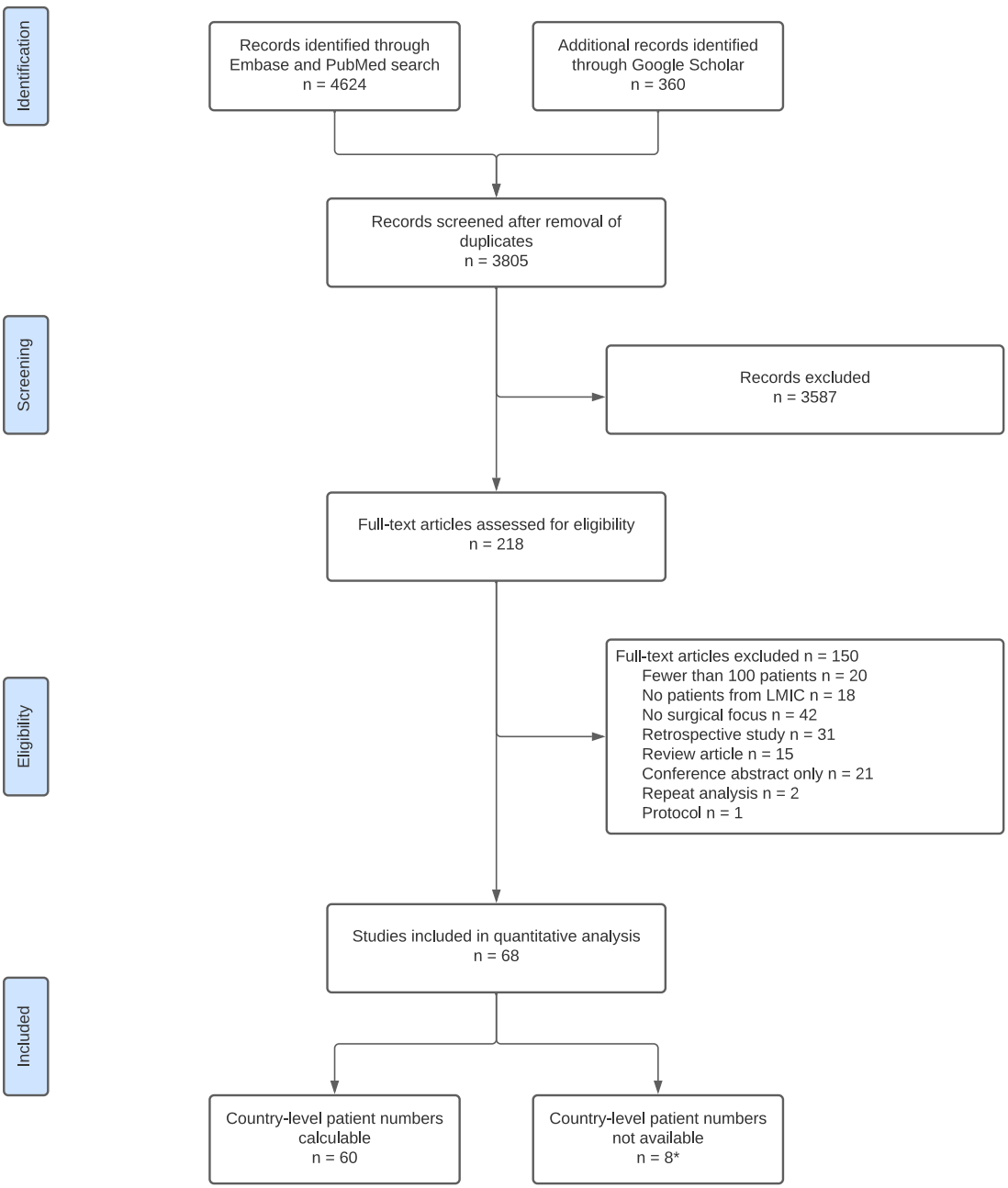


Table 2-3. Studies included within the systematic review.

Author	Year	Patient number	Included countries	Study design	Surgical specialty	Primary outcomes measured
Moghimi-Dehkordi et al[87]	2008	746	Iran	Database	General surgery	Postoperative outcomes
Zhaohui et al[88]	2008	1959	China	Registry	Maxillofacial surgery	Postoperative outcomes
Mariano et al[89]	2009	780	Brazil	Database	Urology	Postoperative outcomes
Rezaianzadeh et al[90]	2009	1148	Iran	Registry	Breast	Postoperative outcomes
Campos et al[91]	2009	4744	Brazil	Registry	General surgery	Patient demographics / Postoperative outcomes
Elbasmi et al[92]	2010	902	Kuwait	Registry vs Database	Breast	Patient demographics
Biglarian et al[93]	2010	436	Iran	Database	General surgery	Postoperative outcomes
Moghimi-Dehkordi et al[94]	2010	742	Iran	Database	General surgery	Postoperative outcomes
Chen et al[95]	2010	945	China	Cohort	General surgery	Postoperative outcomes
Gupta et al[96]	2010	811	India	Database	General	Incidence
ALANEPE (Latin American Pediatric Nephrology Association[97]	2010	1254	Brazil (667), Chile (163), Venezuela (113), Mexico (171), Cuba (36), Colombia (17), Costa Rica (13), Nicaragua (9), Guatemala (3), Ecuador (3),	Registry	Paediatrics / Transplantation	Patient demographics / Postoperative outcomes

			Honduras (18), Paraguay (4) and Peru (5)			
Muleta et al[98]	2010	14928	Ethiopia	Cohort	Gynaecology	Patient demographics
Ercole et al[99]	2011	3543	Brazil	Database	Orthopaedics	Postoperative outcomes
Brisebois et al[100]	2011	4434	Afghanistan	Database	Multiple specialties	Incidence
Ranasinghe et al[101]	2011	1378	Sri Lanka	Registry	Urology	Incidence
Nechuta et al[102]	2011	4877	China	Registry + prospective follow-up	Breast	Postoperative outcomes
Elias et al[103]	2011	625	Brazil	Cohort	Multiple specialties	Postoperative outcomes
Frajzyngier et al[104]	2012	1273*	Uganda, Guinea, Niger, Nigeria, Bangladesh	Cohort	Obstetrics and gynaecology	Postoperative outcomes
Piotto et al[105]	2012	3010	Brazil	Database	Cardiothoracics	Postoperative outcomes
Löfgren et al[106]	2014	563	Uganda	Database	General surgery	Incidence
Tollefson et al[107]	2015	604	Zimbabwe	Database	ENT	Patient demographics
Mejia et al[108]	2015	2565	Brazil	Database	Cardiothoracics	Postoperative outcomes
Sivasubramaniam et al[109]	2015	4211	China	Database	Breast surgery	Patient demographics
Noppakun et al[110]	2015	5729	Thailand	Registry	Transplantation	Patient demographics / Postoperative outcomes
SASOS[111]	2015	3927	South Africa	Cohort	Multiple specialties	Patient demographics / Postoperative outcomes

Moodley et al[112]	2015	3727	South Africa	Database	Multiple	Postoperative outcomes
Zablotska et al[113]	2015	11664	Belarus	Database	ENT	Incidence
Saifuddin et al[114]	2015	2198	Pakistan	Cohort	Cardiothoracics	Postoperative outcomes
Filippi et al[115]	2015	950	Burkina Faso	Cohort	Obstetrics and gynaecology	Postoperative outcomes / Quality of life
Sangkittipaiboon et al[116]	2015	1439	Thailand	Registry	Breast	Incidence
Lalitwongsa et al[117]	2015	2458	Thailand	Registry	Breast	Incidence
Tassanasunthornwong et al[118]	2015	1118	Thailand	Registry	Breast	Incidence
Paula et al[119]	2015	2612	Brazil	Database	Orthopaedics	Postoperative outcomes
Islam et al[120]	2015	3329	Bangladesh	Database	Obstetrics and gynaecology	Incidence
Moreno et al[121]	2015	46539*	Europe	Database	Multiple specialties	Postoperative outcomes
ISOS[122]	2016	15806*	Worldwide	Cohort	Multiple specialties	Postoperative outcomes
Nagoshi et al[123]	2016	479*	India, Turkey, Brazil, China, HIC	Cohort	Spinal surgery	Postoperative outcomes / Quality of life
Tostes et al[124]	2016	3773	Brazil	Database	Multiple specialties	Access
Wang et al[125]	2016	2733	China	Registry	Transplantation	Survival
Garcia et al[126]	2016	2506*	Nepal, India, Zambia	Database	Plastics	Patient demographics / Postoperative outcomes
Xiang et al[127]	2016	335	China	Cohort	General Surgery	Postoperative outcomes / Patient survival
GlobalSurg collaborative[26]	2016	10745*	Worldwide	Cohort	Multiple specialties	Postoperative outcomes

Nandakumar et al[128]	2016	14053	India	Cohort	Head and neck	Incidence / Postoperative outcomes
Reyes et al[129]	2016	2621	Philippines	Registry	General Surgery	Patient demographics
Lei et al[130]	2016	1004	China	Cohort	General surgery	Patient demographics / Postoperative outcomes
Bhandare et al[131]	2017	580	India	Cohort	General surgery	Survival
Acaroglu et al[132]	2017	535*	Turkey	Database	Spinal surgery	Postoperative outcomes
Fang et al[133]	2017	1183	China	Database	General surgery	Survival
Figueiredo et al[134]	2017	2460	Brazil	Cohort	General surgery	Postoperative outcomes
Zheng et al[135]	2017	32040	China	Registry	Cardiothoracics	Postoperative outcomes
Yousefzadeh et al[136]	2017	588	Iran	Registry	Paediatrics	Postoperative outcomes
Gajewski et al[137]	2017	27743	Zambia (3549), Malawi (24194)	Cohort	Multiple specialties	Patient demographics
Shah et al[138]	2017	4143	Nepal	Cohort	Multiple specialties	Patient demographics
Hu et al[139]	2017	3474	China	Cohort	Obstetrics and gynaecology	Patient demographics
Arthur et al[140]	2017	3285	Brazil	Registry	Cardiothoracics	Postoperative outcomes
Hernandez et al[141]	2017	1415	South Africa	Database	General Surgery	Patient demographics
The ACTION study group[142]	2017	9513	Cambodia (206), Indonesia (2335), Lao PDR (101), Malaysia (1662), Myanmar (1178), Philippines (909), Thailand (1206), Vietnam (1916)	Cohort	Multiple specialties	Patient cost / Postoperative outcomes
Doshi et al[143]	2017	787	India	Cohort	Orthopaedics	Postoperative outcomes
Kopp et al[144]	2017	346	Malawi	Cohort	Gynaecology	Postoperative outcomes

Treeprasertsuk et al[145]	2017	34325	Thailand	Database	General Surgery	Incidence / Postoperative outcomes
Carvalho et al[146]	2017	16882	Brazil	Cohort	General surgery	Postoperative outcomes
Wang et al[147]	2018	1977	China	Database	Breast surgery	Survival
van der Spuy et al[148]	2018	382	South Africa	Cohort	Multiple specialties	Patient demographics
George et al[149]	2018	1075	India	Cohort	Multiple specialties	Patient demographics
Augusto et al[150]	2018	428346	Brazil	Registry	Gynaecology	Postoperative outcomes / Patient cost
Brand et al[151]	2018	3412	South Africa	Database	General surgery	Survival
ASOS (African Surgical Outcomes Study)[25]	2018	11422	Congo, Dem. Rep. (315), Gambia, The (82), Madagascar (192), Mali (329), Mauritius (418), Namibia (325), Niger (186), Nigeria (395), South Africa (5522), Uganda (620), Zimbabwe (640), Algeria (184), Benin (220), Burundi (127), Cameroon (223), Congo (3), Egypt (10), Ethiopia (252), Ghana (225), Kenya (324), Libya (667), Senegal (7), Tanzania (97), Togo (19), Zambia (40)	Cohort	Multiple specialties	Postoperative outcomes
GlobalSurg collaborative[27]	2018	12539	Worldwide	Cohort	Multiple specialties	Postoperative outcomes

*Country-specific numbers not available

Table 2-4. Aims of included studies grouped by primary outcome measure and surgical specialty.

Primary outcome measure	Author	Year	Patient number	Surgical specialty	Article aim
Patient demographics	Elbasmi et al[92]	2010	902	Breast surgery	To determine reliability of Kuwait cancer registry
	Sivasubramaniam et al[109]	2015	4211	Breast surgery	Identify breast cancer disparities compared to American SEER database
	Tollefson et al[107]	2015	604	ENT	Estimate the burden of cleft lip-palate in Zimbabwe
	*Campos et al[91]	2009	4744	General surgery	Evolution of laparoscopic colorectal surgery in Brazil
	Reyes et al[129]	2016	2621	General Surgery	Colorectal cancer characteristics across metro Cebu district over a ten year period
	*Lei et al[130]	2016	1004	General surgery	Pathological data and prediction of microvascular invasion pre-operatively in patients with HCC
	Hernandez et al[141]	2017	1415	General Surgery	Severity of appendicitis at presentation in South African cohort
	Muleta et al[98]	2010	14928	Gynaecology	Presence of obstetric fistula across Ethiopia
	Hu et al[139]	2017	3474	Obstetrics and gynaecology	Measurement of placental response in low-risk childbirth
	*Garcia et al[126]	2016	2506	Plastics	Factors Affecting Burn Contracture Outcome in Developing Countries
	*ALANEPE (Latin American Pediatric Nephrology Association)[97]	2010	1254	Paediatrics / Transplantation	Latin American registry of paediatric renal transplantation

	*Noppakun et al[110]	2015	5729	Transplantation	25-year experience of kidney transplantation in Thailand
	Gajewski et al[137]	2017	27743	Multiple specialties	Access to surgery in Sub-Saharan Africa
	*SASOS[111]	2015	3927	Multiple specialties	7-day surgical outcomes in South Africa
	Shah et al[138]	2017	4143	Multiple specialties	Use of tablet elogbooks by 14 non-medical anaesthetic providers to measure complications
	van der Spuy et al[148]	2018	382	Multiple specialties	Presence of hypertensive disease in elective surgery cohort
	George et al[149]	2018	1075	Multiple specialties	Myocardial injury after non-cardiac surgery
Incidence	Sangkittipaiboon et al[116]	2015	1439	Breast	Measurement of breast cancer incidence in Thailand district
	Lalitwongsa et al[117]	2015	2458	Breast	Measurement of breast cancer incidence in Thailand district
	Tassanasunthornwong et al[118]	2015	1118	Breast	Measurement of breast cancer incidence in Thailand district
	Zablotska et al[113]	2015	11664	ENT	Malignant thyroid pathological findings following radiation exposure
	Gupta et al[96]	2010	811	General surgery	Presentation of renal tumours over a 20-year period
	Löfgren et al[106]	2014	563	General surgery	Prevalence of groin herniae in eastern Uganda
	*Treeprasertsuk et al[145]	2017	34325	General Surgery	Burden and mortality of intrahepatic cholangiocarcinoma in Thailand

	Islam et al[120]	2015	3329	Obstetrics and gynaecology	Rate of caesarean section in hospitals providing emergency obstetric care
	Ranasinghe et al[101]	2011	1378	Urology	Incidence of prostate cancer
	Brisebois et al[100]	2011	4434	Multiple specialties	Multi-national medical unit experience in Afghanistan
Access	Tostes et al[124]	2016	3773	Multiple specialties	Access to surgical care in Brazil
Postoperative outcomes	Rezaianzadeh et al[90]	2009	1148	Breast	Survival analysis of patients with breast cancer in Iran
	Nechuta et al[102]	2011	4877	Breast	Vitamin supplement use during breast cancer treatment
	Piotto et al[105]	2012	3010	Cardiothoracics	Independent predictors of prolonged mechanical ventilation after coronary artery bypass surgery
	Mejia et al[108]	2015	2565	Cardiothoracics	Age, creatinine and ejection fraction score in Brazil: Comparison with InsCor and the EuroSCORE
	Saifuddin et al[114]	2015	2198	Cardiothoracics	Developing cardiac surgery service in Pakistan
	Zheng et al[135]	2017	32040	Cardiothoracics	Comparing Outcomes of Coronary Artery Bypass Grafting among Large Teaching and Urban Hospitals
	Arthur et al[140]	2017	3285	Cardiothoracics	Renal dysfunction following cardiac surgery
	Nandakumar et al[128]	2016	14053	Head and neck	Incidence / Postoperative outcomes
	Moghimi-Dehkordi et al[87]	2008	746	General surgery	Survival following gastric cancer resection
	*Campos et al[91]	2009	4744	General surgery	Evolution of laparoscopic colorectal surgery in Brazil
	Biglarian et al[93]	2010	436	General surgery	Determining of prognostic factors in gastric cancer patients

	Moghimi-Dehkordi et al[94]	2010	742	General surgery	Impact of age on prognosis in Iranian patients with gastric carcinoma
	Chen et al[95]	2010	945	General surgery	Effect of diabetes mellitus on prognosis for patients undergoing resection for colorectal cancer
	*Xiang et al[127]	2016	335	General Surgery	Prospective cohort study of laparoscopic and open hepatectomy for hepatocellular carcinoma
	*Lei et al[130]	2016	1004	General surgery	Pathological data and prediction of microvascular invasion pre-operatively in patients with HCC
	Figueiredo et al[134]	2017	2460	General surgery	Early exit site infection following peritoneal dialysis catheter insertion
	*Treeprasertsuk et al[145]	2017	34325	General Surgery	Burden and mortality of intrahepatic cholangiocarcinoma in Thailand
	Carvalho et al[146]	2017	16882	General surgery	Incidence and risk factors for surgical site infection in general surgery
	Frajzyngier et al[104]	2012	1273	Obstetrics and gynaecology	Surgical methods for repair of genitourinary fistula
	Filippi et al[115]	2015	950	Obstetrics and gynaecology	The effects of life-saving caesarean sections in Burkina Faso
	Kopp et al[144]	2017	346	Gynaecology	Continence status in women after obstetric vesicovaginal fistula repair
	Augusto et al[150]	2018	428346	Gynaecology	Costs and mortality rates of surgical approaches to hysterectomy in Brazil
	Ercole et al[99]	2011	3543	Orthopaedics	Risk of surgical site infection following orthopaedic surgery

	Paula et al[119]	2015	2612	Orthopaedics	Readmission and death following hip fracture in elderly population
	Doshi et al[143]	2017	787	Orthopaedics	Infection following internal fixation of tibial fractures
	Zhaohui et al[88]	2008	1959	Maxillofacial surgery	Design and implementation of a maxillofacial trauma registry
	*Garcia et al[126]	2016	2506	Plastics	Factors Affecting Burn Contracture Outcome in Developing Countries
	Nagoshi et al[123]	2016	479	Spinal surgery	Outcomes following surgery for degenerative cervical myelopathy
	Acaroglu et al[132]	2017	535	Spinal surgery	Surgery for adult spinal deformity
	Yousefzadeh et al[136]	2017	588	Paediatrics	Mortality, length of stay and surgery associated with paediatric trauma
	*ALANEPE (Latin American Pediatric Nephrology Association)[97]	2010	1254	Paediatrics / Transplantation	Latin American registry of paediatric renal transplantation
	*Noppakun et al[110]	2015	5729	Transplantation	25-year experience of kidney transplantation in Thailand
	Mariano et al[89]	2009	780	Urology	Laparoscopic radical prostatectomy
	Elias et al[103]	2011	625	Multiple specialties	Incidence and risk factors for sepsis in surgical patients
	*SASOS[111]	2015	3927	Multiple specialties	7-day surgical outcomes in South Africa

	Moodley et al[112]	2015	3727	Multiple	Predictors of in-hospital mortality following non-cardiac surgery
	Moreno et al[121]	2015	46539	Multiple specialties	Utility of American Society of Anaesthesiologist score in predicting in-hospital mortality
	ISOS[122]	2016	15806	Multiple specialties	Global patient outcomes after elective surgery
	GlobalSurg collaborative[26]	2016	10745	Multiple specialties	Mortality of emergency abdominal surgery in high-, middle- and low-income countries
	*The ACTION study group[142]	2017	9513	Multiple specialties	Policy and priorities for national cancer control planning in low- and middle-income countries
	ASOS (African Surgical Outcomes Study)[25]	2018	11422	Multiple specialties	7-day peri-operative patient outcomes in Africa
	GlobalSurg collaborative[27]	2018	12539	Multiple specialties	Surgical site infection following gastrointestinal surgery
Patient cost	*The ACTION study group[142]	2017	9513	Multiple specialties	Policy and priorities for national cancer control planning in low- and middle-income countries
Survival	Wang et al[147]	2018	1977	Breast surgery	Predictors and survival in presence of internal mammary lymph nodes metastasis
	*Xiang et al[127]	2016	335	General Surgery	Prospective cohort study of laparoscopic and open hepatectomy for hepatocellular carcinoma
	Bhandare et al[131]	2017	580	General surgery	Radical gastrectomy in Indian tertiary centre
	Fang et al[133]	2017	1183	General surgery	Clinicopathologic characteristics and prognosis of gastroenteropancreatic neuroendocrine neoplasms

	Brand et al[151]	2018	3412	General surgery	Long-term outcomes for colorectal cancer in South Africa
	Wang et al[125]	2016	2733	Transplantation	Preoperative sodium concentration, hepatitis B virus cirrhosis and liver transplantation

*More than one outcome measured in study

Figure 2-3. Distribution of patient number across included studies.

Distribution of patient number across individual studies (A) and cumulative count (B) for each year. Material from [81].

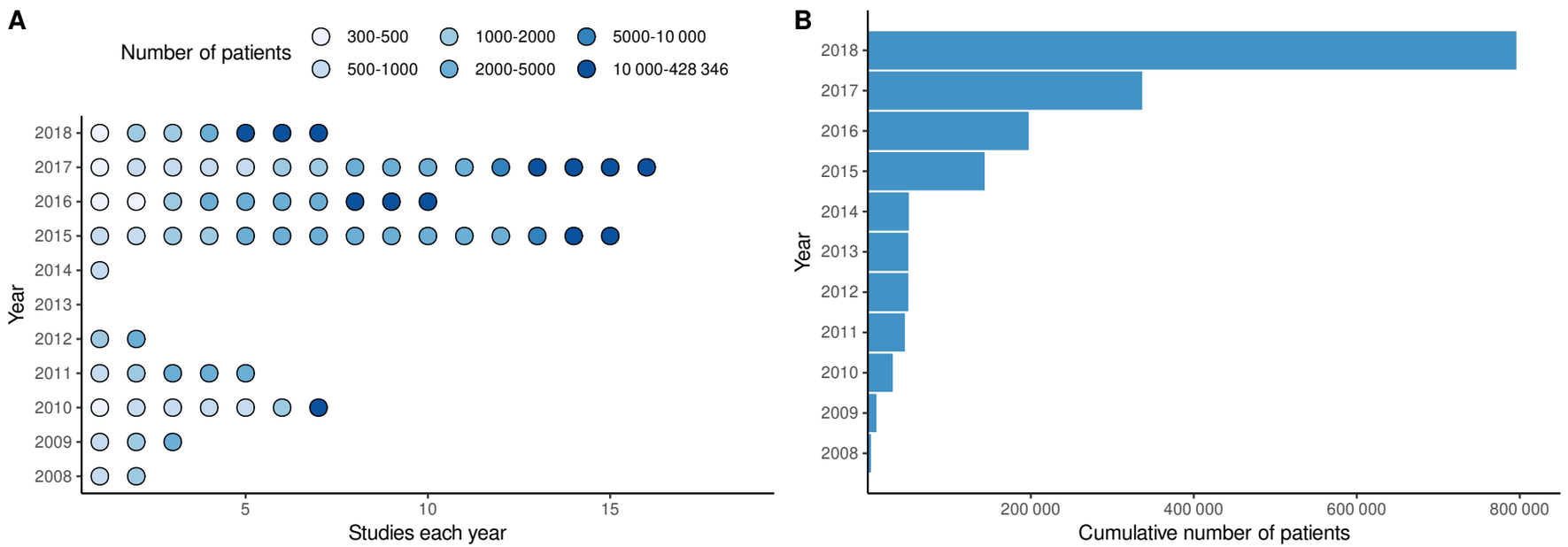


Figure 2-4. Global distribution of patients across low- and middle-income countries for included articles.

High-income countries are coloured white. Countries with <100 patients recruited for a multi-national study were excluded from (a), as were studies where LMIC-specific patient numbers were unspecified[119–121,126,130,151]. Material from [81].

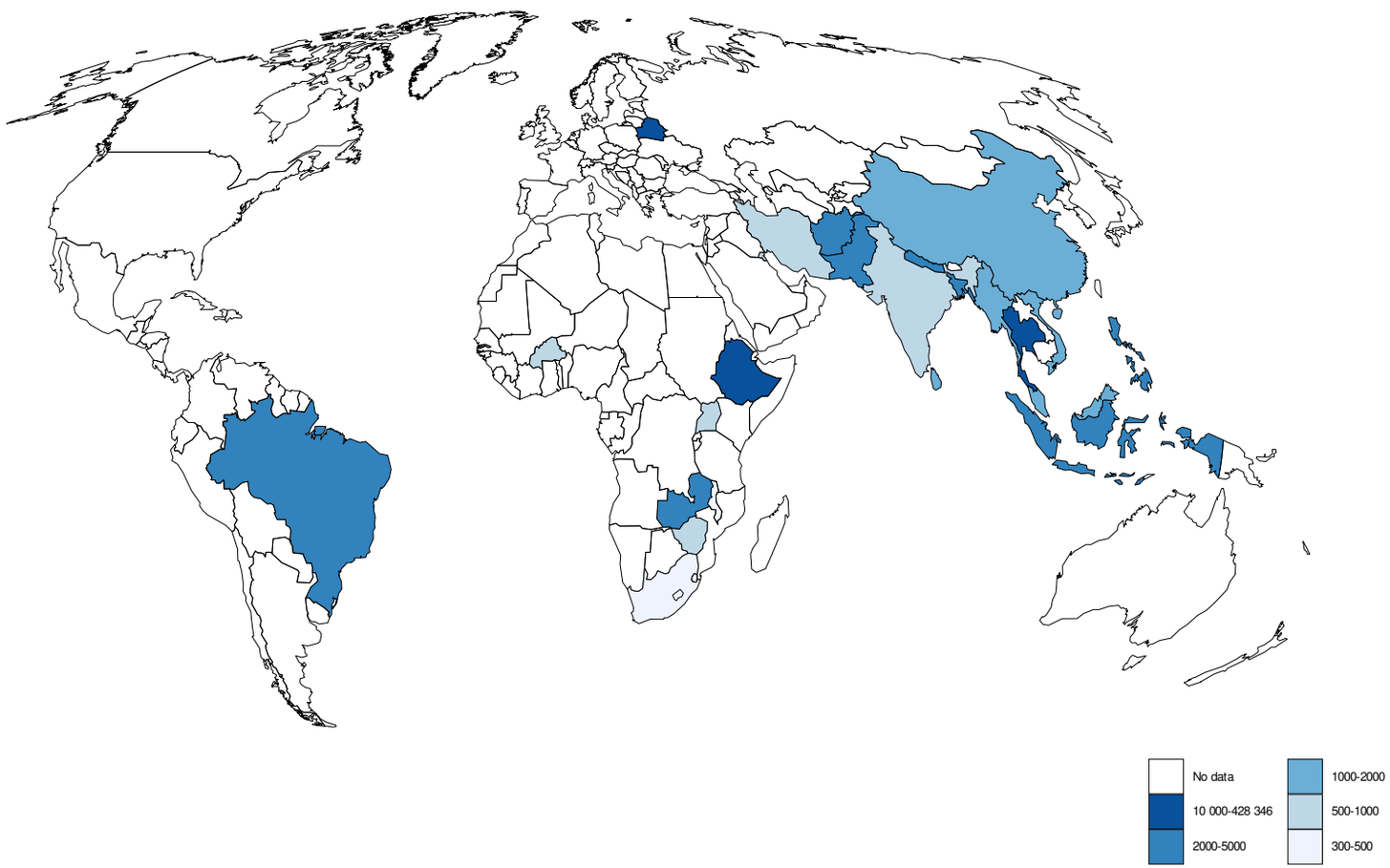
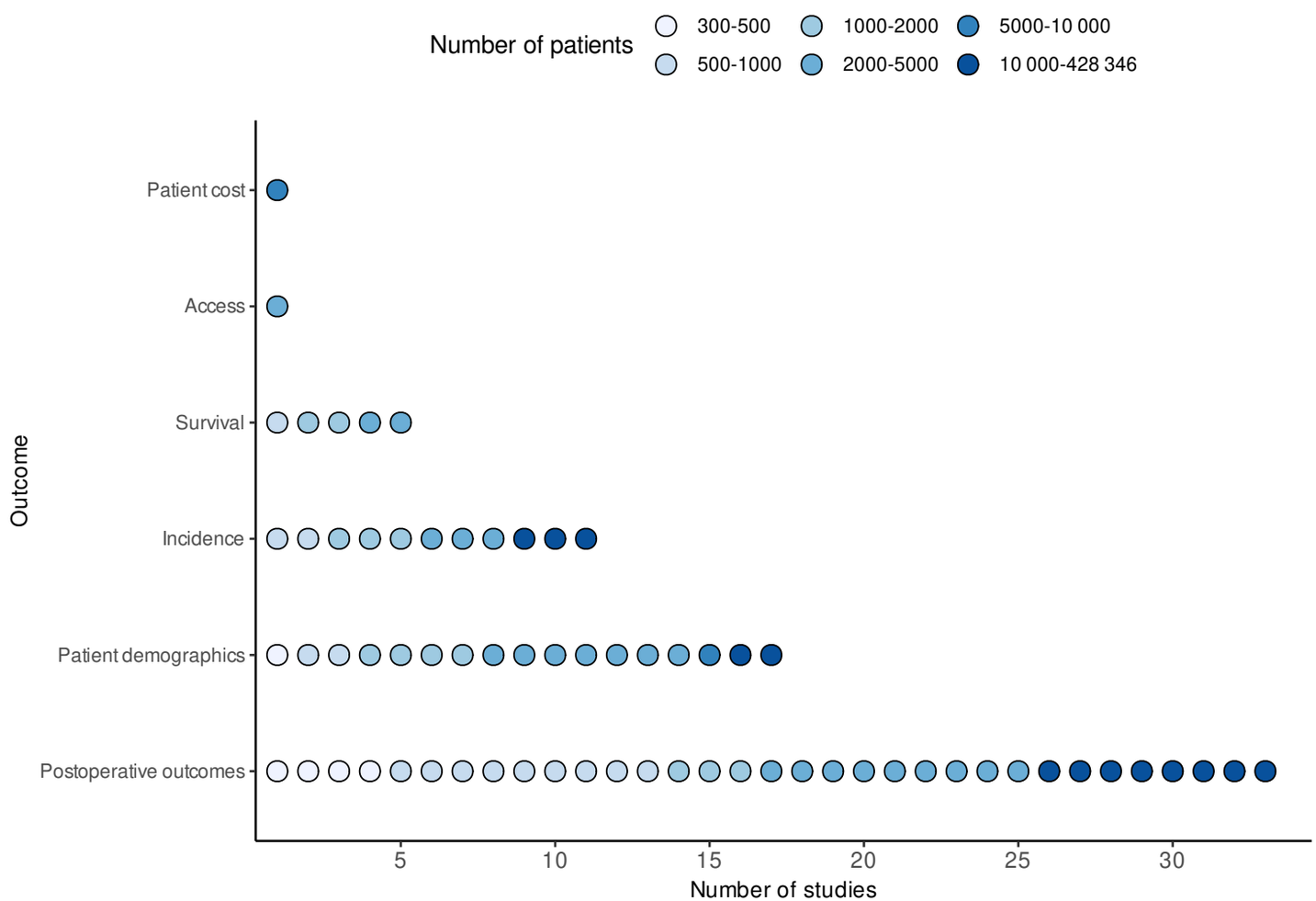


Figure 2-5. Subject area of large volume studies of surgery in low- and middle-income countries.

Material from [81].



2.3.5 Studies including surgery for cancer

Overall, 25 studies solely recruited patients undergoing surgery for cancer[87,89,90,92–96,101,102,109,113,116–118,127–131,133,142,145,147,151]. Breast cancer was the most common (8)[90,92,102,109,116–118,125], followed by gastric (4)[87,93,94,131], colorectal (3)[95,129,151], and hepatic (3)[127,130,145] neoplasms. Only one large international prospective cohort study collected data across multiple cancers[142], however this study was limited to countries in south-east Asia. A further four multicentre, international studies included patients undergoing surgery for cancer[25–27,122], however these patients represented a small subgroup (<20%) within each study.

2.4 Discussion

2.4.1 Summary of key findings

The last five years has seen an exponential rise in the number of studies with a high volume of patient-level data in surgery within LMICs, including some very large patient cohorts seen in countries such as Brazil, China and India. Geographical disparities are apparent and are particularly obvious in Africa, where far fewer large studies have been published. The focus is predominately on short-term outcomes after surgery, together with the epidemiology of diseases commonly treated by surgery. Few studies focus on the specific needs of resource-poor environments, within no study comparing outcomes following cancer surgery across different income settings. It is perhaps too early to determine any positive effects of such work on outcomes in populations of individuals receiving surgical care.

2.4.2 Implications of this work

The combination of multiple data sources to draw population-level conclusions worldwide is epitomised by the Global Burden of Disease (GBD) project by the Institute for Health Metrics and Evaluation at the University of Washington. This is a global effort to comprehensively examine the prevalence, incidence, and impact of multiple diseases and environmental factors using an extensive network of more than 2500 collaborators from 133 countries[152]. Recent publications include global predictions on cancer burden[33], child mortality[15], causes of adult disability[153], and alcohol use[154]. Such projects require accurate national data, something which does not exist in many regions. National registries can be expensive to establish and run, but are becoming more common in middle-income countries, such as the Chinese Guangzhou Occupational Cohort[155] and the Brazilian DATASUS registry[150].

Comprehensive patient-level databases or registries are yet to be adopted in the majority of LMICs. Barriers including a lack of resources and infrastructure, such as electricity and reliable internet connectivity, combine with skill shortages in medical informatics to limit broad adoption. The advent of the Electronic Patient Record (EPR) may present the best opportunity for routine data analysis at a health system level[156]. Although the costs of set-up and maintenance can be a barrier, multiple open-source EPRs now exist which can potentially alleviate some of these[157]. Recently, Rwanda announced the rollout of the OpenMRS system[158] across the country to 250 clinics and hospitals. This will bring EPRs into national practice and offer the opportunity for real-time data collection within a healthcare system to be utilised for infrastructure planning and research.

Linked to this is the explosion in mobile phone technology. Already 75% of the population in sub-Saharan Africa live in an area with mobile internet connectivity[159]. On-board sensors within mobile phones offer the ability to capture data remotely, without need for specialised equipment. The increasing availability of mobile phone use is already supplementing existing forms of patient data, particularly in high-income settings. In surgery, this presents exciting avenues for diagnosis and routine follow-up, particularly in settings where patients cannot easily attend hospitals.

There are important areas of study which are more specific to resource-poor areas, such as access to surgical care and the cost of surgical care to patients. We identified only one study exploring the economic consequences of surgery[142], which reflects previous findings highlighting large-scale health economic studies in cancer being focused in high-income countries or heavily modelled using data from high-income countries[52,160]. Evaluating patient cost following surgery is likely to require frequent and long-term follow-up, potentially explaining the difficulties in measuring this outcome. Utilisation of mobile technology to circumvent current logistical issues and capture expenditure data following surgery is an exciting avenue.

The landscape of healthcare data is changing rapidly. Ensuring LMICs have the resources to keep up-to-date with technological advances will ensure future global health equality[80]. New developments such as artificial intelligence, virtual reality, mobile computing and new molecular techniques present exciting opportunities for surgeons across the world. Embedding these technologies within 'learning' healthcare systems will ensure data contribute to the incremental development of safe practice.

In parallel with future advances, ensuring electronic data is kept secure is of utmost importance. The respect of an individual patient's rights to confidentiality, autonomy,

and privacy is fundamental to ensuring public trust in electronic data collection methods. Beyond good data governance practice, technologies such as blockchain may facilitate the safe and secure sharing of healthcare data within increasingly complex interconnected systems.

2.4.3 Study limitations

There are weaknesses to the approach taken in this review. Pragmatic limitations around the scope of the review search were required and important studies may have been omitted. The synthesis of such a heterogenous group of studies is difficult and conclusions must be made at a high level.

2.4.4 Conclusion

We have demonstrated a significant growth in the use of large volume patient-level data across many surgical specialties and LMICs. We have found at least 71 LMICs currently involved in big data projects, with evidence of an exponential growth in patient numbers totalling more than 700 000 patients. However, currently the majority of studies utilising big data are limited to short-term outcomes after surgery and few address the needs which are particular to LMICs. Funders, policy-makers and specialists in medical informatics urgently need to re-orientate this focus if the potential of big data to improve surgical outcomes, particularly in LMICs, is to be fully realised.

2.5 Contribution statement

This chapter included a systematic review of previously reported studies. I led the work from conception to completion and dissemination. Thank you to Riinu Pius, Mayaba Maimbo and Thomas Drake who help perform article screening.

2.6 Outputs relating to this chapter

This study is published in the *British Journal of Surgery*:

Knight SR, Ots R, Maimbo M, Drake TM, Fairfield CJ, Harrison EM (2019). Systematic review of the use of big data to improve surgery in low- and middle-income countries. **British Journal of Surgery.** 106, e62–e72.

https://doi.org/10.1002/bjs.11052

In addition, I led a follow-up study from conception to completion which evaluated the use of mobile and wearable technology to measure patient outcomes after surgery and is published in *Nature Digital Medicine*:

Knight SR, Ng N, Tsanas A, Mclean K, Pagliari C, Harrison EM (2021). Mobile devices and wearable technology for measuring patient outcomes after surgery: a systematic review. **npj Digit Med.** 4: 1–14.

https://doi.org/10.1038/s41746-021-00525-1

Chapter 3 Measuring early postoperative outcomes in global cancer surgery: the GlobalSurg 3 study

3.1 Introduction

Previous prospective, observational cohort studies performed by the GlobalSurg collaborative (GlobalSurg 1 and 2)[27,161] have demonstrated that patients in LMICs have an increased risk of early death and morbidity following gastrointestinal cancer surgery. These differences persisted in multivariable models accounting for confounders in mortality (OR 3.18, 95% CI 2.12-4.76), major complication (2.14, 1.19-3.84) and surgical site infection (1.32, 1.04-1.68) at 30 days after surgery. Postoperative complications are known to have more severe consequences in LMICs, including death, long-term disability, and catastrophic healthcare expenditure[162].

The measures used to determine the quality of surgical cancer care are controversial and subject to on-going debate. Guidelines produced by bodies such as the National Institute for Health and Care Excellence (NICE, UK) and American College of Surgeons in high-income countries provide some consensus[163,164]. However, there is little evidence on the appropriateness of such guidelines in LMICs, or what specific measures may indicate quality in cancer surgery in resource-poor settings.

The GlobalSurg 3 study aimed to determine variation in the quality of cancer surgery worldwide, focusing on patient outcomes, infrastructure and care processes. This study was driven from within the GlobalSurg collaborative, a well-established global network of over 80 countries.

3.2 Methods

3.2.1 Study design and setting

This international, multicentre, prospective cohort study was conducted according to a published protocol[165], which was prospectively registered (NCT03471494). The study was designed in a collaborative research prioritisation workshop[31]. Breast, colorectal, and gastric cancers were prioritised on the basis of 1) global prevalence and mortality, and 2) relevance to the majority of GlobalSurg collaborators, who are predominantly general surgeons and manage these cancers regularly. To maximise case ascertainment, ensure data quality, and enable engagement across a global network, a pragmatic decision was taken not to collect data on additional cancer types. All study documents, training materials, and language translations were available at online to collaborators throughout the study[166].

Teams of local investigators undertook the study and were coordinated by a network of national lead investigators. The collaborative network methodology has been described in detail previously[161,167]. Any healthcare facility providing emergency or elective surgery for breast, colorectal, or gastric cancer worldwide was eligible to participate. All investigators and national leads are listed in Appendix 10.2.

A UK National Health Service Research Ethics proportionate review considered this study exempt from formal research registration (South East Scotland Research Ethics Service, reference NR/161AB6) as it was deemed clinical audit. Individual centres obtained their own audit or institutional approval, together with ethical approval as per local regulations. This study is reported according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE)[168] and the Statistical Analyses and Methods in the Published Literature (SAMPL)[169] guidelines.

3.2.2 Participants

Investigators included consecutive patients undergoing surgery for breast, colorectal, or gastric cancer, from one or more 28-day period between 1st April 2018 and 31st January 2019, with validation performed until 23rd April 2019. Consecutive sampling is a common non-probability sampling strategy and all patients fulfilling the inclusion criteria within the defined period were enrolled. A 28-day period was chosen to balance sample size requirements and pragmatism for the working clinicians who were enrolling patients and contributing data.

The inclusion of primary breast, colorectal, or gastric cancer was based on global prevalence, potential for cure with surgical treatment, and relevance to general surgeons working in resource-constrained settings. There was an absolute requirement for all cases in the chosen period to be included, but no minimum number was set to avoid bias against smaller centres. Patients provided consent to participate if required by local research regulations and could withdraw at any time during the study period. Adult patients aged 18 or over undergoing their first surgical procedure for the treatment of one of the three cancers were included. Due to potential limitations in preoperative diagnosis in some settings, all patients receiving surgical treatment for suspected cancer were enrolled. Patients subsequently found to have a non-oncological diagnosis were excluded from data analysis.

Emergency procedures were defined as unplanned, non-elective operations. Open and minimally invasive procedures, for example laparoscopic or robotic-assisted, were eligible. Patients were excluded if the primary pathology was not suspected to be breast, colorectal, or gastric cancer; if the pathology was a suspected cancer recurrence; or if they were undergoing a procedure that did not require a skin incision (Table 3-1).

Table 3-1. Patient inclusion and exclusion criteria.

Inclusion criteria
1. Adult patients aged 18 or over
2. Consecutive patients undergoing therapeutic surgery (curative or palliative) for breast, colorectal, or gastric cancer
3. Patients with suspected benign pathology preoperatively whom were subsequently found to have a diagnosis of cancer following their surgery
4. Undergoing emergency or elective procedure requiring a skin incision performed under general or neuraxial (e.g. regional, epidural or spinal) anaesthesia.
5. Includes open, laparoscopic, laparoscopic converted and robotic cases
Exclusion criteria
1. Operations with a sole diagnostic or staging intent
2. Procedures which do not require a skin incision
3. Patients with recurrence of breast, colorectal or gastric cancer

3.2.3 Data collection: Patient-level data

Data variables were selected to be objective, standardised, easily transcribed, and internationally relevant to maximise completeness and accuracy. Local investigators uploaded records to a secure online website, provided using the Research Electronic Data Capture (REDCap) system[170]. The lead investigator at each site checked the accuracy of all cases before data submission. To ensure data quality, real-time assessment upon entry into the database were performed and disparities highlighted to the local collaborator for immediate review. The submitted data were then checked centrally and when missing data were identified, the local lead investigator was contacted and asked to complete the record. Online data visualisation tools aided this process. Once vetted, the record was accepted into the dataset for analysis. Records that

were vetted but remained incomplete were included in the patient flowchart but excluded from analysis.

Patient variables included age, sex, performance status according to the Eastern Cooperative Oncology Group (ECOG status), physical status according to the American Society of Anesthesiologists (ASA) grading system, and smoking status. Disease-related variables included cancer type, disease stage, timing of surgery (elective or emergency), intent of surgery (curative or palliative), and use of the WHO surgical checklist. Presence of preoperative perforation or obstruction, and operative approach (open or minimally invasive) were also included for colorectal and gastric cancers.

3.2.4 Standardisation of disease stage

Disease stage was defined according to the Essential TNM classification of malignant tumours system[171], to account for differences in local protocols and availability of investigations for preoperative staging. The Essential TNM classification system for breast cancer is shown in Figure 3-1 as an example. A pragmatic view was taken to the confirmation of cancer diagnosis, as postoperative pathological examination worldwide is dependent on the availability of patient and healthcare resources. To reflect this, I recorded the basis of cancer diagnosis using a hierarchical scale ranging from clinical diagnosis only to pathological confirmation (Figure 3-2).

Figure 3-1. **Breast cancer Essential TNM classification**

Reproduced from Brierley *et al* (2016)[172], by permission of Wiley Blackwell. The Union for International Cancer Control TNM Classification of Malignant Tumours (Eighth Edition).

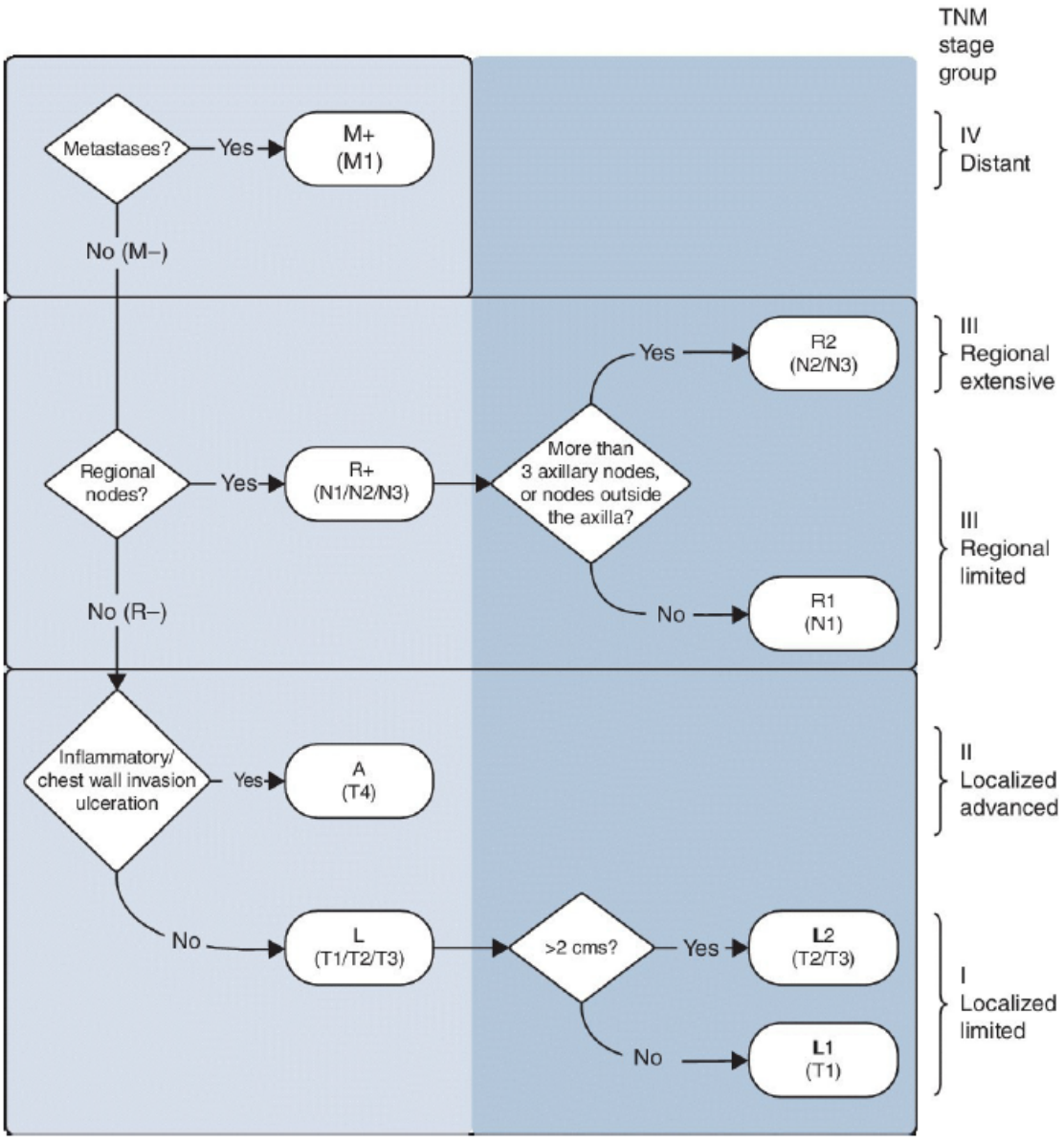
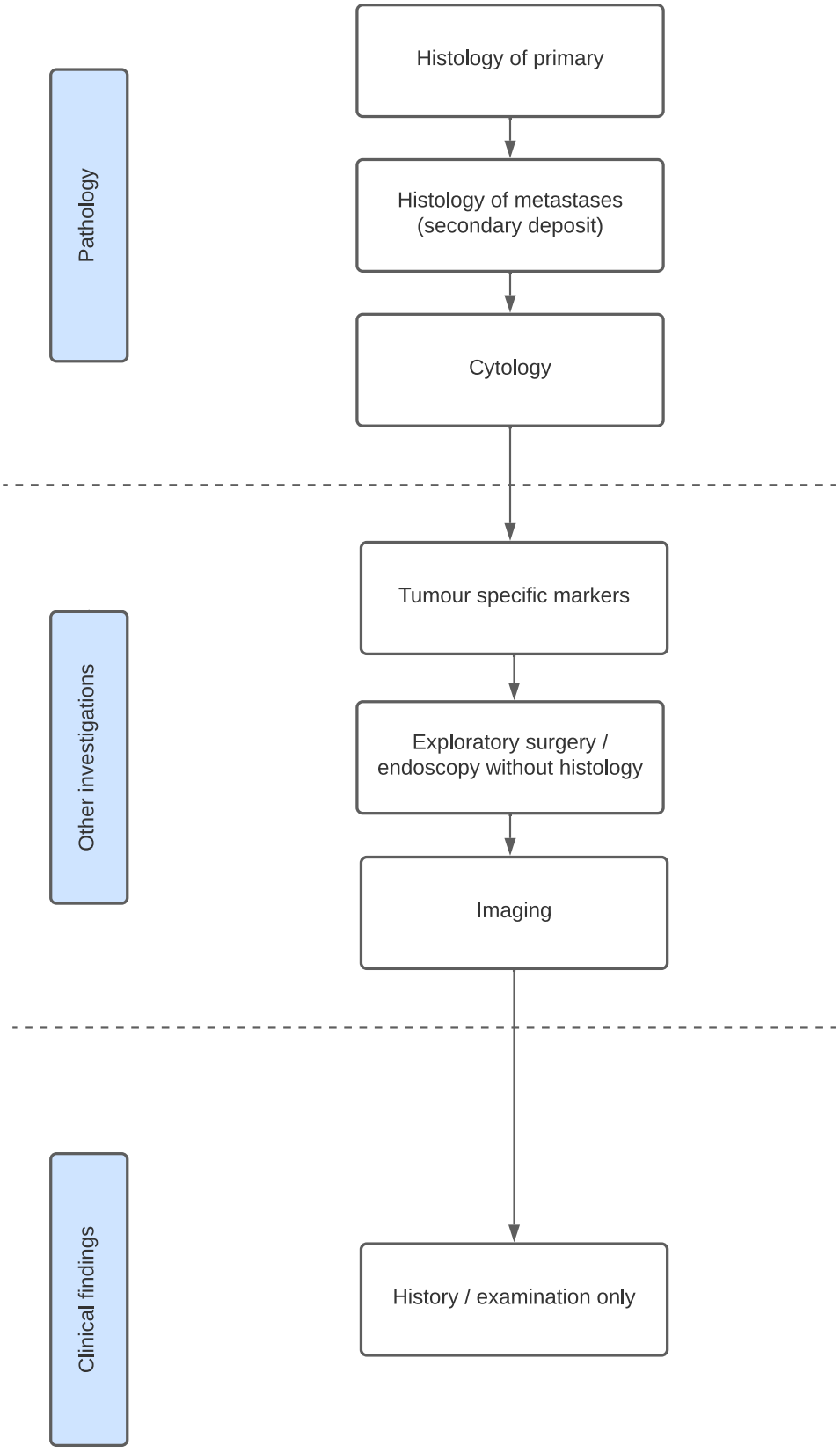


Figure 3-2. Hierarchical scale for basis of cancer diagnosis



3.2.5 Data collection: hospital-level data

The survey design followed a system-based approach adapting the framework for Comprehensive Cancer Centres in LMICs[173]. Hospital infrastructure and process resources identified as core clinical service components to enable access to high quality cancer care were captured, such as the presence of imaging modalities, oncological services, surgical treatment and perioperative care. The ability of hospitals to perform elective operations for eleven globally prevalent cancers was also ascertained[3]. Twenty surgical experts across nine LMICs reviewed multiple survey iterations, with specific criteria to ensure included hospital facility characteristics had relevance in low-income settings.

Definitions for each hospital facility characteristic were taken from the WHO[174], where available, the National Health Service data dictionary[175] or American Association of Clinical Oncology[176]. Members listed within the tumour board structure were taken from the recently published NICE guidelines[177].

Beta testing at two LMIC hospital sites was performed to ensure survey clarity prior to formal release across all collaborating hospitals. Collaborators at hospitals who had entered patient-level data for GlobalSurg 3 were invited to complete the hospital-level survey via a secure online link and entered directly onto the REDCap database. Collaborators were provided with a data extraction sheet to aid completion. The survey remained open for eight weeks, with reminders sent every four weeks if the survey remained incomplete.

3.2.6 Patient outcomes

For all analyses, the primary outcome measures were 30-day mortality and 30-day major complication, as defined by Clavien-Dindo grade III, IV or V (Table 3-2)[178].

Death was included in the definition of major complication and therefore was not a competing risk. *Capacity to rescue* was defined as the absolute risk difference of death in patients sustaining a complication of surgery. Mortality conditional on major complication was analysed *post hoc*.

Table 3-2. **Clavien-Dindo classification of major postoperative complications**

Clavien-Dindo grade III
Unplanned surgical, endoscopic or radiological intervention
IIIa: intervention not under general anaesthesia;
IIIb: intervention under general anaesthesia
Clavien-Dindo grade IV
Life-threatening complication requiring unplanned critical care management
IVa: single organ dysfunction (including dialysis);
IVb: multiorgan dysfunction

The secondary outcome measures were defined in the protocol[165] and designed to describe cancer care quality: (1) 30-day any complication (defined by Clavien-Dindo grade I to V), (2) 30-day unplanned reintervention (defined as operative, radiological, or endoscopic reintervention any time until 30 days after surgery), (3) unplanned readmission to a healthcare facility, (4) cancer-specific complications including seroma (breast), anastomotic leak (colorectal and gastric), surgical site infection (all)[167], abscess formation (all), and post-operative bleed (all), (5) cancer treatment pathways, and (6) hospital-level care processes. Patients were assessed at 30 days to determine postoperative outcomes, with follow-up performed in person, by telephone, or by review of medical/readmission records, dependent on local practices.

3.2.7 Sample size

As described in the protocol, consideration was given to the sample size needed to compare income groups[165]. Estimates of 30-day mortality for gastrointestinal cancer

surgery were determined using data from the GlobalSurg 1 and 2 studies[161,167]. Stratification of results by country income group show differences between high and LMIC groups in both emergency surgery (11.6% [75/644] vs. 27.3% [59/216]) and elective surgery (2.0% [30/1501] vs. 5.5% [23/416]). An indicative sample size calculation using the smaller of these estimates suggests around 500 patients per group at 80% power (P1=0.020, P2=0.055, alpha=0.05) or 640 patients per group at 90% power would be required to conclude a difference in 30-day mortality rate between income groups.

3.2.8 Statistical analysis: patient-level data

Variation across different international health settings was assessed by stratifying countries by World Bank country group classifications. Differences between World Bank tertiles were tested with the Pearson $\chi 2$ test for categorical variables and with the Kruskal-Wallis test for continuous variables. Multilevel logistic regression models were constructed to account for case mix (differing patient, disease, and operative characteristics), with population stratification by hospital and country of residence incorporated as random intercepts with constrained gradients. Further analyses were then performed exploring the relationship between primary outcome measures, patient factors, and hospital care facilities.

All models were constructed using the following principles: (1) variables associated with outcome measures in previous studies were accounted for; (2) demographic variables were included in model exploration; (3) population stratification by hospital and country of residence was incorporated as random effects; (4) all first-order interactions were checked and included in final models if found to be influential (reaching statistical significance and/or resulting in a 10% or greater change in the odds

ratio of the explanatory variable of interest); (5) final model selection was done using a criterion-based approach by minimising the Akaike information criterion (AIC) and discrimination determined using the c-statistic (area under the receiver operator curve).

Effect estimates are presented as adjusted odds ratios (aOR) and 95% confidence intervals (95% CI). The variance explained at each level of multilevel models was determined[179]. The conditional pseudo-R^2 was defined as the sum of the variance components of fixed and all random effects divided by total variance. The variance explained by each component (marginal pseudo-R^2) was expressed as a proportion of the conditional pseudo-R^2.

Mediation analysis was performed by three-way decomposition of total effects into direct, indirect, and interactive effects[180]. The mediators examined were at the level of the hospital, defined as the presence or absence of postoperative care infrastructure, and it was assumed that there was no causal relationship between these and patient-level covariates. Similarly, no mediator-outcome confounders were specified. Uncertainty was determined using bootstrap resampling (5000 draws) and confidence intervals constructed using percentiles.

Quantities of interest were calculated from logistic regression models for different covariate levels (patient and disease characteristics). Absolute risk differences were calculated, and confidence intervals determined using bootstrap resampling. The number needed to treat (NNT) to benefit was defined as the reciprocal of the absolute risk difference.

All analyses were done using the R Foundation Statistical Program version 3.6.3, using the finalfit, tidyverse, regmedint, and lme4. Additional data and analyses which support Chapters 5 to 7 are contained within the Appendix (10.3 to 10.5).

3.2.9 Statistical analysis: hospital-level data

Eleven hospital characteristics were selected *a priori* on the basis of their potential to directly or indirectly affect patient outcomes following cancer surgery[173,181–185]. They were categorised into four areas potentially representing structure and process measures within the hospital that support the management of high-risk surgical patients[173,182]: imaging modalities (ultrasound and CT scan); oncological service organisation (oncologist, pathologist, tumour board); perioperative care organization (postoperative recovery area, opioid analgesia, palliative care, higher level care area (HDU and/or ITU)); and specialist cancer services (specialist hospital and capability to perform elective oesophagecetomy). The relationship between elective oesophagectomy, facility availability, service complexity and mortality is well described in high-income settings[182–184].

I used automated variable selection with backward elimination to select those hospital facility characteristics associated with 30-day mortality, using the Akaike information criterion (corresponding alpha of 0.157) as described by Moon *et al*[186]. All hospital facility characteristics were included as explanatory variables within this model, but with the exclusion of patient-level data. Only main interactions were included to avoid overfitting. Facility characteristics with a P value of <0.05 were identified as candidate covariates. As a sensitivity analysis, a bootstrap procedure (n=5000) was performed to investigate variability in hospital facility characteristic selection.

To obtain adjusted outcomes at hospitals with different numbers of facility characteristics, I created an ordinal variable (0–5) which represented the number of characteristics at each hospital. Hospitals were then categorised into different facility capability tertiles by patient distribution.

Variation across different international health settings was assessed by stratifying countries by World Bank country group classifications. Differences between groups were tested with the Pearson $\chi 2$ test for categorical variables and with the Kruskal-Wallis test for continuous variables. To characterize the relationship between hospital facility capacity and mortality, generalised estimating equations (GEE) were constructed to account for case mix and operative characteristics (differing income group, patient, disease, and operative characteristics) known to be associated with worse outcomes following cancer surgery[187], with population stratification by hospital.

Adjusted outcomes were calculated as predicted probabilities from a GEE logistic regression model, including potential confounders (patient age, sex, American Society of Anesthesiologists (ASA) grade, performance status, disease stage and operative urgency) across income group and cancer type. I obtained confidence intervals (CIs) and a P value for trend by fitting the GEE logistic regression model with facility capability.

Sensitivity analyses for adjusted outcome rates, by imputing the average number of available hospital characteristics by nearest neighbour HDI rank for missing hospitals, was also performed. As an additional comparison, adjusted outcomes were also calculated using all eleven hospital facility characteristics (ordinal value 0-11) across included hospitals using the same methodology.

The relationship between hospital facility capability and 30-day mortality were calculated from logistic regression models for different covariate levels (patient and disease characteristics). Absolute risk differences were calculated, and CIs determined using bootstrap resampling (5000 draws). The number needed to treat to benefit was defined as the reciprocal of the absolute risk difference.

All P values were 2-sided and were considered statistically significant if the P value was less than 0.05. All analyses were done using R (version 3.6.3), using the finalfit, tidyverse, geepack, epitools and bootStepAIC. Additional data and analyses which support Chapters 5 to 7 are contained within the Appendix (10.3 to 10.5).

3.2.10 Validation of patient-level data

Data validation was performed in three parts across a representative sample of centres according a pre-specified protocol[188]. Independent validators (for example, doctors, nurses, or medical students who were not part of the recruiting teams) quantitatively reported case ascertainment and sampled data accuracy. Validators were asked to provide data for a subset of variables, three patient variables (age, sex, and disease stage), two operative variables (surgical urgency and intent) and two outcome measures (30-day mortality and major complication rate) in order to measure data accuracy.

Finally, validators identified any missing eligible patient within the local cohort and collected the missing information for each omission: age, sex, operation urgency, and 30-day mortality. These data were used to determine whether patient data were missing at random. All validators are listed in Appendix 10.2.

3.3 Discussion

I describe a multicentre, international, prospective cohort study investigating the quality and outcomes of surgery for three of the most common global cancers. Despite the likely increased risk of mortality and major morbidity for patients undergoing surgery for cancer in LMICs, high quality, empirical data is currently unavailable. Furthermore, in countries with limited resources applicability of cancer surgery guidelines are yet to be tested.

By using a collaborative methodology and a short four-week data collection period, the study will recruit sufficient patients to measure this, while avoiding burdening low-resource centres that may otherwise be unable to participate. Investigating the morbidity and mortality caused by cancer surgery globally, this study will provide a platform to build future quality improvement programmes and interventional trials as previously demonstrated by the GlobalSurg network[1].

This study will be delivered using an international multidisciplinary collaborative network of healthcare researchers, with the collaborative model having consistently proven its ability to produce high-quality outcomes in international studies[161,167]. A detailed study protocol in multiple languages, mandatory training, data quality control and validation period will ensure standardisation to deliver a reliable and accurate data set.

As the second most common cause of death in 2015, with 8.7 million deaths globally[33], cancer incidence is predicted to become an increasing burden worldwide[33,52] and place further pressure on already limited healthcare systems. Neoplasms already contribute to significant global morbidity and mortality, causing the highest loss of gross domestic product of any surgical disease[32]. Surgery can provide cure for many cancers, particularly in countries where limited access to oncology treatment exists. However, the majority of the world's population lack access to safe, affordable, and timely cancer surgery[21].

This study provides the first opportunity to collect and analyse prospective, observational data for three of the most common global cancers. Current literature is heavily reliant on simulated models based on limited data sources[21,32,33]. My study will

quantify any global inequalities in cancer surgery, highlight differences in patient presentation, treatment interventions, and surgical outcomes.

With information relating to early surgical outcomes and specific quality measures relating to each cancer, collaborators will have the opportunity to appraise their current practice against a global standard. Furthermore, surgeons and other interested parties will be able to use the findings from this study to help develop focused cancer surgery guidelines based on empirical global data.

3.4 Contribution statement

This chapter formed a part of a protocol developed in collaboration with international surgical experts, led by Professor Ewen Harrison. I led the protocol development to completion and dissemination.

3.5 Outputs relating to this chapter

This study is published in *BMJ Open:*

NIHR Global Health Research Unit on Global Surgery [**Knight SR** first author in writing group] (2019). Quality and outcomes in global cancer surgery: protocol for a multicentre, international, prospective cohort study (GlobalSurg 3). **BMJ Open.** 9: e026646.

http://dx.doi.org/10.1136/bmjopen-2018-026646

Chapter 4 Patients undergoing surgery for cancer worldwide

4.1 Introduction

Previous studies have demonstrated the ability to capture large prospective datasets on early surgical outcomes following surgery across multiple nations[81]. However, in patients undergoing surgery for cancer, these data have been limited to single cancers within individual countries. Furthermore, the absence of data quality validation following primary data collection restricts interpretation of data reliability and accuracy[189].

This lack of high-quality data limits global efforts to improve cancer care. Strategic planning mandates detailed and accurate information so that appropriate resource 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.

To address these knowledge gaps, I sought to characterise the patient population undergoing surgery for cancer worldwide through a primary analysis of the data from the GlobalSurg 3 study. I then aimed to evaluate the reliability and accuracy of collected data through an independent validation process.

4.2 Methods

4.2.1 Study design and participants

The GlobalSurg 3 study was performed according to a published protocol[188] and is described in detail within Chapter 3. Briefly, consecutive patients aged 18 or over

undergoing their first surgical procedure for breast, colorectal, or gastric cancer were recruited between 1st April 2018 and 31st January 2019. Inclusion criteria were: patients undergoing an emergency or elective procedure for a suspected cancer diagnosis, who required a skin incision performed under general or neuraxial anaesthesia. Patients who were not suspected to have a primary pathology of breast, colorectal, or gastric cancer were excluded, as were patients presenting with suspected cancer recurrence.

Following completion of patient recruitment, hospital-level data were subsequently collected using a survey designed in conjunction with twenty surgical experts across nine LMICs to ensure included hospital facility characteristics had relevance in low-income settings. Beta testing at two LMIC hospital sites was performed to ensure survey clarity prior to formal release across all collaborating hospitals. Collaborators at hospitals who had entered patient-level data were invited to complete the hospital level survey and provided with a data extraction sheet to aid completion. The survey remained open for eight weeks, with reminders sent every four weeks if the survey remained incomplete.

4.2.2 Data quality and validation

Data variables were selected to be objective, standardised, easily transcribed, and internationally relevant to maximise completeness and accuracy. Furthermore, to ensure data quality, real-time assessment upon entry into the database were performed and disparities highlighted to the local collaborator for immediate review. Submitted data were then subsequently checked centrally and when missing data were identified, the local lead investigator was contacted and asked to complete the record.

Data validation was performed across a representative sample of randomly selected centres. Independent validators, who were not part of the primary data collection

process, quantitatively reported case ascertainment and sampled data accuracy. Validators were provided with the following patient variables: hospital ID, age, sex, date of admission, date of operation, cancer type and primary operation name. These data were complete in the primary dataset. Using this information, validators were asked to confirm variables from the patient's paper or electronic notes in order to measure data accuracy.

For categorical variables, agreement between validation and primary data is described using the Cohen's kappa coefficient. Guidelines on the interpretation of agreement with the kappa coefficient are poor (<0.20), fair (0.20 to 0.40), moderate (0.41 to 0.60), good (0.61 to 0.80), and very good (0.80 to 1.00)[190].

4.3 Results

4.3.1 Overview of study cohort

Between 1st April 2018 and 31st January 2019, 16 838 patient records were submitted for analysis. 880 (5.2%) did not fulfil the inclusion criteria, leaving 15 958 records for the final analysis (Figure 4-1). These patients were from 428 hospitals, across 82 countries: 22 countries in Africa, 17 countries in Asia, 30 countries in Europe, 5 countries in North America, 2 countries in Oceania, and 6 countries in South America (Figure 4-2).

Patients most often received surgery for breast cancer (8406, 52.7%), followed by colorectal (6215, 38.9%) and gastric cancer (1337, 8.4%). On stratification by World Bank country income groups, 9106 (57.1%) patients were from high-income countries, 2721 (17.0%) from upper middle-income countries, and 4131 (25.9%) from low/lower

middle-income countries (Table 4-1). Almost three quarters of patients (11 565, 72.5%) were female, secondary to the inclusion of breast cancer.

Patients from upper middle-income and low/lower middle-income were younger, more likely to have lost weight, and had fewer comorbidities compared with high-income country patients (Table 4-1). However, the physical performance status of patients was comparable across all three income groups. Smoking was more common in high-income countries, however the rates of diabetes mellitus and Human Immunodeficiency Virus (HIV) were similar.

Figure 4-1. Patient flow chart.

Material from [187].

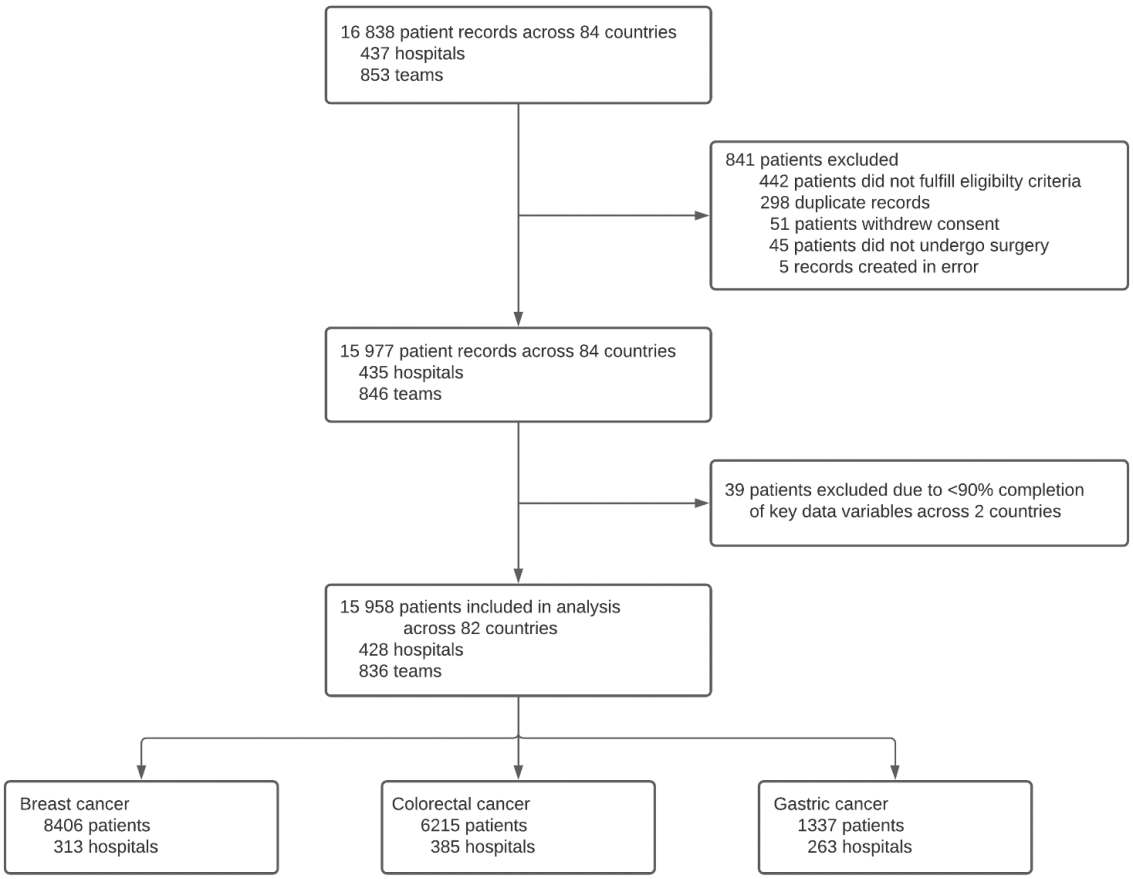


Figure 4-2. Distribution of patients within the GlobalSurg 3 cohort.

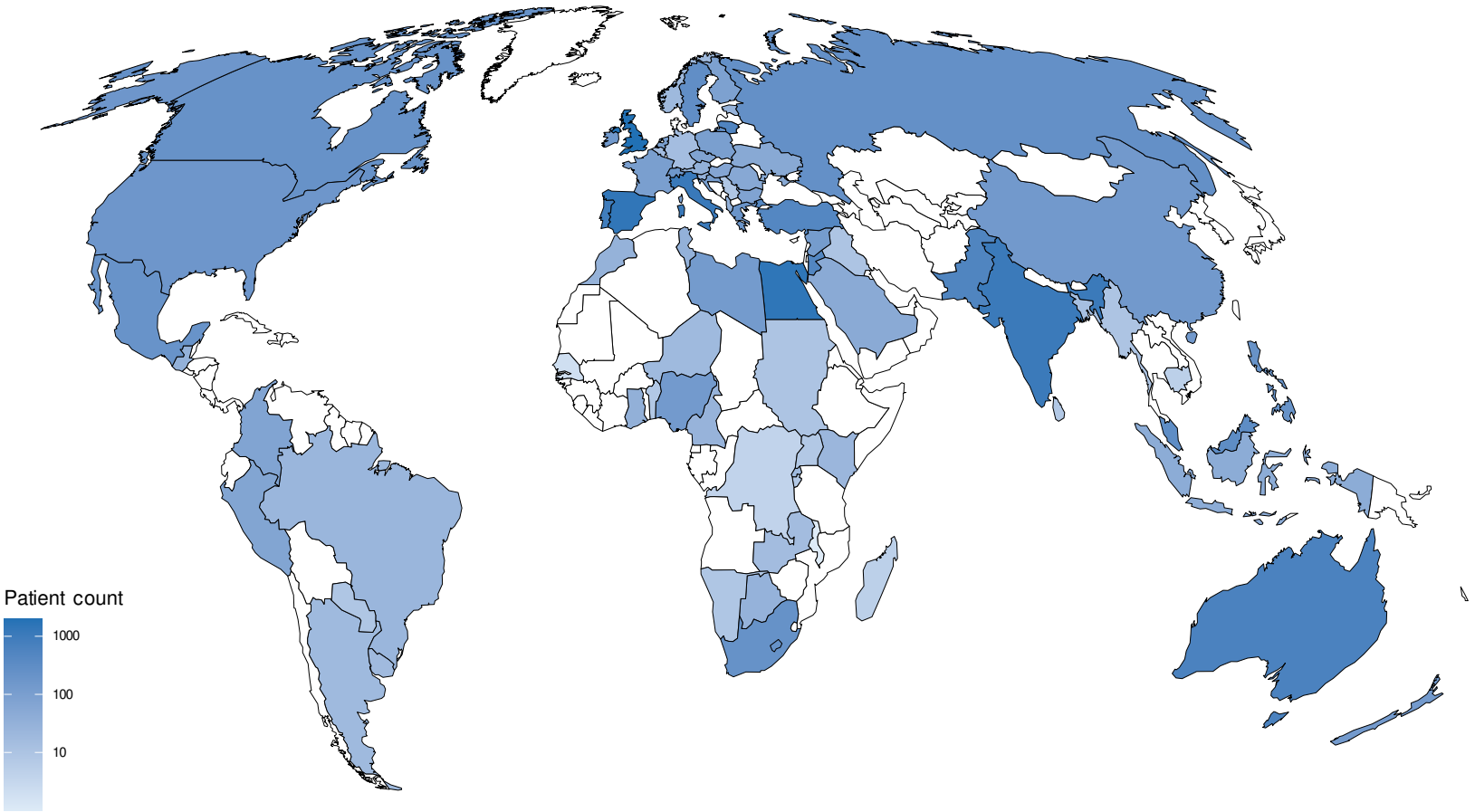


Table 4-1. Patient characteristics by country income group.

Numbers are n (%), unless otherwise indicated. The total column includes patients from 82 countries across 428 hospitals. ASA, American Society of Anesthesiologists operative risk grade; ECOG, Eastern Cooperative Oncology Group; BMI, body mass index; SD, standard deviation.

WB income (tertile)		High	Upper middle	Low/lower middle	P
		N=9106	N=2721	N=4131	
Cancer type	Breast	4220 (46.3)	1319 (48.5)	2867 (69.4)	<0.001
	Colorectal (colon or rectum)	4174 (45.8)	1113 (40.9)	928 (22.5)	
	Gastric (stomach)	712 (7.8)	289 (10.6)	336 (8.1)	
Age (years)	Mean (SD)	65.0 (13.4)	58.0 (13.6)	51.9 (12.7)	<0.001
Sex	Male	2864 (31.5)	791 (29.1)	723 (17.5)	<0.001
	Female	6231 (68.4)	1928 (70.9)	3406 (82.4)	
	(Missing)	11 (0.1)	2 (0.1)	2 (0.0)	
ASA	I	1148 (12.6)	739 (27.2)	1285 (31.1)	<0.001
	II	4769 (52.4)	1474 (54.2)	2242 (54.3)	
	III	2558 (28.1)	391 (14.4)	412 (10.0)	
	IV	217 (2.4)	42 (1.5)	36 (0.9)	
	V	17 (0.2)	1 (0.0)	10 (0.2)	
	(Missing)	397 (4.4)	74 (2.7)	146 (3.5)	
BMI	Normal weight (BMI 18.5 to 24.9)	3267 (35.9)	1148 (42.2)	1511 (36.6)	<0.001
	Underweight (BMI < 18.5)	231 (2.5)	111 (4.1)	234 (5.7)	
	Overweight (BMI 25 to 30)	3079 (33.8)	882 (32.4)	1354 (32.8)	

	Obese (BMI >30)	1773 (19.5)	470 (17.3)	867 (21.0)	
	(Missing)	756 (8.3)	110 (4.0)	165 (4.0)	
>10% weight loss	No	6560 (72.0)	1813 (66.6)	2896 (70.1)	<0.001
	Yes	1049 (11.5)	673 (24.7)	917 (22.2)	
	(Missing)	1497 (16.4)	235 (8.6)	318 (7.7)	
ECOG performance status	0	5090 (55.9)	1732 (63.7)	2136 (51.7)	<0.001
	1	2152 (23.6)	639 (23.5)	1085 (26.3)	
	2	961 (10.6)	201 (7.4)	570 (13.8)	
	3	299 (3.3)	94 (3.5)	176 (4.3)	
	4	32 (0.4)	9 (0.3)	31 (0.8)	
	(Missing)	572 (6.3)	46 (1.7)	133 (3.2)	
Smoking	No, never	5363 (58.9)	1902 (69.9)	3631 (87.9)	<0.001
	Stopped >6 weeks ago	1650 (18.1)	322 (11.8)	181 (4.4)	
	Yes, current smoker	1174 (12.9)	347 (12.8)	170 (4.1)	
	(Missing)	919 (10.1)	150 (5.5)	149 (3.6)	
Diabetes	No	7594 (83.4)	2179 (80.1)	3100 (75.0)	<0.001
	Diet	209 (2.3)	42 (1.5)	45 (1.1)	
	Medication (non-insulin)	895 (9.8)	324 (11.9)	422 (10.2)	
	Insulin	279 (3.1)	120 (4.4)	191 (4.6)	
	(Missing)	129 (1.4)	56 (2.1)	373 (9.0)	
HIV tested	No	8650 (95.0)	1626 (59.8)	2118 (51.3)	<0.001
	Yes - negative	404 (4.4)	1067 (39.2)	2001 (48.4)	
	Yes - positive	9 (0.1)	26 (1.0)	12 (0.3)	
	(Missing)	43 (0.5)	2 (0.1)	0 (0.0)	

4.3.2 Diagnosis and stage at presentation

Patients were more likely to present first to a family doctor (n=5163, 32.4%) or hospital out-patient clinic (5564, 34.9%; Table 4-2) for all three cancers. Across income group, methods of first presentation and surgical urgency were similar. However, patients in upper-middle and low/lower-middle income countries were more likely to present symptomatically and travel distances >100km for surgical treatment. For colorectal and gastric cancers, two thirds of patients in LMIC settings presented initially to a specialist clinic and a higher rate of emergency surgery was seen in low/lower-middle income settings (Table 4-3).

Patients from upper middle-income and low/lower middle-income generally presented with a more advanced disease stage for breast, colorectal, or gastric cancer (Table 4-4). The presence of metastatic disease at the time of surgery was higher for all included cancers in upper middle-income and low/lower middle-income compared to high-income countries. Where available, final pathological staging using histology demonstrated good correlation with the Essential TNM Classification of Malignant Tumours (Figure 4-3).

4.3.3 Postoperative patient follow-up

Patients were reviewed in clinic, by telephone, or whilst still an in-patient to determine 30-day follow-up in ≥75% across all three cancers (Figure 4-4). In the majority of patients primary histology was the main method of diagnosis, when stratified by income group and cancer type. However, a trend towards diagnosis by another method, particularly by imaging, was seen in upper middle-income and low/lower middle-income groups. This pattern was identified across all three cancer types, with a higher rate in patients undergoing surgery for colorectal cancer.

Table 4-2. Method of presentation: all patients.

WB income (tertile)		High	Upper middle	Low/lower middle	P
		N=9106	N=2721	N=4131	
First consultation	Local clinic: family doctor / general practitioner	3646 (40.0)	444 (16.3)	1073 (26.0)	<0.001
	Local clinic: nurse	60 (0.7)	38 (1.4)	22 (0.5)	
	Local clinic: specialist doctor	1577 (17.3)	717 (26.4)	1171 (28.3)	
	Hospital: out-patient clinic	2827 (31.0)	1189 (43.7)	1548 (37.5)	
	Hospital: in-patient	796 (8.7)	264 (9.7)	146 (3.5)	
	Other/non-medical/traditional healer	37 (0.4)	4 (0.1)	27 (0.7)	
	(Missing)	163 (1.8)	65 (2.4)	144 (3.5)	
Mode of diagnosis	Symptomatic	5589 (61.4)	2219 (81.6)	3610 (87.4)	<0.001
	Screening	2707 (29.7)	225 (8.3)	126 (3.1)	
	Detected incidentally	662 (7.3)	257 (9.4)	371 (9.0)	
	(Missing)	148 (1.6)	20 (0.7)	24 (0.6)	
Distance to home (km)	< 10 km	3497 (38.4)	677 (24.9)	575 (13.9)	<0.001
	10-20 km	1798 (19.7)	617 (22.7)	673 (16.3)	
	20-50 km	1756 (19.3)	479 (17.6)	768 (18.6)	
	50-100 km	738 (8.1)	195 (7.2)	514 (12.4)	
	>100 km	576 (6.3)	439 (16.1)	1409 (34.1)	
	(Missing)	741 (8.1)	314 (11.5)	192 (4.6)	
Urgency	Elective	8525 (93.6)	2534 (93.1)	3915 (94.8)	0.006
	Emergency	579 (6.4)	187 (6.9)	213 (5.2)	
	(Missing)	2 (0.0)	0 (0.0)	3 (0.1)	

Table 4-3. Method of presentation: colorectal and gastric cancer only.

WB income (tertile)		High	Upper middle	Low/lower middle	P
		N=4886	N=1402	N=1264	
First consultation	Local clinic: family doctor / general practitioner	1958 (40.1)	219 (15.6)	194 (15.3)	<0.001
	Local clinic: nurse	13 (0.3)	7 (0.5)	2 (0.2)	
	Local clinic: specialist doctor	893 (18.3)	449 (32.0)	417 (33.0)	
	Hospital: out-patient clinic	1216 (24.9)	490 (35.0)	487 (38.5)	
	Hospital: in-patient	702 (14.4)	210 (15.0)	107 (8.5)	
	Other/non-medical/traditional healer	12 (0.2)	1 (0.1)	13 (1.0)	
	(Missing)	92 (1.9)	26 (1.9)	44 (3.5)	
Mode of diagnosis	Symptomatic	3516 (72.0)	1284 (91.6)	1213 (96.0)	<0.001
	Screening	876 (17.9)	48 (3.4)	11 (0.9)	
	Detected incidentally	419 (8.6)	61 (4.4)	33 (2.6)	
	(Missing)	75 (1.5)	9 (0.6)	7 (0.6)	
Distance to home (km)	< 10 km	1860 (38.1)	337 (24.0)	223 (17.6)	<0.001
	10-20 km	939 (19.2)	345 (24.6)	213 (16.9)	
	20-50 km	947 (19.4)	238 (17.0)	257 (20.3)	
	50-100 km	392 (8.0)	117 (8.3)	129 (10.2)	
	>100 km	357 (7.3)	240 (17.1)	370 (29.3)	
	(Missing)	391 (8.0)	125 (8.9)	72 (5.7)	
Urgency	Elective	4325 (88.5)	1225 (87.4)	1073 (84.9)	0.002
	Emergency	560 (11.5)	177 (12.6)	191 (15.1)	
	(Missing)	1 (0.0)	0 (0.0)	0 (0.0)	

4.3.4 Postoperative complications

The unadjusted rates of postoperative complications are shown in Figure 4-5. Higher rates of any complication in upper-middle and low/lower-middle income groups were found across all three cancer types, particularly influenced by the incidence of surgical site infection and minor complications. However, no differences in cancer-specific complications were identified across income group, including major complication rates, postoperative haemorrhage, abscess formation, and anastomotic leak.

4.3.5 Hospital facilities

Hospitals in high-income (n = 241), upper middle-income (n = 81) and low/lower middle-income (n = 106) groups were sampled. Hospitals in upper middle-income and low/lower-middle income groups were less likely to have postoperative care infrastructure (designated postoperative recovery areas, consistently available critical care facilities, and an available and working CT) and cancer care pathways (tumour board review, oncology services and palliative care services; Figure 4-6 and Table 4-5). However, patients were more likely to be treated in hospitals with specialist cancer centre status and a larger patient catchment population compared to high-income countries.

4.3.6 Missing data

Missingness was low and no patterns were seen when comparing included and missing data by income group and cancer type (Table 4-6) or across patient variables (Figure 4-7). Variables relating to nutritional status (BMI and >10% weight loss) and smoking status were most likely to be missing, with levels of missingness elevated in high-income countries.

Table 4-4. **Stage of presentation by region.**

Essential TNM Classification of Malignant Tumours (eTNM) as defined by the Union for International Cancer Control (UICC).

World Bank income (tertile)		High	Upper middle	Low/lower middle	P
eTNM pre-op (breast)	Tis	427 (10.1)	45 (3.4)	42 (1.5)	<0.001
	L1	1760 (41.8)	298 (22.7)	245 (8.7)	
	L2	1129 (26.8)	361 (27.5)	741 (26.2)	
	A	38 (0.9)	25 (1.9)	74 (2.6)	
	R1	646 (15.3)	404 (30.8)	1184 (41.8)	
	R2	141 (3.3)	109 (8.3)	406 (14.3)	
	M+	70 (1.7)	71 (5.4)	140 (4.9)	
eTNM pre-op (colorectal)	L	1457 (35.1)	198 (17.9)	147 (16.2)	<0.001
	A	911 (21.9)	269 (24.3)	206 (22.7)	
	R+	1276 (30.7)	437 (39.4)	415 (45.8)	
	M+	511 (12.3)	204 (18.4)	138 (15.2)	
eTNM pre-op (gastric)	L	316 (44.5)	77 (27.3)	57 (17.2)	<0.001
	A	108 (15.2)	58 (20.6)	69 (20.8)	
	R+	243 (34.2)	115 (40.8)	147 (44.4)	
	M+	43 (6.1)	32 (11.3)	58 (17.5)	

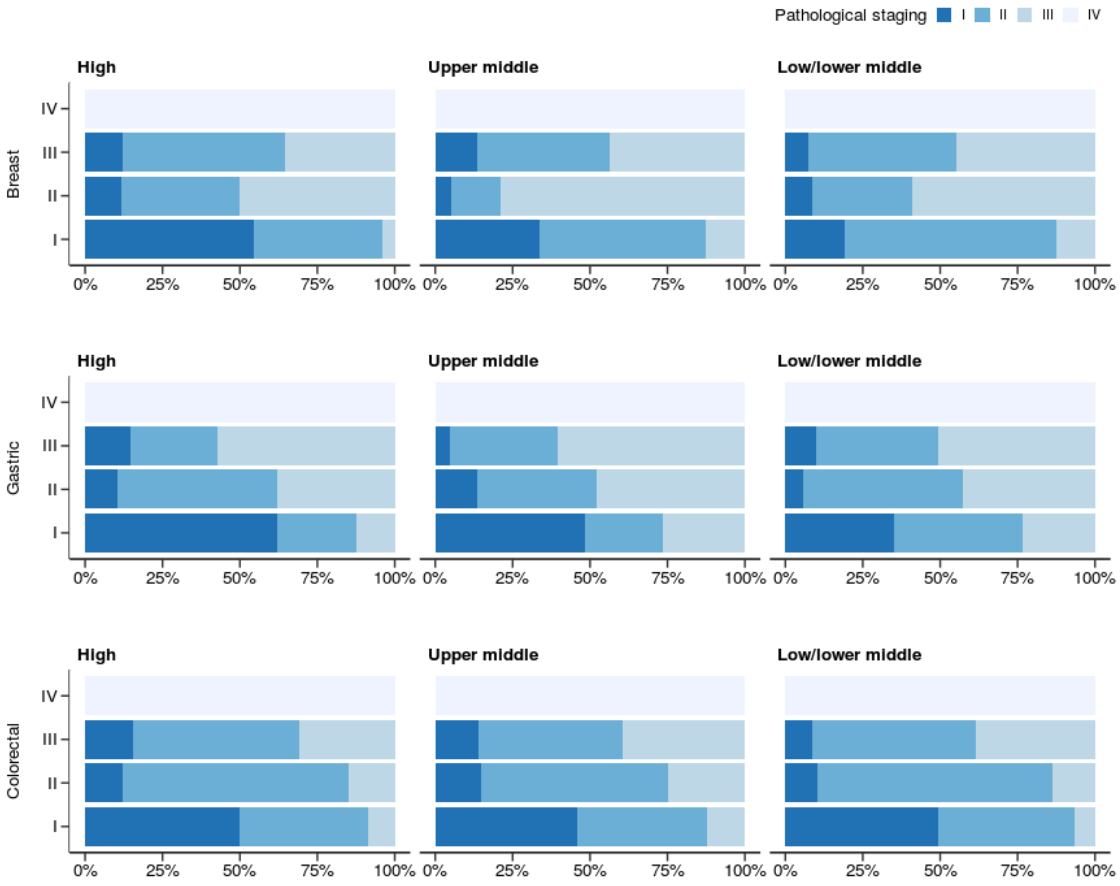
Breast cancer: Tis, No invasive cancer (e.g. DCIS); L1, Tumour ≤2 cm in size (T1); L2, Tumour >2 cm in size (T2/T3); A, Inflammatory cancer, chest wall invasion or ulceration present (T4); R1, 1 to 3 nodes involved inside axilla but none outside axilla (N1); R2, >3 nodes involved inside axilla or nodal involvement outside axilla (N2/N3); M+, Metastases present (M1).

Gastric cancer: L, Tumour contained within stomach wall with no nodal involvement (Stage I); A, Tumour through stomach wall with no nodal involvement (Stage II); R+, Regional lymph node involvement (Stage III); M+, Metastases present (Stage IV)

Colorectal cancer: L, Tumour contained within bowel wall with no nodal involvement (Stage I); A, Tumour through bowel wall with no nodal involvement (Stage II); R+, Regional lymph node involvement (Stage III); M+, Metastases present (Stage IV).

Figure 4-3. Comparison between preoperative clinical and postoperative final pathological staging.

Preoperative clinical staging performed using Essential TNM Classification of Malignant Tumours (eTNM), as defined by the Union for International Cancer Control (UICC). Material from [187].



4.3.7 Data validation

Validation was performed in 265 hospitals (high 156, upper middle 48, low/lower middle 61) across 69 countries, representing 1060 hospital-weeks of data collection. In primary data collection there were 3669 patients included across hospitals selected for validation. Validators identified 3805 cases that fulfilled inclusion criteria for the validation period, equating to a case ascertainment rate of 96.4% (3669/3805; Figure 4-8).

The validation cohort were representative of the primary data collected by 838 mini-teams (Figure 4-9). There was no difference in case ascertainment rates between World Bank country income groups (chi-squared statistic 1.04, df 2, P=0.595).

4.3.8 Data accuracy

Availability of sampled variables during the validation process is detailed in Table 4-7. Overall availability of variables for validation was good, however validators highlighted limited availability of reliable written notes. This pattern was reflected particularly in operation records. The ability of validators to identify outcome measures was lower across all countries (30-day major complication available, high 87.9%, upper middle 86.6%, low/lower middle 79.6% World Bank income group).

Accuracy was high for the validated continuous predictor (age; Pearson's correlation coefficient 0.99; Figure 4-10). There was good or very good agreement between validation and primary data for patient (sex, kappa coefficient 0.99), operative (urgency 0.77; intent 0.75) and cancer staging (pT stage 0.93; pN stage 0.67) variables (Table 4-8). Agreement for 30-day mortality (0.89) was also excellent, however, for 30-day major complication (0.63) the agreement was lower.

Figure 4-4. Patient follow-up and method of diagnosis.

Method of determination of 30-day follow-up variables (A). Basis for cancer diagnosis stratified by cancer type and country income group (B). Material from [187].

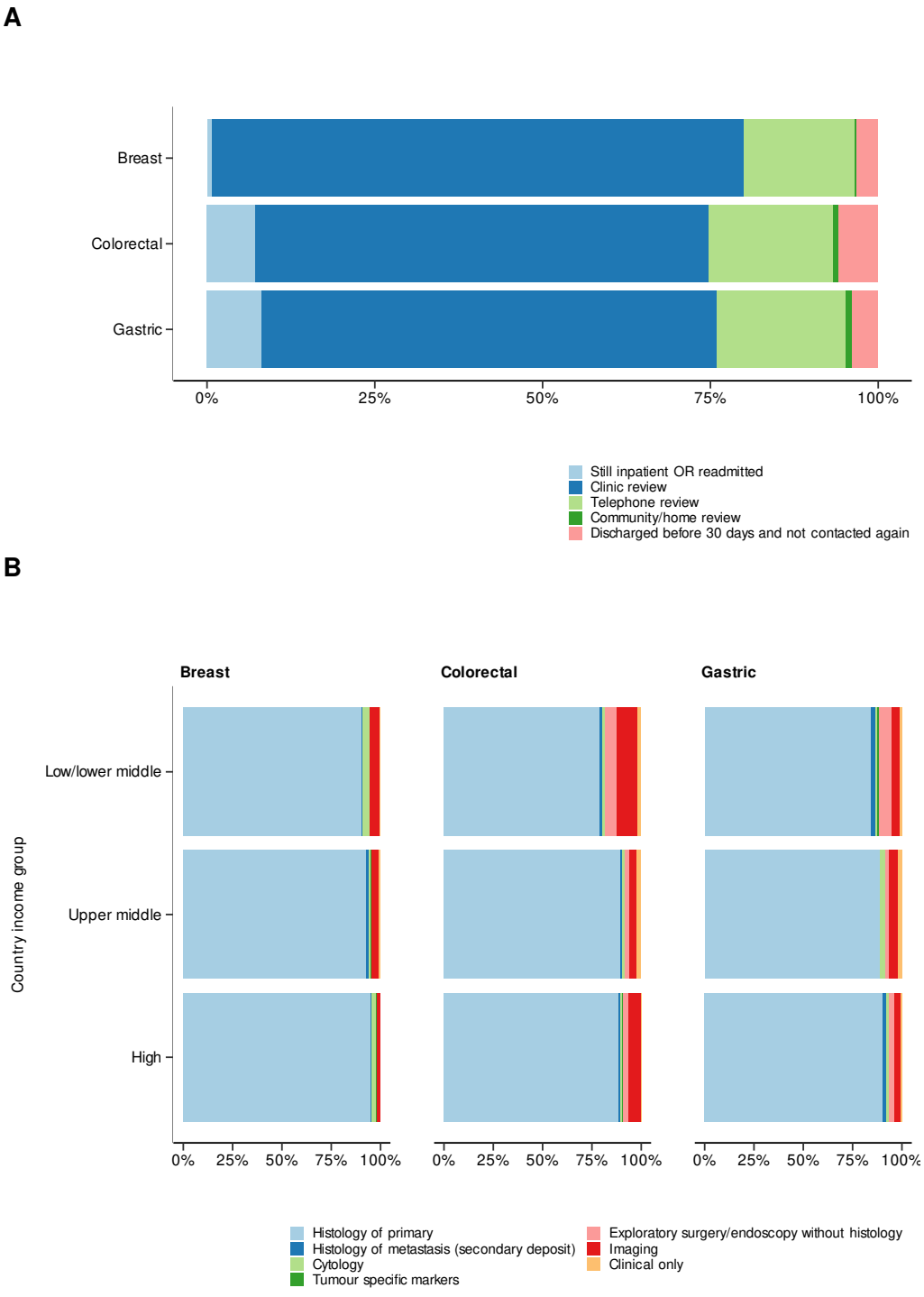


Figure 4-5. Proportion of all patients who sustained specific complications, stratified by cancer-type and country income group.

Ordered by overall frequency. CD, Clavien-Dindo complication grade; OSI, organ space infection. Material from [187].

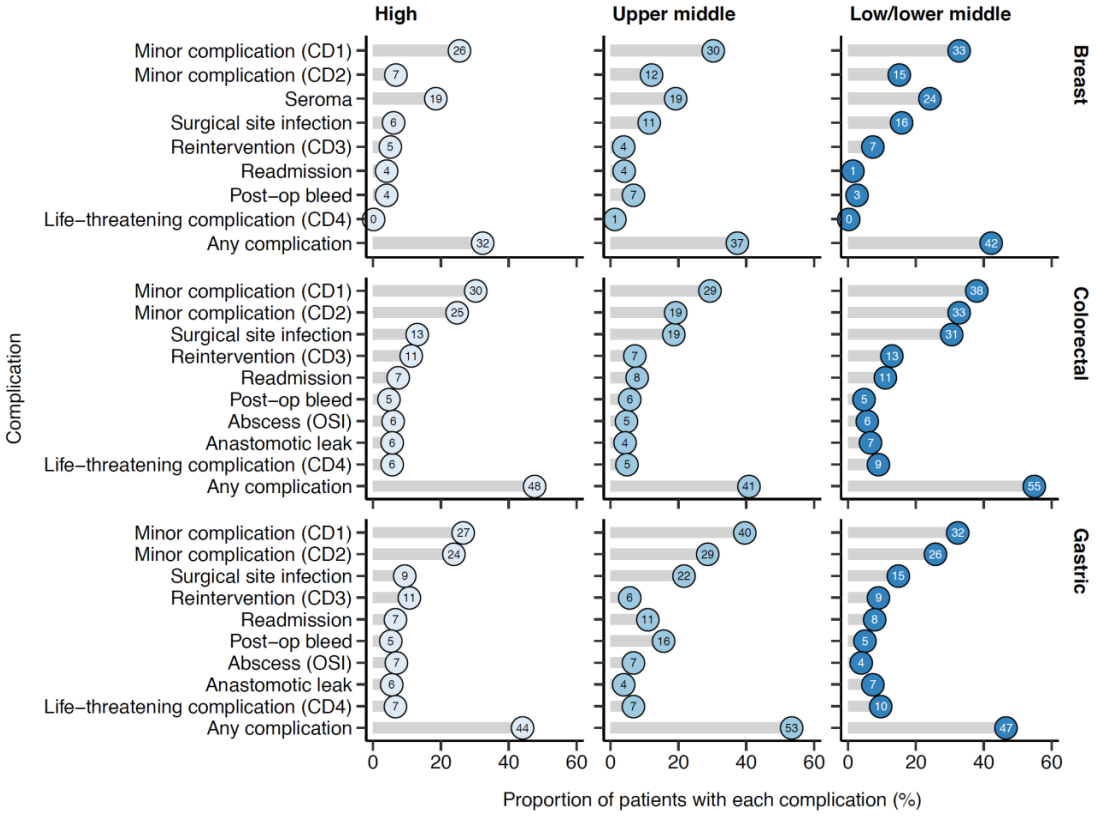


Figure 4-6. Hospital type and facilities for centres treating cancer, stratified by country income group.

MDT, multidisciplinary team. Material from [187].

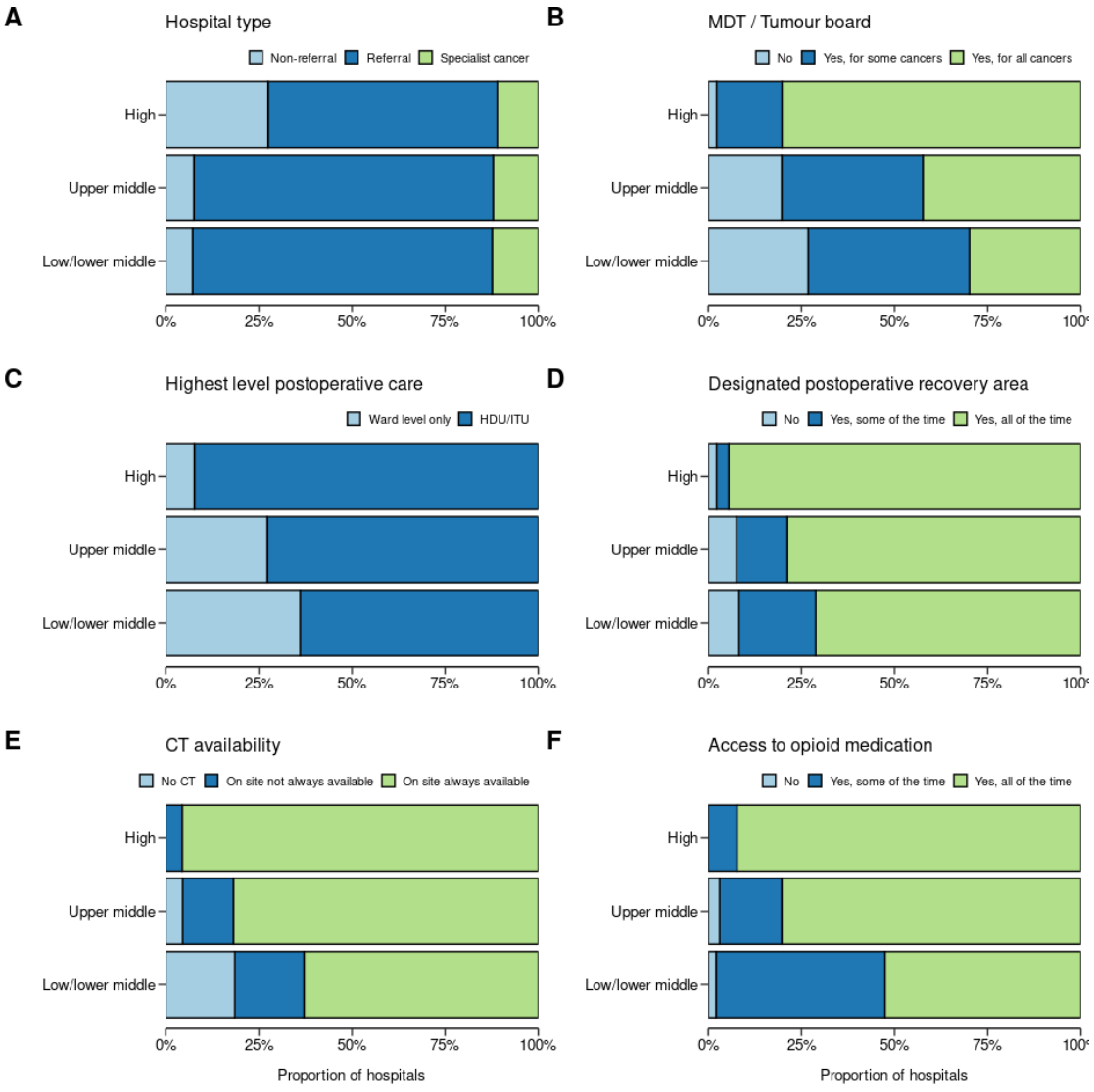


Table 4-5. Summary of hospital care services for centres treating cancer stratified by country income group.

WB income (tertile)		High	Upper middle	Low/lower middle	P
		N=241	N=81	N=106	
Hospital type	Non-referral hospital	25 (10.4)	5 (6.2)	7 (6.6)	0.001
	Referral hospital	56 (23.2)	53 (65.4)	78 (73.6)	
	Specialist cancer hospital	10 (4.1)	8 (9.9)	12 (11.3)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
Hospital catchment	< 50 000	5 (2.1)	12 (14.8)	22 (20.8)	<0.001
	50 000 - 199 999	32 (13.3)	14 (17.3)	7 (6.6)	
	200 000 - 499 999	30 (12.4)	3 (3.7)	8 (7.5)	
	500 000 - 999 999	13 (5.4)	11 (13.6)	12 (11.3)	
	1 000 000 - 1 999 999	6 (2.5)	11 (13.6)	14 (13.2)	
	Over 2 000 000	5 (2.1)	15 (18.5)	34 (32.1)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
MDT / Tumour board	None	2 (0.8)	13 (16.0)	26 (24.5)	<0.001
	Yes, for some cancers	16 (6.6)	25 (30.9)	42 (39.6)	
	Yes, for all cancers	73 (30.3)	28 (34.6)	29 (27.4)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
Oncologist	Not available	6 (2.5)	11 (13.6)	27 (25.5)	<0.001
	Available in hospital	85 (35.3)	46 (56.8)	63 (59.4)	
	(Not sampled)	150 (62.2)	24 (29.6)	16 (15.1)	
Palliative care specialist	Not available	23 (9.5)	35 (43.2)	59 (55.7)	<0.001
	Available in hospital	68 (28.2)	31 (38.3)	38 (35.8)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	

CT scan	No CT scan	0 (0.0)	3 (3.7)	18 (17.0)	<0.001
	On site, not always available	4 (1.7)	9 (11.1)	18 (17.0)	
	On site, always available	87 (36.1)	54 (66.7)	61 (57.5)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
Opioid medication	No	0 (0.0)	2 (2.5)	2 (1.9)	<0.001
	Yes, some of the time	7 (2.9)	11 (13.6)	44 (41.5)	
	Yes, all of the time	84 (34.9)	53 (65.4)	51 (48.1)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
Designated perioperative recovery area	No	2 (0.8)	5 (6.2)	8 (7.5)	0.001
	Yes, some of the time	3 (1.2)	9 (11.1)	20 (18.9)	
	Yes, all of the time	86 (35.7)	52 (64.2)	69 (65.1)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
Highest level of postoperative care	Ward level only	7 (2.9)	18 (22.2)	35 (33.0)	<0.001
	ICU/HDU	84 (34.9)	48 (59.3)	62 (58.5)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
Pathology services	Not available	0 (0.0)	1 (1.2)	3 (2.8)	0.191
	Available at another hospital	9 (3.7)	7 (8.6)	17 (16.0)	
	On site, not always available	16 (6.6)	6 (7.4)	10 (9.4)	
	On site, always available	66 (27.4)	52 (64.2)	67 (63.2)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
Radiotherapy	No radiotherapy available	1 (0.4)	3 (3.7)	18 (17.0)	0.001
	> 50 km from hospital	15 (6.2)	7 (8.6)	21 (19.8)	

	10 - 50 km from hospital	12 (5.0)	9 (11.1)	13 (12.3)	
	Within 10 km from hospital	21 (8.7)	16 (19.8)	11 (10.4)	
	Radiotherapy on site	42 (17.4)	31 (38.3)	34 (32.1)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
Chemotherapy	No chemotherapy available	0 (0.0)	2 (2.5)	3 (2.8)	0.001
	> 50 km from hospital	0 (0.0)	2 (2.5)	13 (12.3)	
	10 - 50 km from hospital	2 (0.8)	5 (6.2)	8 (7.5)	
	Within 10 km from hospital	13 (5.4)	9 (11.1)	7 (6.6)	
	Chemotherapy on site	76 (31.5)	48 (59.3)	66 (62.3)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
Perioperative care pathway	Absent	12 (5.0)	29 (35.8)	62 (58.5)	<0.001
	Present	79 (32.8)	37 (45.7)	35 (33.0)	
	(Not sampled)	150 (62.2)	15 (18.5)	9 (8.5)	
Cancer care pathway	Absent	49 (20.3)	35 (43.2)	63 (59.4)	0.219
	Present	42 (17.4)	28 (34.6)	33 (31.1)	
	(Not sampled)	150 (62.2)	18 (22.2)	10 (9.4)	

Table 4-6. Patient and operative characteristics by country income group stratified by cancer type, including missing data.

Numbers are n (%), unless otherwise indicated. ASA, American Society of Anesthesiologists operative risk grade. ECOG, Eastern Cooperative Oncology Group. High income included 31 countries and 241 hospitals. Upper middle income included 23 countries and 81 hospitals. Lower middle/low income included 28 countries and 106 hospitals. The total column therefore includes 82 countries and 428 hospitals.

		Breast High	Breast Upper middle	Breast Low/lower middle	Colorectal High	Colorectal Upper middle	Colorectal Low/lower middle	Gastric High	Gastric Upper middle	Gastric Low/lower middle
Total N		4220	1319	2867	4174	1113	928	712	289	336
Age (years)	Mean (SD)	61.0 (13.4)	53.4 (13.1)	50.7 (11.9)	68.6 (12.4)	62.4 (12.3)	54.5 (14.4)	67.4 (12.8)	62.5 (13.2)	55.4 (12.9)
Sex	Male	43 (1.0)	13 (1.0)	32 (1.1)	2394 (57.4)	596 (53.5)	485 (52.3)	427 (60.0)	182 (63.0)	206 (61.3)
	Female	4172 (98.9)	1306 (99.0)	2833 (98.8)	1774 (42.5)	515 (46.3)	443 (47.7)	285 (40.0)	107 (37.0)	130 (38.7)
	(Missing)	5 (0.1)	0 (0.0)	2 (0.1)	6 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ASA	I	767 (18.2)	462 (35.0)	937 (32.7)	319 (7.6)	219 (19.7)	238 (25.6)	62 (8.7)	58 (20.1)	110 (32.7)
	II	2383 (56.5)	726 (55.0)	1576 (55.0)	2042 (48.9)	612 (55.0)	506 (54.5)	344 (48.3)	136 (47.1)	160 (47.6)
	III	744 (17.6)	83 (6.3)	223 (7.8)	1545 (37.0)	227 (20.4)	141 (15.2)	269 (37.8)	81 (28.0)	48 (14.3)
	IV	28 (0.7)	11 (0.8)	10 (0.3)	166 (4.0)	23 (2.1)	18 (1.9)	23 (3.2)	8 (2.8)	8 (2.4)
	V	2 (0.0)	0 (0.0)	0 (0.0)	15 (0.4)	1 (0.1)	6 (0.6)	0 (0.0)	0 (0.0)	4 (1.2)
	(Missing)	296 (7.0)	37 (2.8)	121 (4.2)	87 (2.1)	31 (2.8)	19 (2.0)	14 (2.0)	6 (2.1)	6 (1.8)

BMI	Normal weight (BMI 18.5 to 24.9)	1443 (34.2)	462 (35.0)	887 (30.9)	1510 (36.2)	521 (46.8)	456 (49.1)	314 (44.1)	165 (57.1)	168 (50.0)
	Underweight (BMI < 18.5)	74 (1.8)	23 (1.7)	62 (2.2)	119 (2.9)	63 (5.7)	111 (12.0)	38 (5.3)	25 (8.7)	61 (18.2)
	Overweight (BMI 25 to 30)	1341 (31.8)	458 (34.7)	1077 (37.6)	1517 (36.3)	348 (31.3)	206 (22.2)	221 (31.0)	76 (26.3)	71 (21.1)
	Obese (BMI >30)	928 (22.0)	308 (23.4)	736 (25.7)	749 (17.9)	145 (13.0)	115 (12.4)	96 (13.5)	17 (5.9)	16 (4.8)
	(Missing)	434 (10.3)	68 (5.2)	105 (3.7)	279 (6.7)	36 (3.2)	40 (4.3)	43 (6.0)	6 (2.1)	20 (6.0)
>10% weight loss	No	3321 (78.7)	1091 (82.7)	2468 (86.1)	2817 (67.5)	606 (54.4)	337 (36.3)	422 (59.3)	116 (40.1)	91 (27.1)
	Yes	98 (2.3)	84 (6.4)	187 (6.5)	732 (17.5)	427 (38.4)	514 (55.4)	219 (30.8)	162 (56.1)	216 (64.3)
	(Missing)	801 (19.0)	144 (10.9)	212 (7.4)	625 (15.0)	80 (7.2)	77 (8.3)	71 (10.0)	11 (3.8)	29 (8.6)
ECOG performance status	0	2688 (63.7)	984 (74.6)	1657 (57.8)	2056 (49.3)	583 (52.4)	379 (40.8)	346 (48.6)	165 (57.1)	100 (29.8)
	1	838 (19.9)	242 (18.3)	621 (21.7)	1116 (26.7)	319 (28.7)	318 (34.3)	198 (27.8)	78 (27.0)	146 (43.5)
	2	311 (7.4)	48 (3.6)	400 (14.0)	557 (13.3)	125 (11.2)	117 (12.6)	93 (13.1)	28 (9.7)	53 (15.8)
	3	73 (1.7)	17 (1.3)	68 (2.4)	188 (4.5)	63 (5.7)	81 (8.7)	38 (5.3)	14 (4.8)	27 (8.0)
	4	6 (0.1)	1 (0.1)	14 (0.5)	22 (0.5)	6 (0.5)	12 (1.3)	4 (0.6)	2 (0.7)	5 (1.5)
	(Missing)	304 (7.2)	27 (2.0)	107 (3.7)	235 (5.6)	17 (1.5)	21 (2.3)	33 (4.6)	2 (0.7)	5 (1.5)
Smoking	No, never	2800 (66.4)	1056 (80.1)	2728 (95.2)	2236 (53.6)	688 (61.8)	684 (73.7)	327 (45.9)	158 (54.7)	219 (65.2)
	Stopped >6 weeks ago	517 (12.3)	86 (6.5)	34 (1.2)	965 (23.1)	170 (15.3)	103 (11.1)	168 (23.6)	66 (22.8)	44 (13.1)
	Yes, current smoker	562 (13.3)	133 (10.1)	27 (0.9)	496 (11.9)	173 (15.5)	100 (10.8)	116 (16.3)	41 (14.2)	43 (12.8)

	(Missing)	341 (8.1)	44 (3.3)	78 (2.7)	477 (11.4)	82 (7.4)	41 (4.4)	101 (14.2)	24 (8.3)	30 (8.9)
Diabetes	No	3696 (87.6)	1074 (81.4)	2107 (73.5)	3311 (79.3)	859 (77.2)	720 (77.6)	587 (82.4)	246 (85.1)	273 (81.2)
	Diet	71 (1.7)	16 (1.2)	27 (0.9)	125 (3.0)	20 (1.8)	14 (1.5)	13 (1.8)	6 (2.1)	4 (1.2)
	Medication (non-insulin)	307 (7.3)	139 (10.5)	312 (10.9)	510 (12.2)	161 (14.5)	84 (9.1)	78 (11.0)	24 (8.3)	26 (7.7)
	Insulin	92 (2.2)	55 (4.2)	136 (4.7)	160 (3.8)	52 (4.7)	43 (4.6)	27 (3.8)	13 (4.5)	12 (3.6)
	(Missing)	54 (1.3)	35 (2.7)	285 (9.9)	68 (1.6)	21 (1.9)	67 (7.2)	7 (1.0)	0 (0.0)	21 (6.2)
Distance to home (km)	< 10 km	1637 (38.8)	340 (25.8)	352 (12.3)	1630 (39.1)	270 (24.3)	179 (19.3)	230 (32.3)	67 (23.2)	44 (13.1)
	10-20 km	859 (20.4)	272 (20.6)	460 (16.0)	814 (19.5)	266 (23.9)	170 (18.3)	125 (17.6)	79 (27.3)	43 (12.8)
	20-50 km	809 (19.2)	241 (18.3)	511 (17.8)	791 (19.0)	206 (18.5)	200 (21.6)	156 (21.9)	32 (11.1)	57 (17.0)
	50-100 km	346 (8.2)	78 (5.9)	385 (13.4)	324 (7.8)	89 (8.0)	97 (10.5)	68 (9.6)	28 (9.7)	32 (9.5)
	>100 km	219 (5.2)	199 (15.1)	1039 (36.2)	279 (6.7)	176 (15.8)	235 (25.3)	78 (11.0)	64 (22.1)	135 (40.2)
	(Missing)	350 (8.3)	189 (14.3)	120 (4.2)	336 (8.0)	106 (9.5)	47 (5.1)	55 (7.7)	19 (6.6)	25 (7.4)

Figure 4-7. Map of missing values.

Missing values for main explanatory and dependent variables by observation. Material from [187].

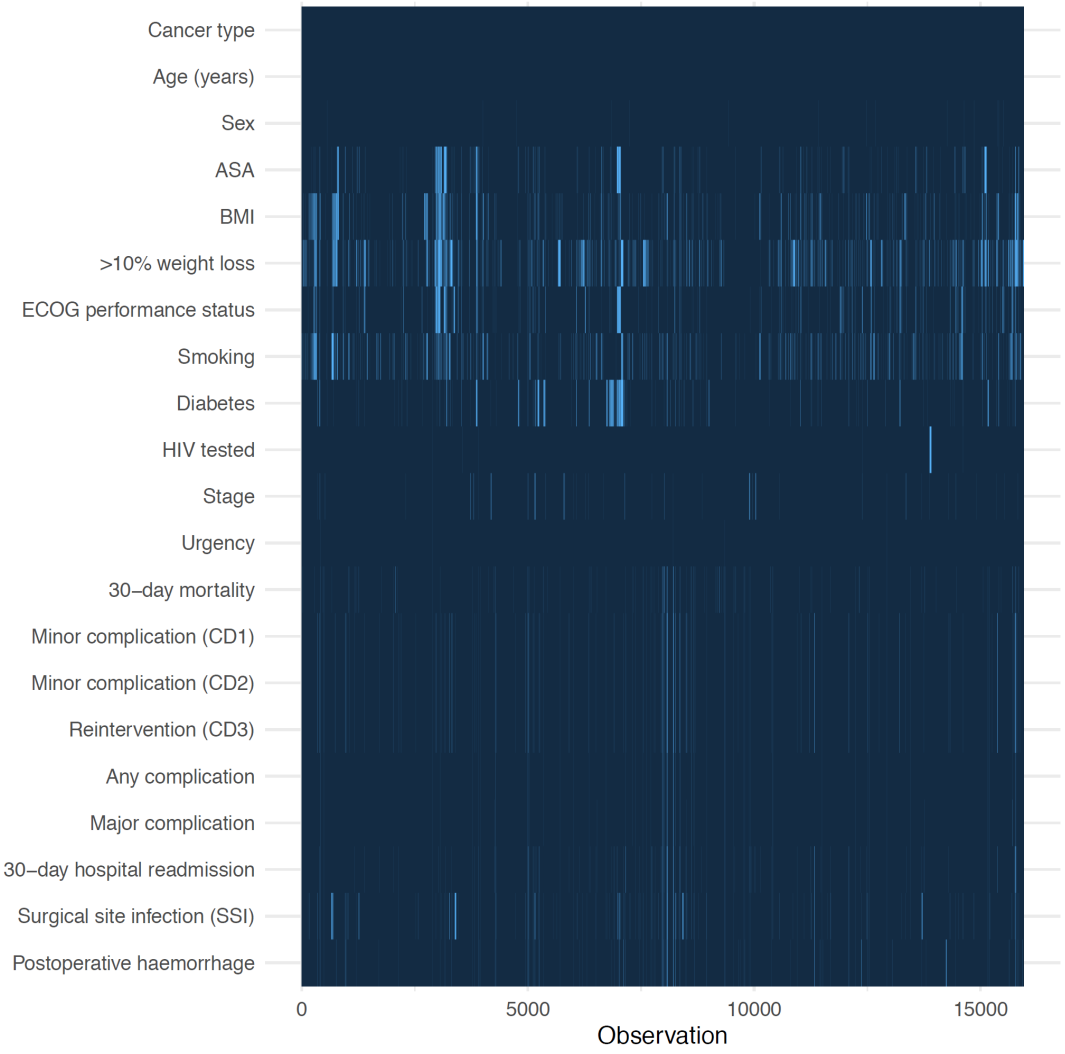


Figure 4-8. Case ascertainment.

Correlation of number of patients fulfilling inclusion criteria identified by validators against those included in primary data collection. Dotted lines represent 50% and 95% concordance. Material from [187].

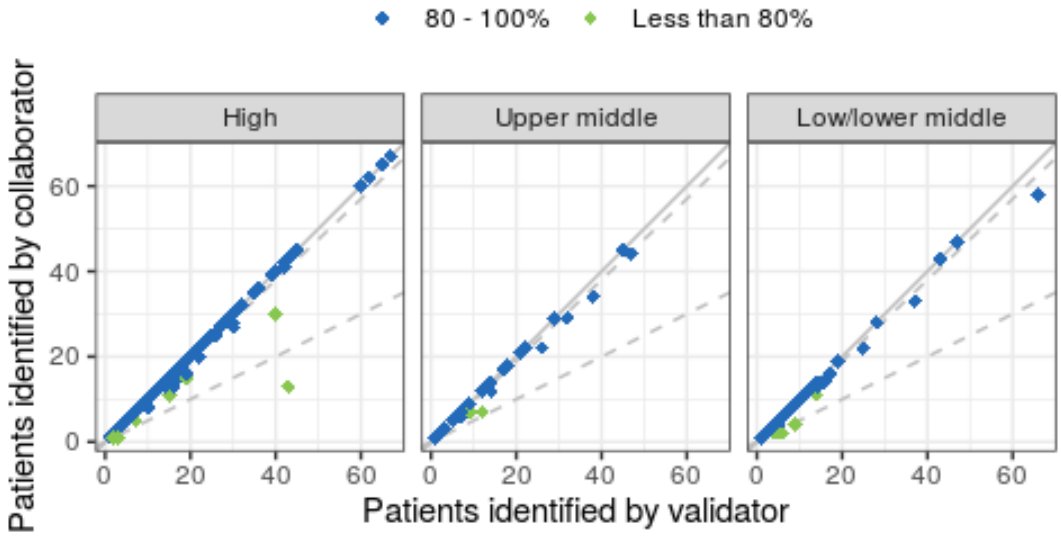


Figure 4-9. Distribution of patients enrolled per hospital stratified by validation.

Material from [187].

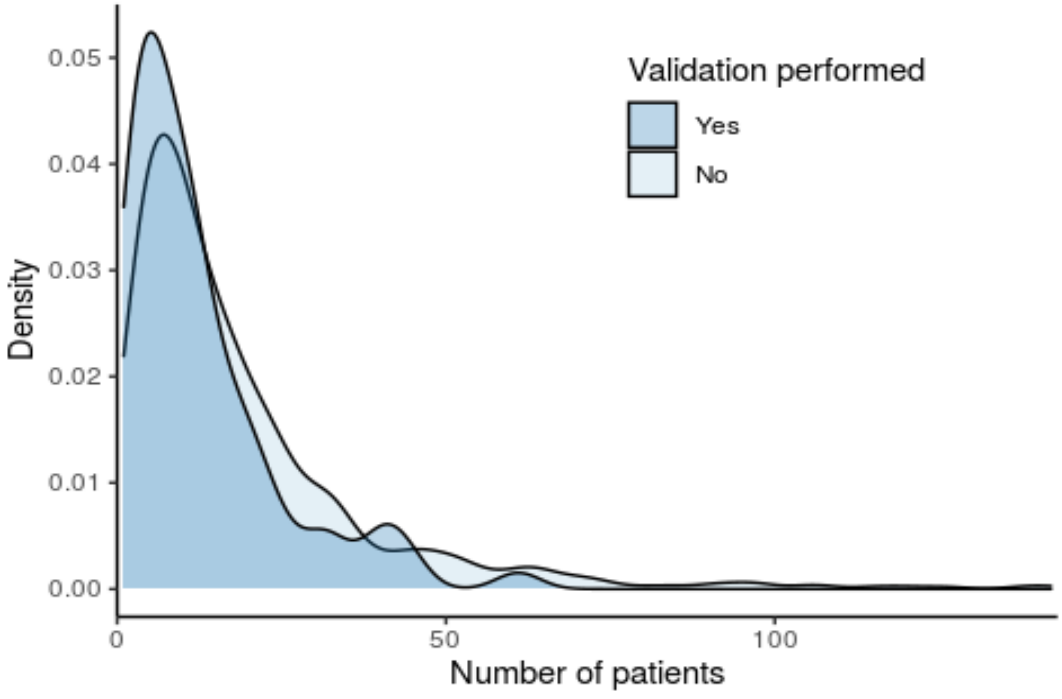


Table 4-7. Availability of sampled variables to validators by country income group.

		World Bank income group			
		High N=3168	Upper middle N=694	Low/lower middle N=658	P*
Pathological staging available	No	128 (5.0)	13 (2.4)	79 (14.0)	<0.001
	Yes	2441 (95.0)	523 (97.6)	485 (86.0)	
Urgency available	No	32 (1.2)	5 (0.9)	7 (1.2)	0.854
	Yes	2537 (98.8)	531 (99.1)	557 (98.8)	
Operative intent	No	175 (6.8)	5 (0.9)	52 (9.2)	<0.001
	Yes	2393 (93.2)	531 (99.1)	512 (90.8)	
30-day major complication available	No	312 (12.1)	72 (13.4)	115 (20.4)	<0.001
	Yes	2256 (87.9)	464 (86.6)	448 (79.6)	
30-day mortality available	No	158 (6.2)	19 (3.5)	79 (14.0)	<0.001
	Yes	2410 (93.8)	517 (96.5)	485 (86.0)	

*Chi-squared or Fisher's exact test where expected cell count <5. Data are n (%).

Figure 4-10. Correlation of patient age in validation compared to primary datasets.

Number of patients included: 4520. Material from [187].

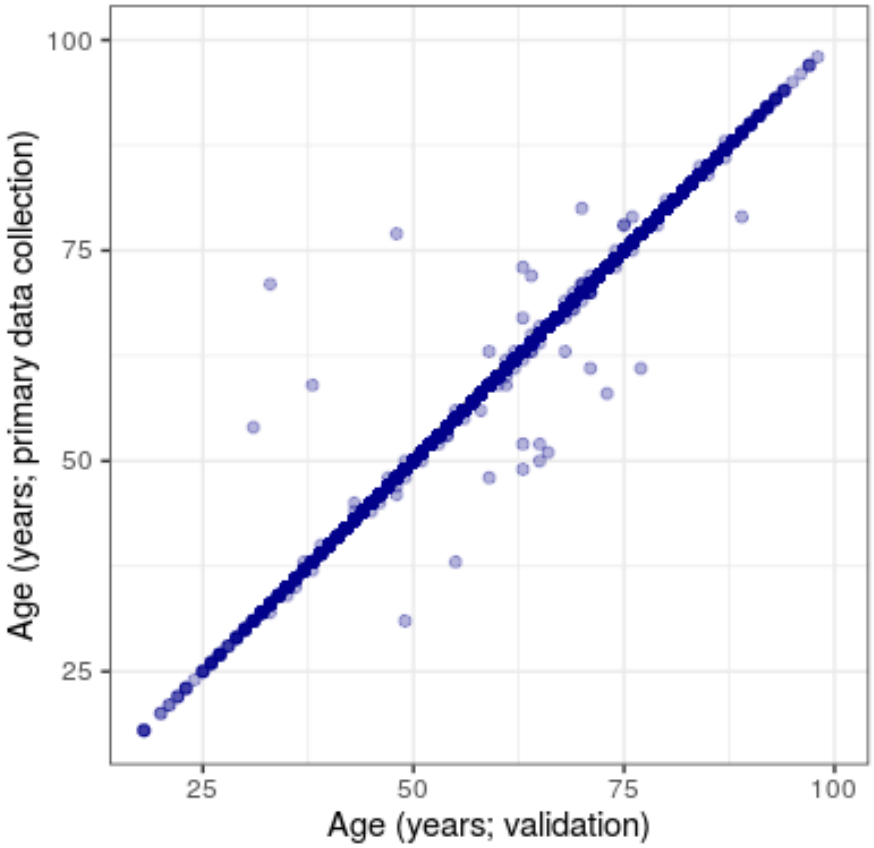


Table 4-8. Validation study for categorical variables.

Data are counts.

	Primary data	Validation data				Kappa
Sex		Female			Male	0.99
	Female	3169			1	
	Male	6			1340	
Pathological T stage		T0	T1	T2	T3	T4	0.93
	T0	140	23	6	4	1	
	T1	11	722	29	12	4	
	T2	9	41	720	34	6	
	T3	4	12	20	818	11	
	T4	2	3	5	20	380	
Pathological N stage		N0	N1	N2	N3		0.67
	N0	1350	135	56	16		
	N1	181	491	71	17		
	N2	73	69	247	38		
	N3	3	4	3	34		
Urgency		Elective			Emergency	0.77
	Elective	3270			71	
	Emergency	55			229	
Intent		Curative			Palliative	0.75
	Curative	3066			77	
	Palliative	61			231	
30-day major complication		No			Yes	0.63
	No	2696			123	
	Yes	96			226	
30-day mortality		Alive			Died	0.89
	Alive	3321			9	
	Died	4			55	

4.4 Discussion

4.4.1 Summary of key findings in context of previous literature

For the first time, I provide comprehensive data across income settings for patients undergoing surgery for three globally common cancers. In this prospective, international cohort of 15 958 patients in 82 countries undergoing surgery for breast, colorectal, or gastric cancer, I demonstrate that patients in low-resource settings were younger and had fewer comorbidities, but presented with more advanced disease. Furthermore, these patients were more likely to be treated in hospitals with fewer postoperative care facilities and more limited cancer care pathways.

Patients commonly presented to a healthcare professional in the community or hospital out-patient setting, which is different to that described in previously[191]. Often patients turn to informal care providers due to accessibility and trust[192], increasing the delay in seeking appropriate healthcare. My patient population is likely to represent those who have the means to seek and afford cancer care, and therefore further conclusions are limited. However, patients were more likely to present with advanced disease in LMICs, potentially reflecting additional delays in presentation secondary to patient knowledge, care availability, and/or public health policy[12,193].

With at least five billion people worldwide not having access to safe surgical care[12], it is perhaps not surprising I demonstrate hospital facilities are limited in LMICs. The hospital facility and resource deficits are well described in low-resource settings for basic surgical care[194–196], yet accurate estimates for the provision of cancer care are currently limited[52]. The scaling up of high-quality surgical systems for cancer requires high-quality data to assess the current state of care, prioritise improvements and

evaluate their effects[52]. I further describe and explore the impact of hospital infrastructure on early outcomes following cancer surgery in Chapters 5 and 6.

Standard TNM classifications of malignant tumours were first described in 1943[197], with accurate information on the extent of disease at diagnosis important for patient prognostication, treatment planning, and evaluation of cancer control policies[197]. Despite its importance, the availability and standardisation of cancer staging is currently limited[198], making contemporary international comparisons and benchmarking studies difficult[199]. Recently a simplified scheme, the Essential TNM classification system (eTNM)[200], has been introduced to enable the accurate recording of disease stage at diagnosis.

However, the global application of the eTNM staging system has yet to be performed[197]. I demonstrate that clinical application in low-resourced environments is possible, with preoperative disease staging correlating with histological diagnosis across all income settings after minimal collaborator training. As a result, the eTNM classification system is likely to represent a key cornerstone in enabling population-based cancer registries to develop and evaluate cancer control through public health policies, together with facilitating global comparisons.

4.4.2 Study strengths

I used standardised, validated, prospective methodology to gather global, contemporaneous, and comprehensive data. This study represents the largest known prospectively collected dataset of patients undergoing surgery for globally prevalent cancers. The use of a prespecified protocol using standardised variable definitions, developed with LMIC surgical experts, allows for meaningful comparisons of early surgical outcomes and quality of cancer care across income settings. In particular,

mandatory collaborator training and real-time data quality control delivered high-quality data collection.

Few large scale cohort studies have previously performed independent validation following primary data collection, with significant variation in patient number, countries and hospitals sampled[27,201–203]. The validation of over 20% patients in the primary dataset and case ascertainment above 95% compares favourably to similar studies.

4.4.3 Study limitations

A limitation of this study was that only patients undergoing primary surgery for breast, colorectal, or gastric cancers were included, and therefore patient characteristics, modes of presentation, and treatment for those receiving conservative or oncological therapy were not examined. The denominator in this study is therefore patients undergoing surgery, rather than a population-level measure of prevalence.

Data were limited to those routinely collected during patient care and prioritised by LMIC surgical experts during protocol development. For example, out-of-pocket payment for surgical cancer care is a major cause of catastrophic expenditure[56] and its collection would have helped to answer key questions relating to the financing of surgical systems for cancer[52]. However, pragmatic decisions were required to ensure data collection provided a limited burden to collaborators within already stretched low-resource clinical environments. Despite such decisions, over 100 variables were collected for nearly 16 000 patients with low missingness and high reliability.

There are many cancers of critical importance in global health, with certain cancers having higher prevalence than breast, colorectal, or gastric cancer[54]. Included cancers were prioritised due to their high global prevalence and relevance to the majority of the

GlobalSurg collaborators. Therefore, to maximise case ascertainment, ensure data quality, and enable engagement across a global network, a pragmatic decision was taken not to collect data on additional cancer types. Despite certain aspects being generalisable across surgical systems for cancer care, further high-quality observational data is still required for other cancers. This methodology has been made publicly available and I hope it can be utilised to capture detailed oncological outcome data for additional, globally prevalent cancers.

Lastly, hospital-level data were not validated. Despite demonstrating high case ascertainment, data reliability and accuracy for patient-level data, only assumptions can be made relating to the hospital-level component of this study. However, the use of standardised definitions, data extraction sheets, beta testing within LMIC hospital sites prior to formal release and completion by existing collaborators is likely to have maximised data reliability.

4.4.4 Conclusion

In summary, I describe the patient and hospital characteristics for patients undergoing surgery for breast, colorectal, or gastric cancer. Data were collected to a high level of case ascertainment, accuracy and reliability. Further Chapters (5, 6 and 7) will explore the variation in patient outcomes and the factors which influence these across income settings.

4.6 Outputs relating to this chapter

This study is published in *The Lancet:*

NIHR Global Health Research Unit on Global Surgery [**Knight SR** first author in writing group] (2021). Global variation in postoperative mortality and complications

after cancer surgery: a multicentre, prospective cohort study in 82 countries. **Lancet.** 397; 387–97.

https://doi.org/10.1016/S0140-6736(21)00001-5

I presented this work as an oral presentation at the American College of Surgeons Conference, Washington in July 2019.

Chapter 5 Global variation in postoperative mortality and complications after cancer surgery

5.1 Introduction

Irrespective of the development status of a country, surgery remains one of the cornerstones of cancer treatment. Solid tumours are often untreated in LMICs and this carries significant macroeconomic consequences, with cumulative GDP losses estimated to be as high as 1.2% between 2016 and 2030[204]. However, operations for cancer are often highly invasive, with the potential for patients to experience substantial postoperative morbidity.

Previous work identified significant global disparities in surgical outcomes, with patients in LMICs two to three times more likely to sustain a major complication or die[27,161]. These consequences are devasting for patients and their families, and in the context of cancer treatment, complications can lead to long-term morbidity, increased treatment costs, and delays in adjuvant treatment. Rescuing patients who sustain a major complication from death has become an important focus of quality improvement in surgery[205]. Not only must complications be minimised, but the timely recognition and management of complications is essential if avoidable mortality is to be minimised. Little is known about factors contributing to early death and complication after cancer surgery in LMICs.

To address these issues, I conducted an international, multicentre, prospective cohort study which aimed to determine the variation in mortality and complication rates for breast, colorectal, or gastric cancers in low-income, middle-income, and high-income country settings.

5.2 Methods

5.2.1 Study design and participants

The study methods and patient cohort are described in detail within Chapter 3 and Chapter 4, respectively. Briefly, 15 958 consecutive patients underwent a primary procedure for breast, colorectal, or gastric cancer across 82 countries between 1st April 2018 and 31st January 2019. Case ascertainment and data accuracy were found to be high[187].

5.2.2 Primary outcomes

The primary outcome measures were 30-day mortality and 30-day major complication, as defined by Clavien-Dindo grade III, IV or V[178]. Death was included in the definition of major complication and therefore was not a competing risk. *Capacity to rescue* was defined as the absolute risk difference of death in patients sustaining a complication of surgery.

5.2.3 Statistical analysis

Multilevel logistic regression models were constructed to account for case mix, with population stratification by hospital and country of residence incorporated as random intercepts with constrained gradients. Further analyses were then performed exploring the relationship between primary outcome measures, patient factors, and hospital care facilities. The variance explained at each level of multilevel models was determined[179], with variance explained by each component (marginal pseudo-R^2) expressed as a proportion of the conditional pseudo-R^2.

Mediation analysis was performed by three-way decomposition of total effects into direct, indirect, and interactive effects[180], with uncertainty determined using bootstrap

resampling (5000 draws) and confidence intervals constructed using percentiles. Further detail on all statistical analyses for this study can be found in Chapter 3. Additional data and analyses which support this Chapter are contained within Appendix 10.3.

5.3 Results

5.3.1 Mortality, complications, and stage of presentation

Overall, 8406 (52.7%) patients underwent surgery for breast cancer, 6215 (38.9%) for colorectal cancer, and 1337 (8.4%) for gastric cancer (Figure 5-1). The distribution of cancer type, unadjusted mortality, and complication rates across country income group are shown in Figure 5-1.

The proportion of patients with later stage disease being operated upon was greater in upper middle-income and low/lower middle-income countries for all three cancer groups (Figure 5-2). There was a strong positive correlation between cancer stage and performance status for gastric cancer patients, and a weaker relationship in breast and colorectal cancer patients (Table 5-1 to 5-3). No strong relationship between operative risk (ASA grade) and cancer stage was seen.

Adjusted 30-day mortality was higher for gastric cancer in the low/lower middle-income group (33/336, 9.8%) and for colorectal cancer in upper middle-income (47/1113, 4.2%) and low/lower middle-income (63/928, 6.8%) groups, compared to the high-income group (gastric: 27/712, 3.8%; colorectal 94/4172, 2.3%) (Figure 5-2). However, the proportion of patients with a major complication or any complication was similar across all income groups.

Figure 5-1. Patients and outcomes by cancer-type and country income group.

Crude outcome rates are shown for 30-day mortality, 30-day major complication (Clavien Dindo ≥III) and 30-day any complication. Material from [187].

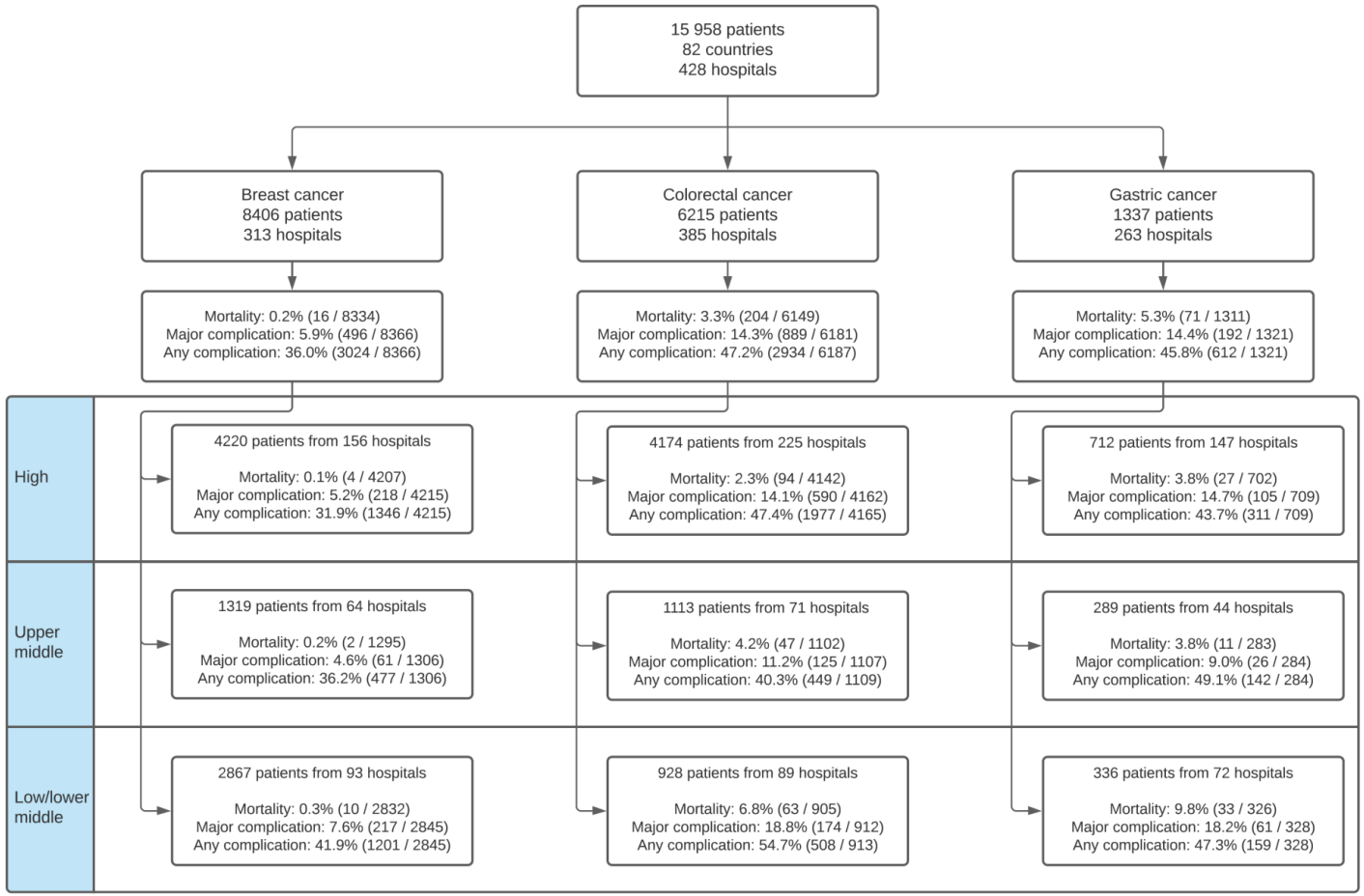


Figure 5-2. Stage of presentation, 30-day mortality, and 30-day complications by cancer and country income group.

Proportion of patients enrolled by cancer stage by country income group (A). Proportion of patients dying or sustaining a major complication or any complication by day 30 after surgery stratified by country income group (B). Proportion of patients sustaining a major complication who died within 30 days (C). Material from [187].

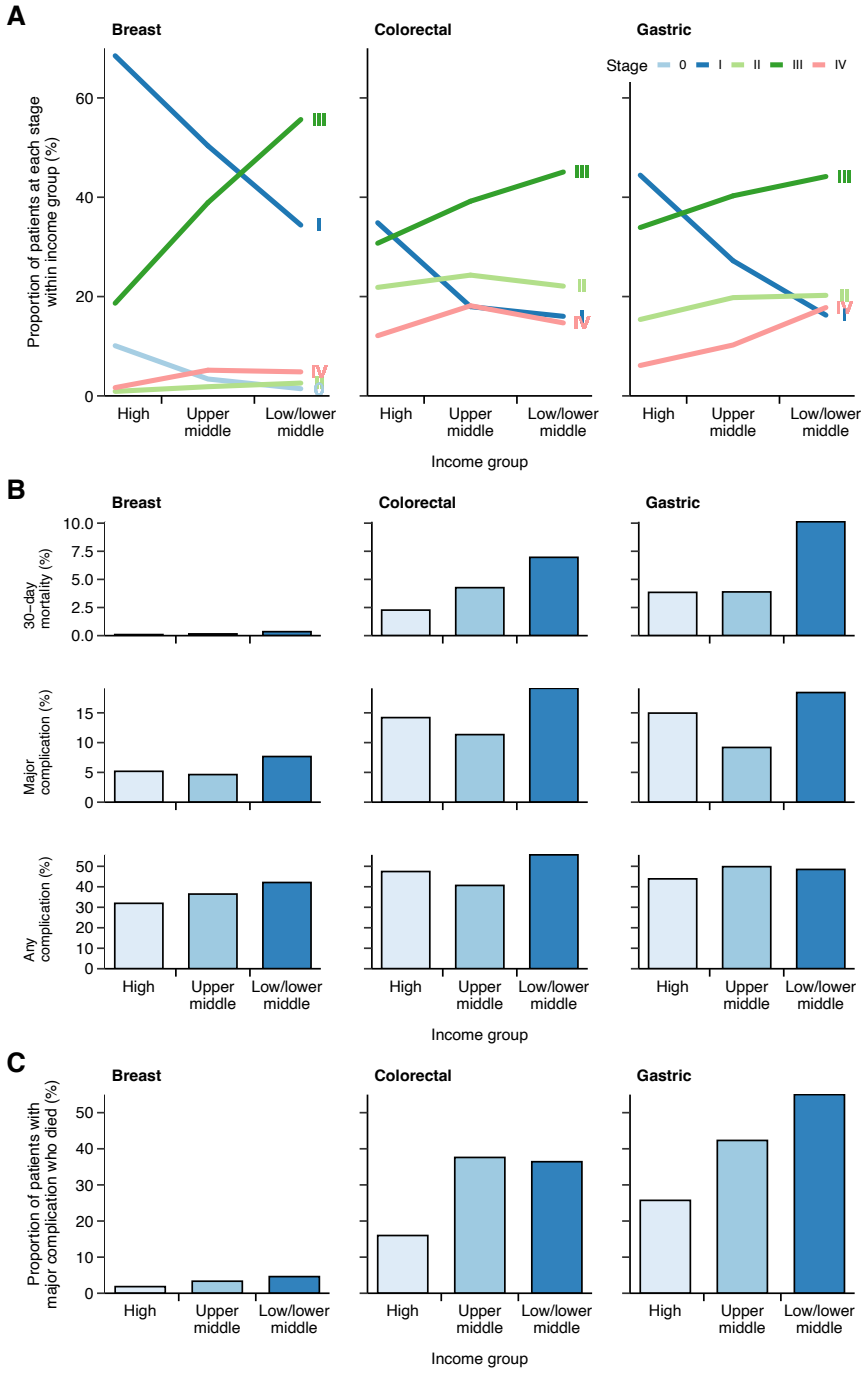


Table 5-1. Cancer stage by other predictors (breast).

Essential TNM Classification of Malignant Tumours (eTNM), as defined by the Union for International Cancer Control (UICC), for breast cancer:

Tis, No invasive cancer (e.g. DCIS); L1, Tumour ≤2 cm in size (T1); L2, Tumour >2 cm in size (T2/T3); A, Inflammatory cancer, chest wall invasion or ulceration present (T4); R1, 1 to 3 nodes involved inside axilla but none outside axilla (N1); R2, >3 nodes involved inside axilla or nodal involvement outside axilla (N2/N3); M+, Metastases present (M1). ASA, American Society of Anesthesiologists operative risk grade; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; HIV, human immunodeficiency virus; SNLB, sentinel lymph node biopsy; SD, standard deviation. Data are n (%).

		Tis N=514	L1/L2 N=4534	A N=137	R1/R2 N=2890	M+ N=281	P
Age (years)	Mean (SD)	56.9 (12.9)	58.4 (13.8)	57.3 (16.9)	53.0 (13.1)	53.9 (13.3)	<0.001
Sex	Male	3 (0.6)	40 (0.9)	5 (3.6)	37 (1.3)	3 (1.1)	0.013
	Female	510 (99.4)	4491 (99.1)	132 (96.4)	2850 (98.7)	278 (98.9)	
ASA	I	122 (26.2)	1108 (25.9)	31 (23.7)	816 (29.6)	69 (25.7)	<0.001
	II	273 (58.7)	2553 (59.6)	69 (52.7)	1625 (59.0)	142 (52.8)	
	III	66 (14.2)	599 (14.0)	30 (22.9)	303 (11.0)	48 (17.8)	
	IV	2 (0.4)	23 (0.5)	1 (0.8)	12 (0.4)	10 (3.7)	
	V	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
BMI	Normal weight (BMI 18.5 to 24.9)	172 (37.2)	1537 (36.9)	45 (34.4)	933 (34.2)	92 (34.3)	0.122
	Underweight (BMI < 18.5)	5 (1.1)	90 (2.2)	2 (1.5)	54 (2.0)	7 (2.6)	
	Overweight (BMI 25 to 30)	153 (33.1)	1529 (36.7)	45 (34.4)	1040 (38.1)	90 (33.6)	
	Obese (BMI >30)	132 (28.6)	1010 (24.2)	39 (29.8)	705 (25.8)	79 (29.5)	

>10% weight loss	No	397 (98.5)	3730 (96.5)	109 (90.8)	2388 (93.0)	216 (87.1)	<0.001
	Yes	6 (1.5)	136 (3.5)	11 (9.2)	179 (7.0)	32 (12.9)	
ECOG performance status	0	359 (76.9)	2903 (67.8)	72 (55.4)	1823 (65.8)	142 (52.0)	<0.001
	1	78 (16.7)	928 (21.7)	35 (26.9)	573 (20.7)	76 (27.8)	
	2	25 (5.4)	361 (8.4)	19 (14.6)	319 (11.5)	34 (12.5)	
	3	3 (0.6)	78 (1.8)	4 (3.1)	52 (1.9)	19 (7.0)	
	4	2 (0.4)	12 (0.3)	0 (0.0)	5 (0.2)	2 (0.7)	
Smoking	No, never	354 (76.5)	3373 (78.9)	115 (90.6)	2459 (88.8)	239 (90.9)	<0.001
	Stopped >6 weeks ago	53 (11.4)	420 (9.8)	9 (7.1)	143 (5.2)	9 (3.4)	
	Yes, current smoker	56 (12.1)	481 (11.3)	3 (2.4)	167 (6.0)	15 (5.7)	
Diabetes	No	444 (88.3)	3783 (86.5)	98 (81.0)	2286 (84.1)	228 (84.1)	0.004
	Diet	10 (2.0)	64 (1.5)	4 (3.3)	30 (1.1)	6 (2.2)	
	Medication (non-insulin)	39 (7.8)	392 (9.0)	12 (9.9)	285 (10.5)	24 (8.9)	
	Insulin	10 (2.0)	134 (3.1)	7 (5.8)	117 (4.3)	13 (4.8)	
HIV tested	No	456 (89.4)	3572 (79.3)	92 (67.2)	1809 (62.7)	170 (60.7)	<0.001
	Yes - Negative	52 (10.2)	927 (20.6)	45 (32.8)	1054 (36.6)	110 (39.3)	
	Yes - Positive	2 (0.4)	7 (0.2)	0 (0.0)	20 (0.7)	0 (0.0)	
Distance to home (km)	< 10 km	172 (36.8)	1415 (34.1)	33 (25.8)	617 (22.9)	76 (29.5)	<0.001
	10-20 km	120 (25.6)	909 (21.9)	16 (12.5)	489 (18.1)	52 (20.2)	
	20-50 km	96 (20.5)	840 (20.2)	31 (24.2)	532 (19.7)	59 (22.9)	

	50-100 km	41	415	20	306	22	
		(8.8)	(10.0)	(15.6)	(11.4)	(8.5)	
	>100 km	39	574	28	751	49	
		(8.3)	(13.8)	(21.9)	(27.9)	(19.0)	
Mode of diagnosis	Symptomatic	174	2547	120	2302	220	<0.001
		(34.7)	(56.9)	(89.6)	(80.3)	(78.9)	
	Screening	299	1519	6 (4.5)	267	25	
		(59.7)	(33.9)		(9.3)	(9.0)	
	Detected incidentally	28	410	8 (6.0)	296	34	
		(5.6)	(9.2)		(10.3)	(12.2)	
Urgency	Elective	511	4515	133	2872	273	<0.001
		(99.4)	(99.6)	(97.1)	(99.4)	(97.5)	
	Emergency	3 (0.6)	19 (0.4)	4 (2.9)	18 (0.6)	7 (2.5)	
Treatment intent	Palliative	5 (1.0)	50 (1.1)	10	81 (2.8)	98	<0.001
				(7.3)		(35.0)	
	Curative	509	4483	127	2809	182	
		(99.0)	(98.9)	(92.7)	(97.2)	(65.0)	
Primary procedure	B27 Mastectomy	161	1559	100	1747	193	<0.001
		(31.3)	(34.4)	(73.0)	(60.5)	(69.7)	
	B28 Partial mastectomy / wide local excision / lumpectomy	305 (59.3)	2790 (61.5)	34 (24.8)	1037 (35.9)	61 (22.0)	
	B32 Open biopsy of breast	21 (4.1)	54 (1.2)	1 (0.7)	15 (0.5)	5 (1.8)	
	B37 Other operations on breast	27 (5.3)	131 (2.9)	2 (1.5)	89 (3.1)	18 (6.5)	
SNLB	No, not available in this hospital	9 (1.8)	236 (5.3)	12 (9.0)	309 (11.2)	42 (15.9)	<0.001
	No, but available in this hospital	259 (52.1)	894 (20.1)	89 (66.4)	1784 (64.8)	165 (62.5)	
	Yes, single technique	131	1825	15	431	45	
		(26.4)	(41.1)	(11.2)	(15.7)	(17.0)	
	Yes, dual technique	98	1487	18	227	12	
		(19.7)	(33.5)	(13.4)	(8.3)	(4.5)	
Axilliary lymph node dissection	No	467	3263	50	560	57	<0.001
		(91.7)	(73.2)	(37.0)	(19.9)	(21.1)	
	Yes	42	1197	85	2254	213	
		(8.3)	(26.8)	(63.0)	(80.1)	(78.9)	

Margin check	No, not available in this hospital	23 (4.9)	344 (7.9)	14 (10.4)	307 (11.1)	40 (15.3)	<0.001
	No, but available in this hospital	193 (41.2)	1927 (44.5)	95 (70.4)	1681 (60.8)	139 (53.3)	
	Yes, by x-ray	198 (42.2)	1028 (23.7)	6 (4.4)	236 (8.5)	17 (6.5)	
	Yes, by frozen section	55 (11.7)	1034 (23.9)	20 (14.8)	540 (19.5)	65 (24.9)	
Primary reconstruction	No, not available in this hospital	28 (5.4)	306 (6.8)	13 (9.5)	307 (10.6)	34 (12.1)	<0.001
	No, but available in this hospital	358 (69.6)	3434 (75.8)	96 (70.1)	2116 (73.3)	199 (71.1)	
	Yes, immediate - prosthesis	52 (10.1)	227 (5.0)	2 (1.5)	117 (4.1)	4 (1.4)	
	Yes, immediate - flap	59 (11.5)	449 (9.9)	14 (10.2)	237 (8.2)	32 (11.4)	
	Yes, planned at later stage	17 (3.3)	117 (2.6)	12 (8.8)	109 (3.8)	11 (3.9)	

Table 5-2. Cancer stage by other predictors (colon).

Essential TNM Classification of Malignant Tumours (eTNM), as defined by the Union for International Cancer Control (UICC), for colorectal cancer: L, Tumour contained within bowel wall with no nodal involvement (Stage I); A, Tumour through bowel wall with no nodal involvement (Stage II); R+, Regional lymph node involvement (Stage III); M+, Metastases present (Stage IV). ASA, American Society of Anesthesiologists operative risk grade; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; HIV, human immunodeficiency virus; SD, standard deviation. Data are n (%).

		L N=1802	A N=1386	R+ N=2128	M+ N=853	P
Age (years)	Mean (SD)	66.9 (13.0)	67.1 (13.6)	63.8 (13.8)	63.3 (14.0)	<0.001
Sex	Male	1026 (57.1)	771 (55.6)	1172 (55.1)	480 (56.4)	0.636
	Female	771 (42.9)	615 (44.4)	955 (44.9)	371 (43.6)	
ASA	I	207 (11.7)	193 (14.3)	264 (12.7)	104 (12.5)	<0.001
	II	892 (50.4)	679 (50.2)	1175 (56.5)	391 (46.9)	
	III	608 (34.4)	426 (31.5)	578 (27.8)	292 (35.0)	
	IV	59 (3.3)	45 (3.3)	60 (2.9)	43 (5.2)	
	V	4 (0.2)	9 (0.7)	4 (0.2)	4 (0.5)	
BMI	Normal weight (BMI 18.5 to 24.9)	621 (36.5)	570 (43.9)	900 (44.3)	377 (47.7)	<0.001
	Underweight (BMI < 18.5)	57 (3.4)	69 (5.3)	107 (5.3)	60 (7.6)	
	Overweight (BMI 25 to 30)	666 (39.2)	449 (34.6)	693 (34.1)	253 (32.0)	
	Obese (BMI >30)	356 (20.9)	210 (16.2)	331 (16.3)	100 (12.7)	
>10% weight loss	No	1249 (81.0)	846 (70.4)	1248 (65.4)	399 (53.8)	<0.001
	Yes	293 (19.0)	355 (29.6)	660 (34.6)	342 (46.2)	

ECOG performance status	0	963 (56.3)	640 (48.5)	1024 (50.0)	379 (46.3)	<0.001
	1	454 (26.5)	397 (30.1)	658 (32.1)	231 (28.2)	
	2	208 (12.2)	178 (13.5)	259 (12.6)	146 (17.8)	
	3	76 (4.4)	90 (6.8)	102 (5.0)	56 (6.8)	
	4	10 (0.6)	15 (1.1)	7 (0.3)	7 (0.9)	
Smoking	No, never	994 (61.8)	818 (66.2)	1283 (65.3)	485 (63.3)	0.154
	Stopped >6 weeks ago	390 (24.3)	253 (20.5)	410 (20.9)	176 (23.0)	
	Yes, current smoker	224 (13.9)	164 (13.3)	271 (13.8)	105 (13.7)	
Diabetes	No	1405 (80.1)	1096 (81.3)	1681 (80.7)	677 (81.2)	0.331
	Diet	41 (2.3)	42 (3.1)	61 (2.9)	15 (1.8)	
	Medication (non-insulin)	220 (12.5)	159 (11.8)	264 (12.7)	107 (12.8)	
	Insulin	89 (5.1)	51 (3.8)	78 (3.7)	35 (4.2)	
HIV tested	No	1630 (90.5)	1151 (83.0)	1760 (82.7)	718 (84.3)	<0.001
	Yes - Negative	166 (9.2)	232 (16.7)	365 (17.2)	129 (15.1)	
	Yes - Positive	5 (0.3)	3 (0.2)	2 (0.1)	5 (0.6)	
Distance to home (km)	< 10 km	663 (40.2)	458 (36.1)	688 (34.7)	259 (33.0)	<0.001
	10-20 km	342 (20.7)	296 (23.3)	408 (20.6)	196 (24.9)	
	20-50 km	355 (21.5)	246 (19.4)	414 (20.9)	166 (21.1)	
	50-100 km	142 (8.6)	117 (9.2)	180 (9.1)	70 (8.9)	
	>100 km	147 (8.9)	152 (12.0)	290 (14.6)	95 (12.1)	
Mode of diagnosis	Symptomatic	1101 (62.2)	1140 (82.8)	1815 (85.9)	746 (88.7)	<0.001
	Screening	478 (27.0)	154 (11.2)	205 (9.7)	54 (6.4)	

	Detected incidentally	192 (10.8)	82 (6.0)	92 (4.4)	41 (4.9)	
Urgency	Elective	1661 (92.2)	1191 (85.9)	1888 (88.7)	593 (69.5)	<0.001
	Emergency	141 (7.8)	195 (14.1)	240 (11.3)	260 (30.5)	
Treatment intent	Palliative	46 (2.6)	85 (6.1)	129 (6.1)	442 (51.8)	<0.001
	Curative	1756 (97.4)	1301 (93.9)	1999 (93.9)	411 (48.2)	
WHO checklist	No, not available in this hospital	145 (8.3)	202 (15.0)	235 (11.4)	99 (11.9)	<0.001
	No, but available in this hospital	63 (3.6)	67 (5.0)	106 (5.1)	46 (5.5)	
	Yes	1541 (88.1)	1079 (80.0)	1725 (83.5)	689 (82.6)	
Primary procedure	T309 Abdomen: Laparotomy with no other procedure	7 (0.4)	5 (0.4)	5 (0.2)	12 (1.4)	<0.001
	T43 Abdomen: Diagnostic laparoscopy with no other procedure	2 (0.1)	0 (0.0)	1 (0.0)	2 (0.2)	
	G74 Small bowel: Formation of ileostomy only	5 (0.3)	6 (0.4)	11 (0.5)	24 (2.8)	
	H04 Colon: Total excision of colon and rectum	13 (0.7)	10 (0.7)	16 (0.8)	10 (1.2)	
	H05 Colon: Total excision of colon	34 (1.9)	33 (2.4)	37 (1.7)	11 (1.3)	
	H06 Colon: Extended excision of right hemicolon	80 (4.4)	89 (6.4)	117 (5.5)	36 (4.2)	
	H07 Colon: Excision of right hemicolon	588 (32.7)	324 (23.4)	503 (23.6)	166 (19.5)	
	H08 Colon: Excision of transverse colon	24 (1.3)	14 (1.0)	22 (1.0)	9 (1.1)	
	H09 Colon: Excision of left hemicolon	142 (7.9)	110 (7.9)	139 (6.5)	54 (6.3)	
	H10 Colon: Excision of sigmoid colon	248 (13.8)	177 (12.8)	192 (9.0)	96 (11.3)	

	H11 Colon: Other excision of colon	35 (1.9)	38 (2.7)	26 (1.2)	22 (2.6)	
	H15 Colon: Formation of any colonic stoma	22 (1.2)	26 (1.9)	53 (2.5)	116 (13.6)	
	H19 Colon: Other open operations on colon	15 (0.8)	20 (1.4)	20 (0.9)	33 (3.9)	
	H331 Rectum: Abdominoperineal resection	83 (4.6)	116 (8.4)	217 (10.2)	51 (6.0)	
	H332 Rectum: Resection with anastomosis of colon to anus	57 (3.2)	28 (2.0)	93 (4.4)	17 (2.0)	
	H333 Rectum: Anterior resection with anastomosis	334 (18.6)	292 (21.1)	516 (24.3)	119 (14.0)	
	H335 Rectum: Resection with closure of rectal stump (Hartmanns)	48 (2.7)	74 (5.3)	120 (5.6)	53 (6.2)	
	H46 Rectum: Other open operations on rectum	63 (3.5)	24 (1.7)	39 (1.8)	22 (2.6)	
Approach	Open	763 (42.6)	774 (56.1)	1195 (56.3)	597 (70.4)	<0.001
	Minimally invasive	1027 (57.4)	606 (43.9)	928 (43.7)	251 (29.6)	
Site	Caecum	233 (13.1)	116 (8.4)	196 (9.3)	96 (11.4)	<0.001
	Ascending colon	385 (21.7)	240 (17.5)	372 (17.6)	129 (15.3)	
	Transverse colon	136 (7.7)	105 (7.6)	127 (6.0)	72 (8.6)	
	Descending colon	125 (7.0)	125 (9.1)	116 (5.5)	61 (7.2)	
	Sigmoid colon	402 (22.6)	310 (22.6)	387 (18.3)	212 (25.2)	
	High rectum (>10 to 15 cm)	178 (10.0)	173 (12.6)	256 (12.1)	111 (13.2)	
	Middle rectum (>5 to 10 cm)	131 (7.4)	131 (9.5)	283 (13.4)	68 (8.1)	
	Low rectum (< =5 cm from anal verge)	186 (10.5)	173 (12.6)	379 (17.9)	93 (11.0)	

Anastomosis	Not performed	269	330	495	327	<0.001
		(15.3)	(24.3)	(23.9)	(39.4)	
	Handsewn	330	300	391	153	
		(18.8)	(22.1)	(18.9)	(18.5)	
	Stapled	1161	727	1188	349	
		(66.0)	(53.6)	(57.3)	(42.1)	
Pre-op obstruction	No	1575	1075	1678	496	<0.001
		(91.0)	(79.5)	(81.4)	(60.0)	
	Yes	155	277	383	330	
		(9.0)	(20.5)	(18.6)	(40.0)	
Pre-op perforation	No	1750	1258	1983	745	<0.001
		(98.3)	(93.0)	(94.3)	(89.1)	
	Yes	30 (1.7)	94 (7.0)	120 (5.7)	91	
					(10.9)	
Stoma formed	No	1338	839	1143	423	<0.001
		(75.4)	(61.2)	(54.2)	(49.9)	
	Yes, loop ileostomy	173	173	378	102	
		(9.8)	(12.6)	(17.9)	(12.0)	
	Yes, end ileostomy	47 (2.6)	55 (4.0)	80 (3.8)	31 (3.7)	
	Yes, loop colostomy	51 (2.9)	54 (3.9)	122 (5.8)	105	
					(12.4)	
	Yes, end colostomy	165	251	385	187	
		(9.3)	(18.3)	(18.3)	(22.1)	

Table 5-3. Cancer stage by other predictors (gastric).

Essential TNM Classification of Malignant Tumours (eTNM), as defined by the Union for International Cancer Control (UICC), for gastric cancer: L, Tumour contained within stomach wall with no nodal involvement (Stage I); A, Tumour through stomach wall with no nodal involvement (Stage II); R+, Regional lymph node involvement (Stage III); M+, Metastases present (Stage IV). ASA, American Society of Anesthesiologists operative risk grade; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; HIV, human immunodeficiency virus; SD, standard deviation. Data are n (%).

		L N=450	A N=235	R+ N=505	M+ N=133	P
Age (years)	Mean (SD)	64.6 (14.4)	62.7 (14.2)	63.1 (13.0)	61.2 (13.8)	0.068
Sex	Male	251 (55.8)	152 (64.7)	317 (62.8)	86 (64.7)	0.048
	Female	199 (44.2)	83 (35.3)	188 (37.2)	47 (35.3)	
ASA	I	66 (15.0)	38 (16.3)	101 (20.4)	23 (17.7)	<0.001
	II	222 (50.5)	110 (47.2)	242 (48.8)	60 (46.2)	
	III	142 (32.3)	78 (33.5)	140 (28.2)	34 (26.2)	
	IV	10 (2.3)	7 (3.0)	12 (2.4)	10 (7.7)	
	V	0 (0.0)	0 (0.0)	1 (0.2)	3 (2.3)	
BMI	Normal weight (BMI 18.5 to 24.9)	203 (47.9)	107 (48.6)	263 (54.0)	69 (54.8)	<0.001
	Underweight (BMI < 18.5)	25 (5.9)	21 (9.5)	55 (11.3)	22 (17.5)	
	Overweight (BMI 25 to 30)	134 (31.6)	79 (35.9)	122 (25.1)	29 (23.0)	
	Obese (BMI >30)	62 (14.6)	13 (5.9)	47 (9.7)	6 (4.8)	
>10% weight loss	No	285 (70.2)	104 (48.4)	202 (43.0)	33 (26.6)	<0.001

	Yes	121 (29.8)	111 (51.6)	268 (57.0)	91 (73.4)	
ECOG performance status	0	241 (55.5)	103 (45.2)	216 (43.7)	42 (32.3)	<0.001
	1	117 (27.0)	85 (37.3)	176 (35.6)	44 (33.8)	
	2	53 (12.2)	27 (11.8)	70 (14.2)	23 (17.7)	
	3	20 (4.6)	12 (5.3)	27 (5.5)	19 (14.6)	
	4	3 (0.7)	1 (0.4)	5 (1.0)	2 (1.5)	
Smoking	No, never	241 (62.0)	124 (57.4)	269 (59.1)	65 (58.6)	0.948
	Stopped >6 weeks ago	86 (22.1)	55 (25.5)	106 (23.3)	26 (23.4)	
	Yes, current smoker	62 (15.9)	37 (17.1)	80 (17.6)	20 (18.0)	
Diabetes	No	376 (85.3)	196 (85.2)	417 (84.2)	108 (81.8)	0.962
	Diet	8 (1.8)	5 (2.2)	9 (1.8)	1 (0.8)	
	Medication (non-insulin)	41 (9.3)	20 (8.7)	50 (10.1)	16 (12.1)	
	Insulin	16 (3.6)	9 (3.9)	19 (3.8)	7 (5.3)	
HIV tested	No	363 (80.7)	162 (68.9)	364 (72.1)	85 (63.9)	0.001
	Yes - Negative	86 (19.1)	73 (31.1)	140 (27.7)	47 (35.3)	
	Yes - Positive	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.8)	
Distance to home (km)	< 10 km	136 (32.9)	53 (24.5)	122 (25.7)	25 (20.7)	0.002
	10-20 km	89 (21.5)	41 (19.0)	87 (18.4)	26 (21.5)	
	20-50 km	75 (18.1)	40 (18.5)	106 (22.4)	24 (19.8)	
	50-100 km	51 (12.3)	26 (12.0)	40 (8.4)	10 (8.3)	

	>100 km	63 (15.2)	56 (25.9)	119 (25.1)	36 (29.8)	
Mode of diagnosis	Symptomatic	340 (76.7)	221 (95.7)	475 (95.4)	130 (97.7)	<0.001
	Screening	31 (7.0)	1 (0.4)	7 (1.4)	1 (0.8)	
	Detected incidentally	72 (16.3)	9 (3.9)	16 (3.2)	2 (1.5)	
Urgency	Elective	436 (96.9)	220 (93.6)	474 (93.9)	113 (85.0)	<0.001
	Emergency	14 (3.1)	15 (6.4)	31 (6.1)	20 (15.0)	
Treatment intent	Palliative	17 (3.8)	23 (9.8)	65 (12.9)	89 (66.9)	<0.001
	Curative	433 (96.2)	212 (90.2)	440 (87.1)	44 (33.1)	
WHO checklist	No, not available in this hospital	49 (11.3)	31 (13.4)	48 (9.8)	10 (7.9)	0.114
	No, but available in this hospital	18 (4.1)	20 (8.7)	24 (4.9)	8 (6.3)	
	Yes	367 (84.6)	180 (77.9)	417 (85.3)	108 (85.7)	
Primary procedure	T309 Abdomen: Laparotomy with no other procedure	7 (1.6)	4 (1.7)	13 (2.6)	13 (9.8)	<0.001
	T43 Abdomen: Diagnostic laparoscopy with no other procedure	7 (1.6)	6 (2.6)	9 (1.8)	5 (3.8)	
	G27 Stomach: Total excision of stomach	131 (29.1)	93 (39.6)	214 (42.4)	30 (22.6)	
	G28 Stomach: Partial excision of stomach	265 (58.9)	102 (43.4)	207 (41.0)	36 (27.1)	
	G32 Stomach: Connection of stomach to jejunum	17 (3.8)	20 (8.5)	42 (8.3)	35 (26.3)	
	G38 Stomach: Other open operations on stomach	23 (5.1)	10 (4.3)	20 (4.0)	14 (10.5)	
Approach	Open	280 (62.5)	182 (77.8)	413 (81.8)	117 (88.0)	<0.001

	Minimally invasive	168 (37.5)	52 (22.2)	92 (18.2)	16 (12.0)	
Site	Upper third (cardia/fundus)	87 (19.7)	39 (17.1)	109 (22.0)	25 (19.8)	0.125
	Middle third (body)	104 (23.5)	39 (17.1)	90 (18.2)	20 (15.9)	
	Distal third (antrium/pylorus)	195 (44.1)	109 (47.8)	210 (42.4)	56 (44.4)	
	Entire stomach	56 (12.7)	41 (18.0)	86 (17.4)	25 (19.8)	
Anastomosis	Not performed	83 (18.9)	29 (12.8)	38 (7.7)	28 (21.7)	<0.001
	Handsewn	116 (26.4)	81 (35.7)	152 (30.9)	54 (41.9)	
	Stapled	241 (54.8)	117 (51.5)	302 (61.4)	47 (36.4)	
D2 resection	No	205 (49.0)	97 (43.3)	166 (34.2)	87 (69.6)	<0.001
	Yes	213 (51.0)	127 (56.7)	320 (65.8)	38 (30.4)	
Pre-op obstruction	No	409 (93.4)	200 (87.0)	421 (84.7)	71 (55.9)	<0.001
	Yes	29 (6.6)	30 (13.0)	76 (15.3)	56 (44.1)	
Pre-op perforation	No	436 (98.9)	223 (96.5)	477 (95.8)	120 (91.6)	0.001
	Yes	5 (1.1)	8 (3.5)	21 (4.2)	11 (8.4)	

5.3.2 Adjusted primary outcomes

Outcomes were adjusted in three-level models accounting for patient and disease factors nested within hospitals and country of treatment (Figure 5-3). Higher 30-day mortality was seen in gastric cancer in low/lower middle-income countries (adjusted odds ratio (aOR) 3.72, 95% confidence interval 1.70 to 8.16) and in colorectal cancer in upper middle (aOR 2.06, 1.11 to 3.83) and low/lower middle-income countries (aOR 4.59, 2.39 to 8.80). No difference in mortality was seen in breast cancer.

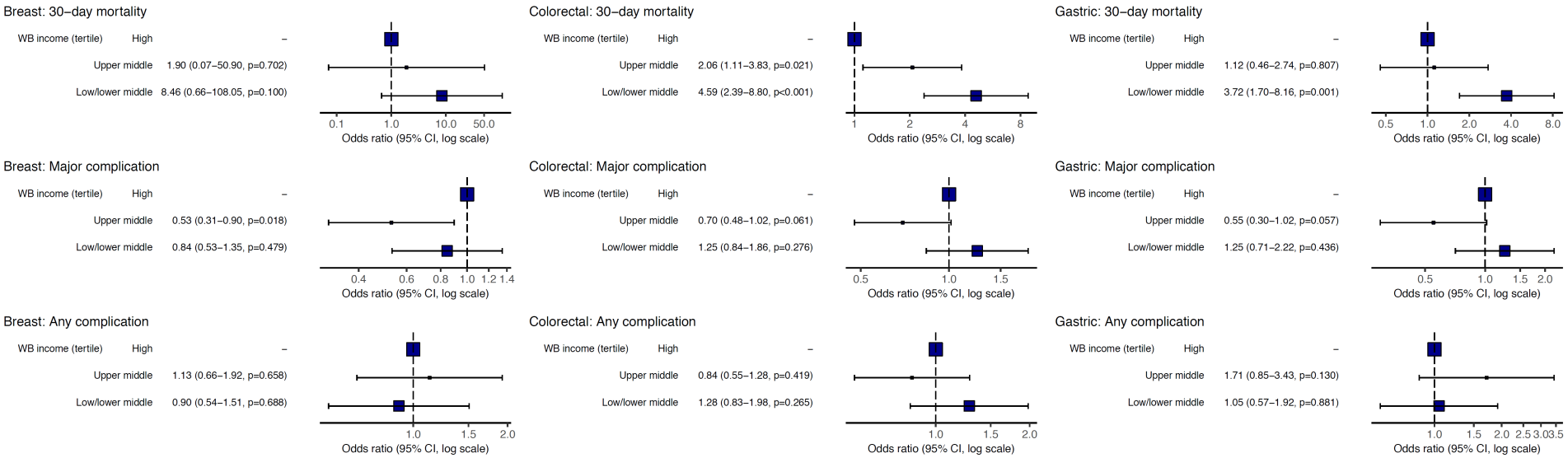
The proportion of patients sustaining a major complication or any complication in these adjusted analyses was again similar across country income groups, with weak evidence of fewer major complications following breast surgery in upper middle-income group (Figure 5-3). No statistical interactions were seen between patient factors and country-income group for mortality or complications; for example, the effect of age, BMI and ASA on outcomes did not differ by country-income group.

5.3.3 Death after major complications

Given similar complication rates across country income groups, I proceeded to an analysis to examine factors predicting mortality after major complications in colorectal and gastric cancer. The proportion of patients sustaining a major complication who subsequently died was higher in upper middle and low/lower middle compared to high-income countries in adjusted analyses (Figure 5-4). The relationship between mortality and country income group was consistent across cancer stage of presentation, except for stage IV gastric cancer, where mortality was high across all country income groups (Figure 5-5). Similarly, the proportion of patients sustaining complications across country income groups was unchanged after stratification by stage of presentation (Figure 5-5).

Figure 5-3. Multilevel logistic regression adjusted outcomes by country income group.

Models were built incorporating patient and disease factors specific to each cancer. Results are adjusted odds ratios (95% confidence intervals, P-value). WB, World Bank. Material from [187].



In a model accounting for patient factors and clustering by country and hospital, patients in upper middle (aOR 3.89, 2.08 to 7.29) and low/lower middle (aOR 6.15, 3.26 to 11.59) groups were more likely to die after a major complication compared to the high-income group (Figure 5-6). Patient performance status and emergency surgery were strong predictors of death after major complication. While patients with stage IV cancer had a greater probability of dying after major complication, stage I to III cancer was not associated with an excess mortality when accounting for other variables in the model. In a four-level model of patients nested in hospitals, countries, and World Bank income groups, 60% of the variation in outcome captured by the model (pseudo-R^2 = 0.42) was explained by patient/disease factors, with the remaining 40% explained by hospital, country, and country income group factors (Figure 5-6).

5.3.4 Hospital facilities and capacity to rescue

The association between country income group and 30-day mortality was examined in a three-way decomposition mediation model of postoperative care infrastructure (Figure 5-7). No interaction was found between this mediator and country income group. A significant proportion of the excess mortality after major complication was mediated by the absence of postoperative care infrastructure in low/lower middle (1.19, 1.01 to 1.42, 10%) and upper middle (1.19, 1.01 to 1.42, 14%) income groups.

The absolute risk differences for 30-day mortality after major complication with and without consistently available postoperative care infrastructure were examined for typical patients (Figure 5-8). The presence of postoperative care infrastructure was associated with fewer deaths in both the low/lower middle-income group (7 to 10 fewer deaths per 100 major complications, number needed to treat [NNT] 10 to 14) and the upper middle-income group (5 to 8 fewer deaths per 100 major complications, NNT 13

to 20). Cancer care pathways were not shown to mediate any association with 30-day mortality.

Figure 5-4. Early outcomes following surgery for cancer by cancer and country income group

Adjusted proportion of patients dying or sustaining a major complication or any complication by day 30 after surgery stratified by country income group (A). Proportion of patients sustaining a major complication who died within 30 days (B). Proportions are adjusted for patient complications using multivariable (reduced) logistic regression models. Material from [187].

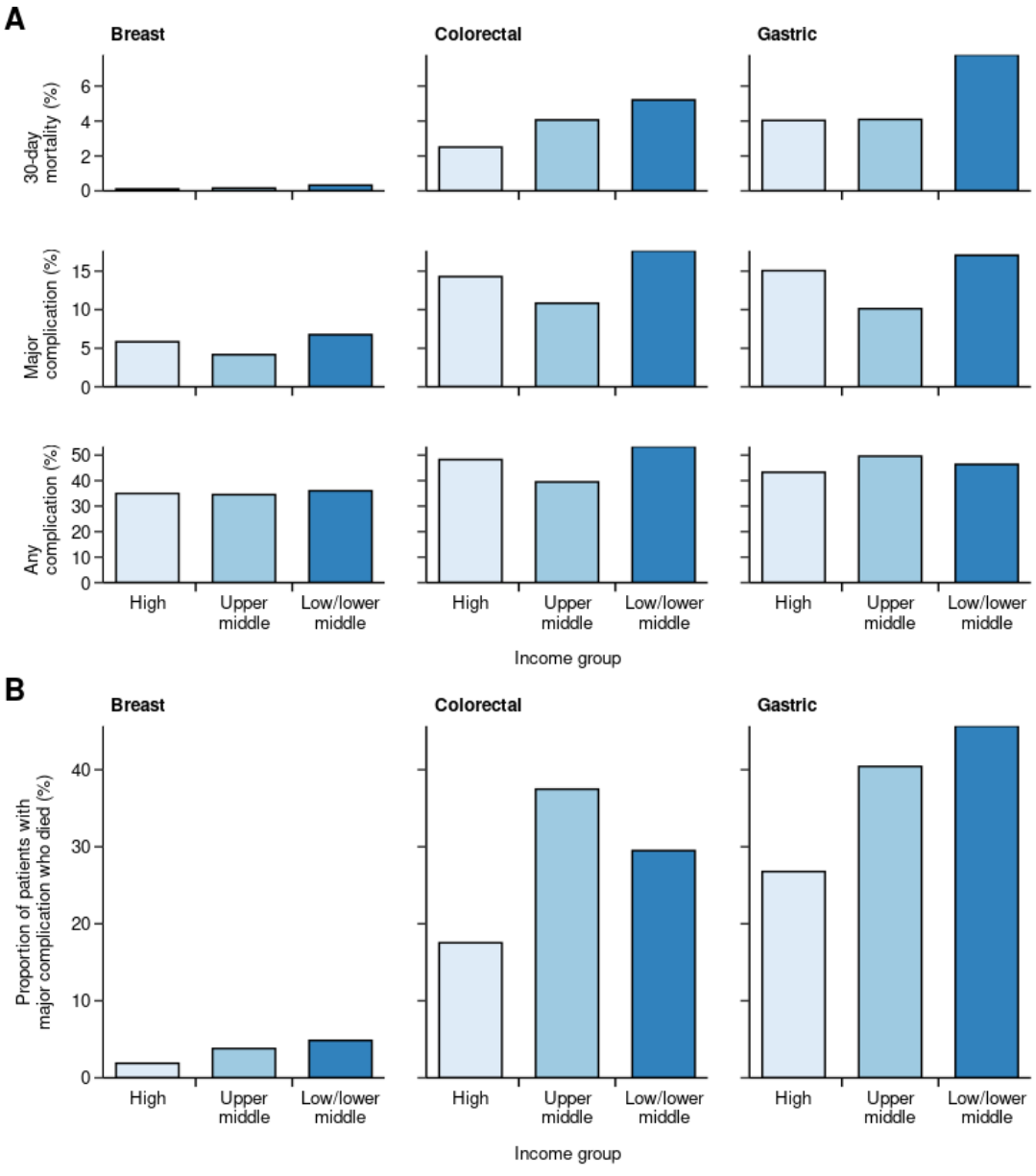


Figure 5-5. Stage of presentation, 30-day mortality, and 30-day complications by cancer and country income group.

30-day mortality (A), major complication (B), and any complication (C) stratified by cancer type, cancer stage, and country income group. Material from [187].

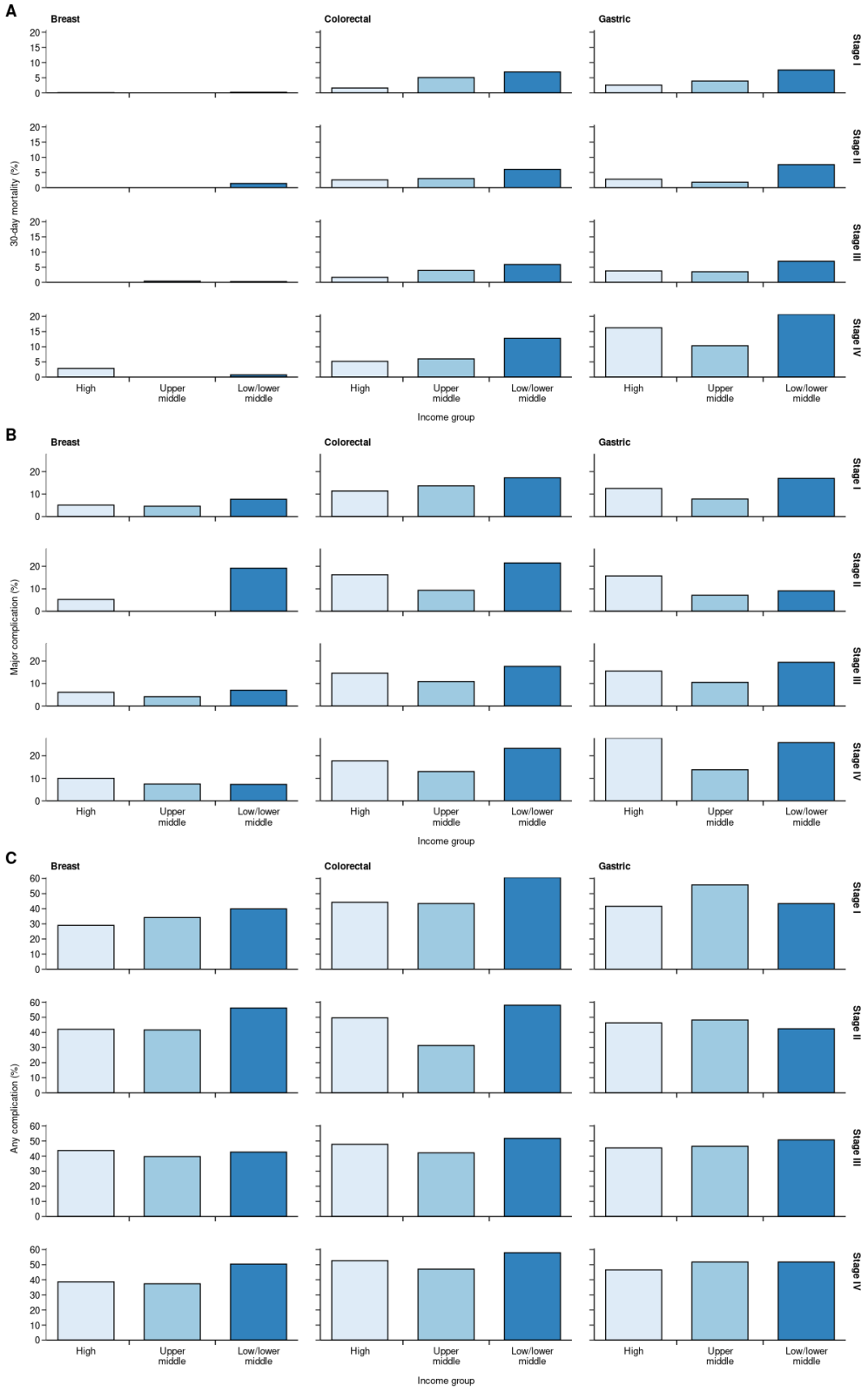


Figure 5-6. Capacity to rescue from major complication.

Multilevel logistic regression model for predictors of death after major complication in colorectal and gastric cancer (A). Proportion of 30-day mortality variation explained at the level of patient/disease, hospital, country, and country income group, in patients with colorectal or gastric cancer who died after major complication (B). The "variance explained" at each of the 4 levels of the model (marginal pseudo-R^2) is expressed as a proportion of the total "variance explained" (conditional pseudo-R^2). WB, World Bank; ECOG, Eastern Cooperative Oncology Group; ASA, American Society of Anesthesiologists; CI, Confidence Interval. Material from [187].

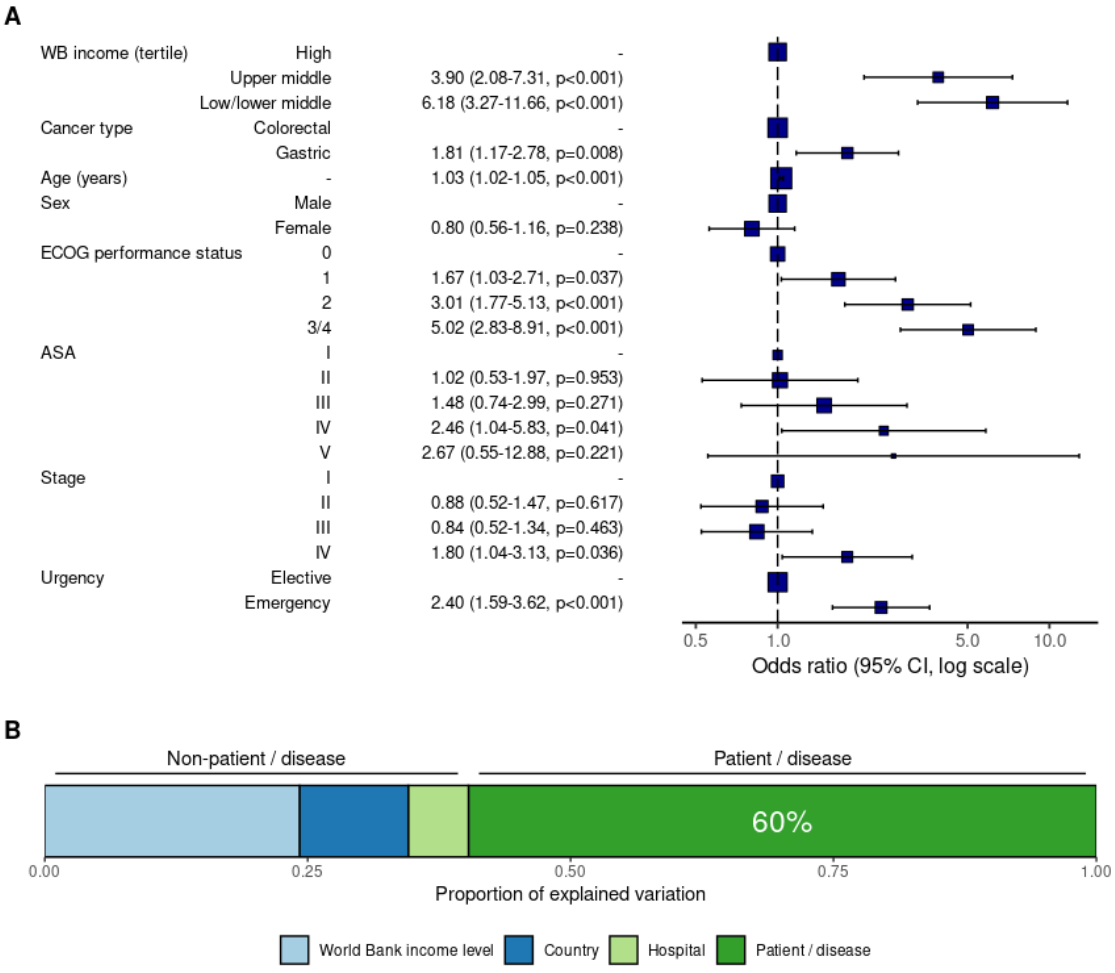


Figure 5-7. Capacity to rescue from major complication mediated by postoperative care infrastructure.

Three-way decomposition mediation model of the proportion of the effect of country income group on 30-day mortality after major complication mediated by postoperative care infrastructure (the consistent presence of a designated postoperative recovery area, the availability of critical care facilities, and the existence of a working CT scanner). ASA, American Society of Anesthesiologists.

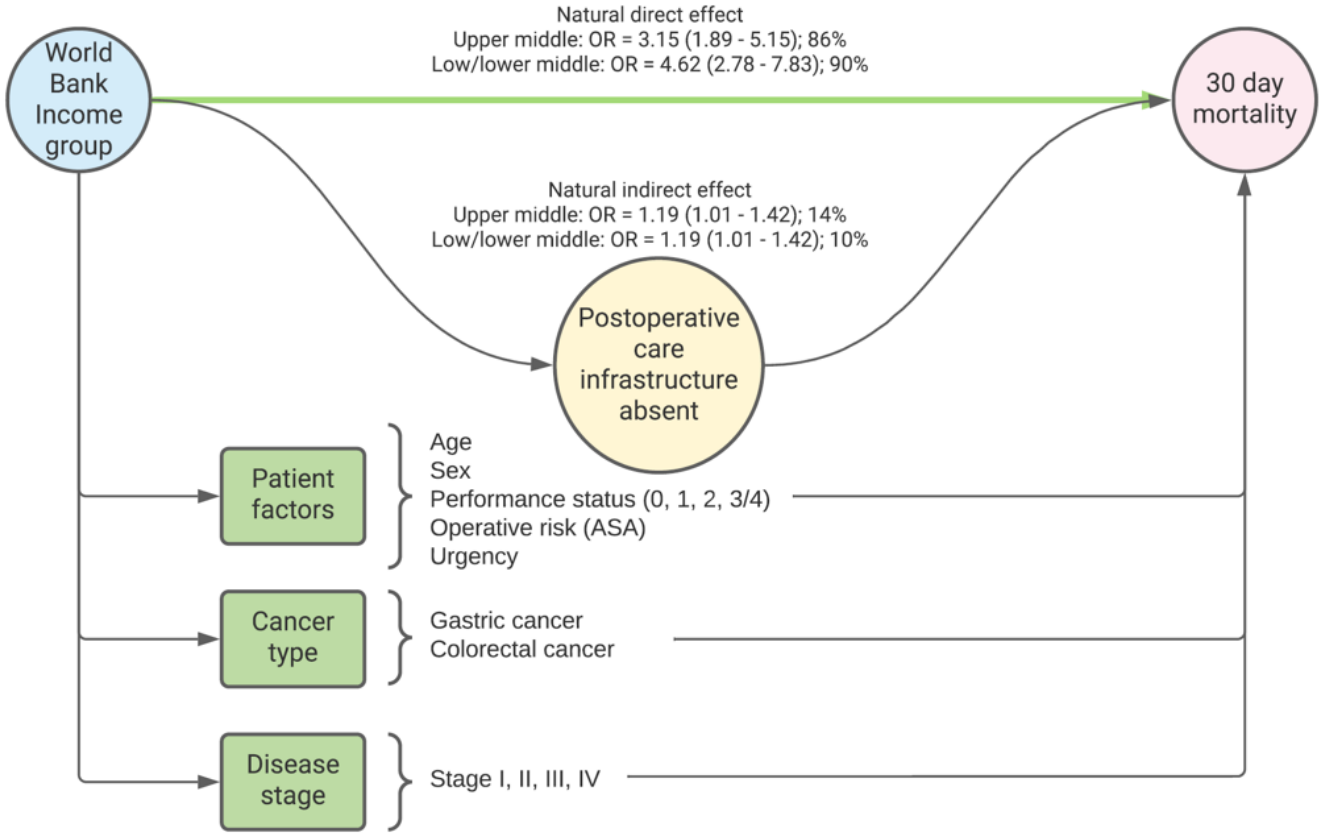
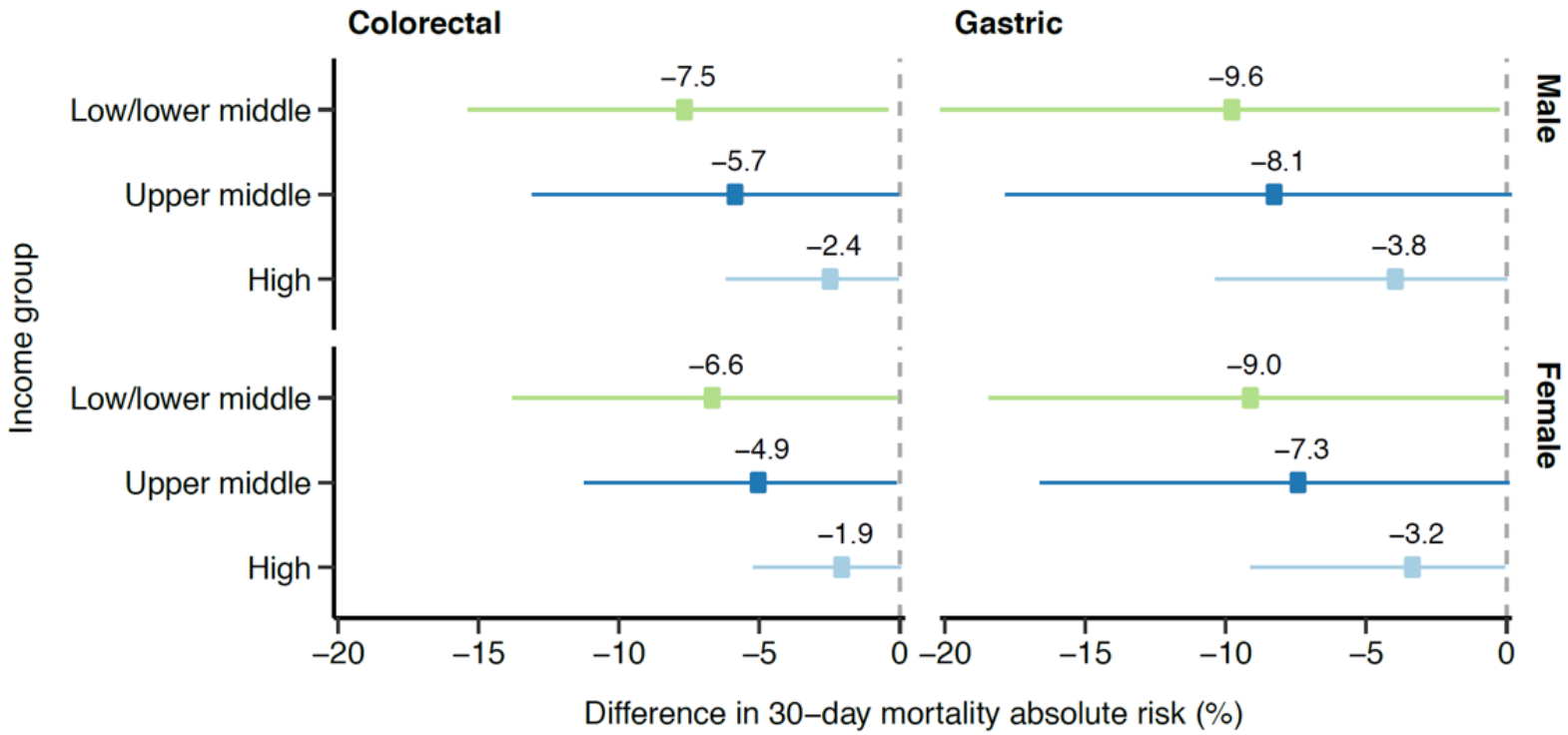


Figure 5-8. Absolute risk difference for 30-day mortality after major complication in the presence of consistently available postoperative care infrastructure.

Estimates for age 55 years, ECOG performance status 1, ASA 2, cancer stage II, and elective surgery. ASA, American Society of Anesthesiologists. Material from [187].



5.4 Discussion

5.4.1 Summary of key findings in context of previous literature

Differences in early cancer outcomes in LMICs compared to high-income countries are often attributed to the advanced stage of presentation, together with a lack of access to cancer-specific treatments. In this prospective, international cohort of 15 958 patients in 82 countries undergoing surgery for breast, colorectal, or gastric cancer, I demonstrate that 30-day postoperative mortality is four-times higher in resource-limited settings, despite patients experiencing similar major complication rates.

While patient factors partially explained the higher postoperative mortality rate in LMICs, health system characteristics, including access to postoperative monitoring, emergent imaging, and critical care facilities also appeared key, resulting in a lack of capacity to rescue after the development of a major complication. This excess mortality after cancer surgery will hamper cancer control efforts in LMICs, and prevent cancer patients, communities, and economies from realising the benefits of cancer-specific treatments.

Cancer is a leading cause of death and disability worldwide[206], exerting substantial economic effects in countries at all stages of development[207], with a disproportionate burden of disease now emerging in LMICs[52]. Surgery is fundamental to the treatment of solid cancers across all income settings, acting as a pivotal component of multidisciplinary care, together with imaging, pathology, chemoradiotherapy, and palliation. Effective surgical care plays a crucial role in the prevention of death from cancer[52], and requires systems of the highest quality throughout the pre- and postoperative periods[68]. If the

opportunity to strengthen surgical cancer systems is not taken, an estimated US$6.2 trillion in gross domestic product will be lost by 2030[52].

5.4.2 Policy implications

Mortality rates reported in my study across LMICs for both colorectal (5.5%) and gastric (7.2%) cancer were higher than current global estimates[208]. Existing perioperative mortality rates in the published literature are limited by the lack of standardised reporting, absence of risk stratification, and are often derived from small, single-centre studies. The 30-day mortality in my study was similar to previous multicentre observational cohorts[27,161]. Across colorectal and gastric cancers, variation in 30-day mortality between high-income countries and LMICs was demonstrated after both emergency (7.1% vs 18.0%) and elective (1.9 vs 4.0%) surgery.

There are well-described factors that may contribute to an early excess mortality following cancer surgery. Locally advanced or metastatic cancer is a common initial presentation in LMICs, due in part to reduced access to timely and affordable surgical services[52]. Delays in presentation result in poorer survival through a combination of cancer progression[209], cancer-related cachexia[210], and the consequences of emergency presentation. Achieving early detection and treatment through cancer screening initiatives is important and often the focus of public health initiatives and funding[211]. However, in this study, I demonstrate that excess mortality after cancer surgery in LMICs is only partly explained by the later presentation of disease. I have shown an excess in postoperative mortality despite similar rates and patterns of complications.

The importance of rescuing patients from common complications is now well-established, with variation described globally[212]. This is the first study to identify capacity to rescue as an important early determinant of outcomes from cancer surgery in resource-restricted settings. Furthermore, I have shown a clear association between the consistent presence of postoperative care infrastructure and lower mortality rates following major complications. The capacity to rescue patients is likely to limit expected reductions in mortality from current global development funds and multilateral investments in cancer control. Better perioperative care systems to detect and intervene upon common complications is essential if early death after cancer surgery is to be reduced.

5.4.3 Strengths of this study

A major strength of this study is its prospective design and granular patient- and hospital-level data collected simultaneously from a wide breadth of global settings. Over one hundred variables were included, making it one of the richest datasets in this area. The use of the Essential TNM system, together with standard TNM eight classifications, make meaningful comparisons of cancer stage possible in settings with limited access to imaging and pathological services[171].

The assessment of cancer stage, treatment, and outcome was standardised, and training provided through an online platform. Data quality was ensured though collaborator-facing web applications and real-time data entry quality assurance. An independent validation study verified data accuracy and case ascertainment, providing reassurance around the credibility of results. Quantification of surgical cancer care in resource-limited settings has been hindered by a lack of high-quality data[208,213,214]. This study therefore contributes to

closing this knowledge gap and allows meaningful comparison from multiple income settings with accurate case-mix adjustment.

5.4.4 Study limitations

Limitations of this study include looking at outcomes only in the 30-days after surgery. Oncological outcomes are clearly essential in capturing the effectiveness of cancer treatments including surgery, and these are also poorly captured and understood in resource-limited settings[52,213]. Disease-free and overall survival following surgery are likely to be significantly lower in LMICs, for many of the reasons described, including presentation with later stage disease across included cancers. The impact of delayed surgery in life-years lost is well described in high-income countries[215], however the impact of this in global settings is less clear.

Only patients undergoing primary surgery for breast, colorectal, or gastric cancers were included, and therefore outcomes in patients receiving non-surgical care were not examined. Furthermore, associations between outcomes and hospital-level facilities are exactly that, associations. Hospitals with CT scanners and critical care facilities are likely to have other differences in infrastructure and processes that may contribute to better outcomes. Finally, the substantial economic and financial costs to patients undergoing cancer treatment are known to be significant but were not measured.

5.4.5 Conclusion

Reducing early mortality after surgery is a key element to improving cancer outcomes and achieving Universal Health Coverage for non-communicable diseases worldwide. The Lancet Oncology Commission on Global Cancer Surgery identified the key requirements

to scale up surgical cancer services by 2030[68]. Improvements in the provision of cancer care remain essential if Sustainable Development Goals are to be met[216]. Yet detailed global information supporting focused initiatives to develop infrastructure, improve quality, and implement effective interventions remains limited. Although complete analysis of the patient pathway was not possible within this analysis, I have identified multiple components of the surgical health system, as well as patient-level risk factors, that could be targeted for further study and intervention. High quality perioperative care requires appropriate recovery and ward space, a sufficient number well-trained staff, the use of early warning systems, and ready access to imaging, operating theatre space, and critical care facilities to deal with complications when they occur. This is even more challenging to deliver in times of COVID-19[217].

Access to cancer surgery is clearly an important barrier to safe and effective care for people with cancer in LMICs[218]. Improved access comes with further opportunities for optimisation of individual patients through, for instance, nutritional interventions and neoadjuvant therapies. Addressing these factors with high-quality interventional trials to build a global evidence base for the delivery of safe cancer surgery, is likely to have significant impact and improve cancer survival.

This work has produced a unique prospective dataset of patients undergoing breast, colorectal, or gastric cancer surgery worldwide. Future research should focus on the detailed characterisation of perioperative care processes and the implementation of strategies to both reduce complication rates, and to rescue patients from complications when they do occur. Policy makers worldwide must balance investments in the early

detection and treatment of cancer, with the simultaneous improvement in safe perioperative care. Without these investments, mortality gains in cancer control will not be fully realised.

5.5 Contribution statement

The primary data for this chapter were collected during the GlobalSurg 3 observational study, an international collaborative led by Professor Ewen Harrison. I led the methodology and analyses presented in this chapter from conception to completion and dissemination.

5.6 Outputs relating to this chapter

This study is published in *The Lancet:*

NIHR Global Health Research Unit on Global Surgery [**Knight SR** first author in writing group] (2021). Global variation in postoperative mortality and complications after cancer surgery: a multicentre, prospective cohort study in 82 countries. **Lancet.** 397; 387–97.

https://doi.org/10.1016/S0140-6736(21)00001-5

I presented this work as an oral presentation at the American College of Surgeons Conference, Washington in July 2019 and as an invited lecture at the NHS Lothian Grand Round in February 2022.

Chapter 6 Effects of hospital facilities on patient outcomes after cancer surgery

6.1 Introduction

I have shown that patients in LMICs have higher mortality after cancer surgery, however the impact of hospital facilities on patient outcomes was not explored[187]. Structural characteristics such as case volume, facility availability, and the presence of specialised services are known to impact surgical outcomes in high-income settings[61,182,183]. Improving hospital facilities through additional infrastructure and resources, translating to greater capacity, is thought to influence clinical outcomes in lower income settings. Current estimates suggest poor-quality health systems cause eight million deaths per year in LMICs[28].

Using a systems-based approach, I aimed to describe critical surgical oncology services available worldwide and determine whether hospital facilities are associated with better outcomes following cancer surgery worldwide, particularly in low-income settings, and the potential effects of improving these resources.

6.2 Methods

6.2.1 Study design and participants

The study methods and patient cohort are described in detail within Chapter 3. Briefly, 15 958 consecutive patients underwent a primary procedure for breast, colorectal, or gastric

cancer across 82 countries between 1st April 2018 and 31st January 2019. Case ascertainment and data accuracy were found to be high[187].

6.2.2 Outcomes

The primary outcome measures were 30-day mortality and 30-day major complication, as defined by Clavien-Dindo grade III, IV or V (Table 3-2)[178]. Death was included in the definition of major complication and therefore was not a competing risk. *Capacity to rescue* was defined as the absolute risk difference of death in patients sustaining a complication of surgery.

Secondary outcome measures were defined in the protocol[165] and designed to describe cancer care quality: (1) 30-day any complication (defined by Clavien-Dindo grade I to V), (2) length of hospital stay, (3) unplanned readmission to a healthcare facility, (4) follow-up method at 30 days, (5) cancer-specific surgical management including multidisciplinary tumour board availability (all), surgical safety checklist use (all), anastomosis formation (colorectal and gastric), achievement of negative resection margin (all), (6) and oncological treatment availability.

6.2.3 Statistical analysis

Eleven hospital characteristics were selected *a priori* on the basis of their potential to directly or indirectly affect patient outcomes following cancer surgery[173,181–185]. All hospital characteristics were included as explanatory variables within an automated variable selection with backward elimination model, but with the exclusion of patient-level data. Only main interactions were included to avoid overfitting. Facility characteristics with a P value of <0.05 were identified as candidate covariates.

To obtain adjusted outcomes at hospitals with different numbers of facility characteristics were obtained, I created an ordinal variable (0–5) from candidate covariates which represented the number of characteristics at each hospital. Hospitals were then categorised into tertiles by patient distribution to define different facility levels.

Adjusted outcomes were calculated as predicted probabilities from a GEE logistic regression model, including potential confounders (patient age, sex, American Society of Anesthesiologists (ASA) grade, performance status, disease stage and operative urgency) across income group and cancer type. I obtained confidence intervals (CIs) and a P value for trend by fitting the GEE logistic regression model with facility level. The relationship between hospital facility level and 30-day mortality were calculated from logistic regression models for different covariate levels (patient and disease characteristics). Absolute risk differences were calculated, and CIs determined using bootstrap resampling (5000 draws). The number needed to treat to benefit was defined as the reciprocal of the absolute risk difference.

Further detail on all statistical analyses for this analysis can be found in Chapter 3. Additional data and analyses which support this Chapter are contained within Appendix 10.4.

6.3 Results

6.3.1 Overview of study cohort

Hospital-level data were available for 9685 patients in 238 hospitals across 66 countries (high income 91 hospitals, 20 countries, 3636 patients; upper middle income 57 hospitals,

19 countries, 2119 patients; low/lower middle income 90 hospitals, 27 countries, 3930 patients; Figure 6-1). The characteristics of included hospitals across income-group is summarised in Table 6-1. Hospital facility characteristics varied across income group except for the presence of ultrasound and pathology services.

A stepwise increase in all hospital facility characteristics was seen as the total number of characteristics present within a hospital increased (Figure 6-3). Across all included cancers, unadjusted mortality rates reduced as overall hospital facility count increased (Figure 6-3). For hospitals where hospital-level data were not available, adjusted mortality rates were found to be similar across each income group (Table 6-2).

6.3.2 Hospital system characteristic selection

Five hospital facility characteristics were strongly associated with 30-day mortality and covered a broad range of resources within the Donabedian framework of Structure and Process[219] (Imaging: Ultrasound and CT scanner; Provider: Oncologist; Supplies: Opioid analgesia; Process: HDU/ITU; Table 6-3). The same characteristics were identified in a sensitivity analysis (Table 6-4). Of the 238 hospitals included, 47% (n=113) had all five facility characteristics present (Figure 6-4). Hospital structure and process resources declined with worsening Human Development Index (HDI), particularly in countries with a HDI rank above 150 (Figure 6-4).

Figure 6-1. Study flowchart for hospital facility analysis.

Material from [220].

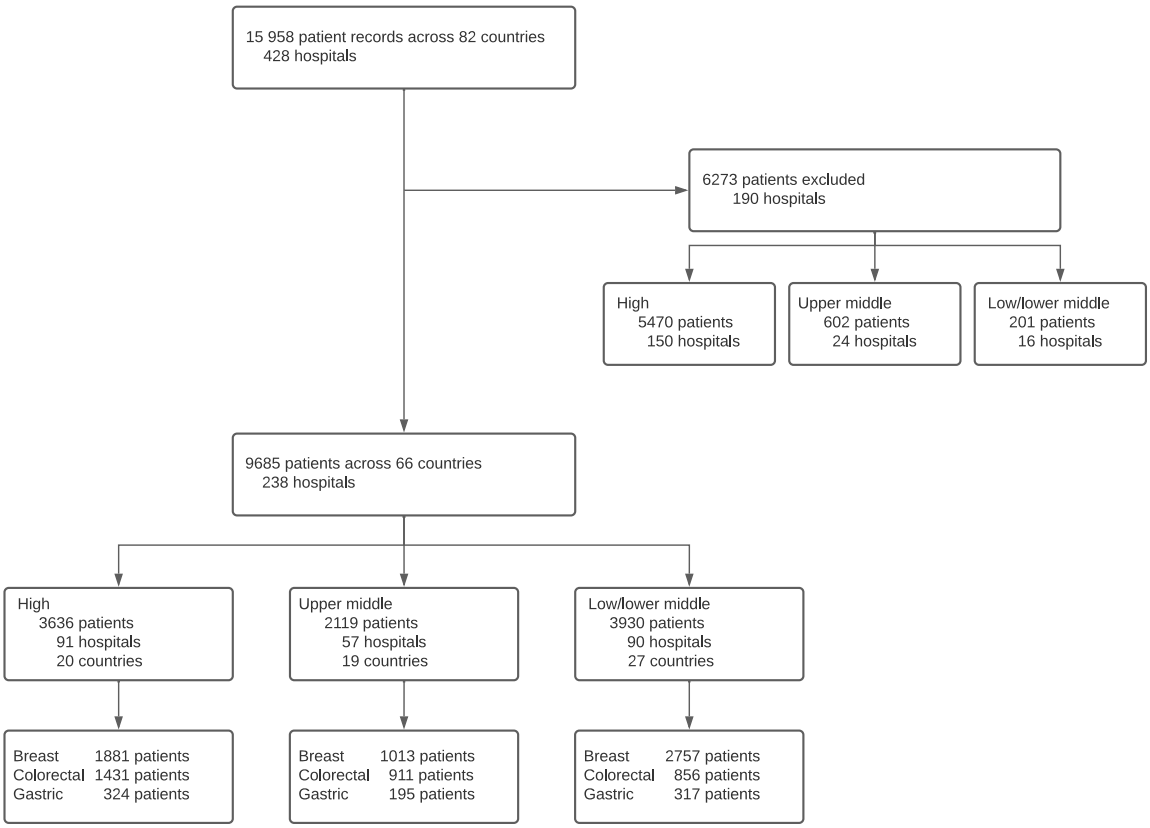


Table 6-1. Distribution of hospital-level infrastructure and resources by country income group.

WB income (tertile)		High (n = 91)	Upper middle (n = 57)	Low/lower middle (n = 90)	P
MDT availability		89 (97.8)	53 (93.0)	71 (78.9)	<0.001
Oncologist available in hospital		85 (93.4)	46 (80.7)	63 (70.0)	<0.001
Palliative care available in hospital		68 (74.7)	28 (49.1)	37 (41.1)	<0.001
Opioid medication available		84 (92.3)	48 (84.2)	47 (52.2)	<0.001
Ultrasound available		77 (84.6)	52 (91.2)	75 (83.4)	0.382
CT scan available		87 (95.6)	48 (84.2)	54 (60.0)	<0.001
Postoperative care facilities		86 (94.5)	45 (78.9)	62 (68.9)	<0.001
Critical care bed available		84 (92.3)	44 (77.2)	60 (66.7)	<0.001
Pathology available in hospital		66 (72.5)	46 (80.7)	62 (68.9)	0.295
Hospital type	Non-referral hospital	25 (27.5)	3 (5.3)	5 (5.6)	0.001
	Referral hospital	56 (61.5)	46 (80.7)	73 (81.1)	
	Specialist cancer hospital	10 (11.0)	8 (14.0)	12 (13.3)	
Elective oesophagectomy available		44 (48.4)	34 (59.6)	46 (51.1)	0.403

Figure 6-2. Relationship between hospital facilities and country income group.

Material from [220].

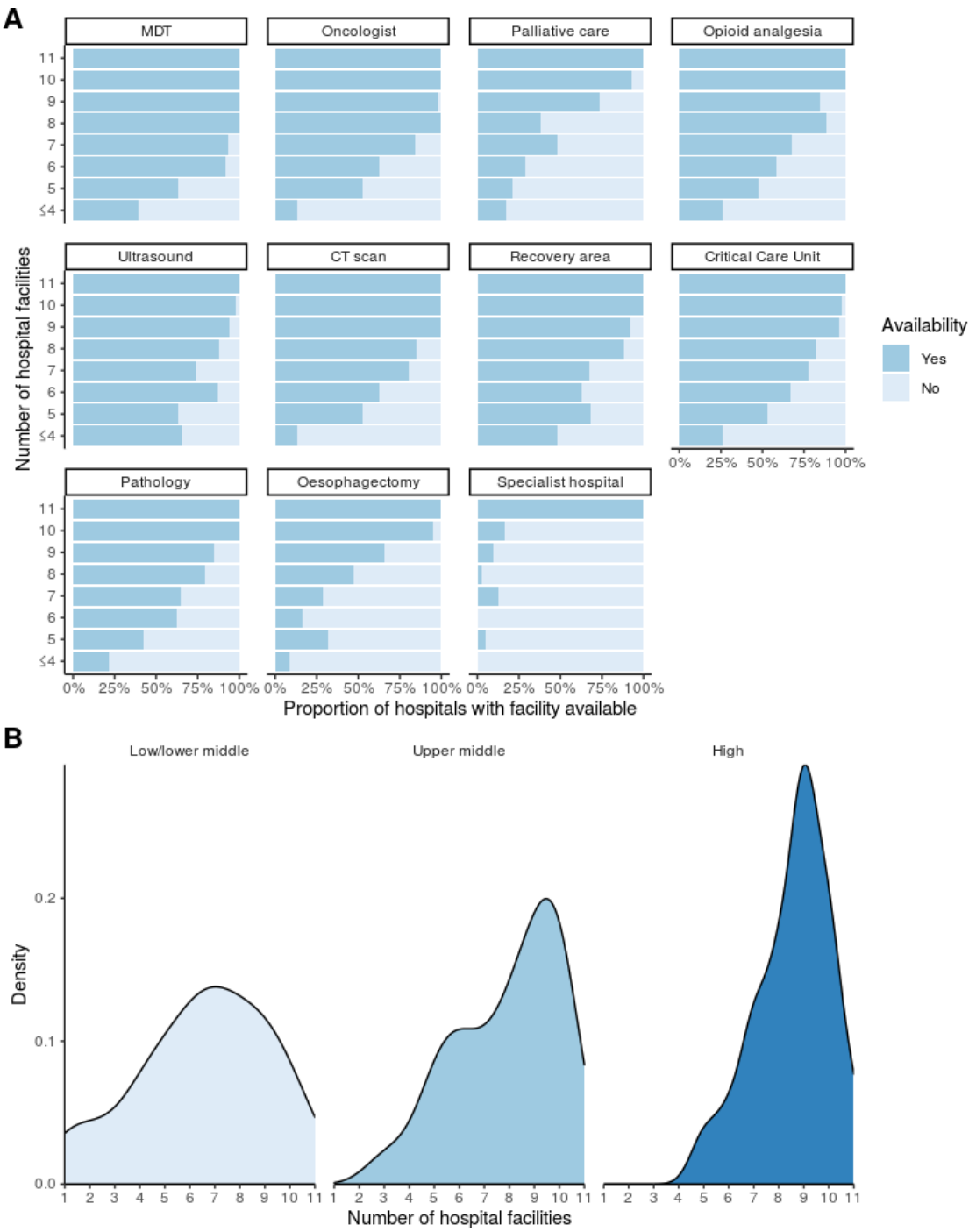


Figure 6-3. Distribution of outcomes across total number of hospital facility characteristics.

Minor complication: Clavien-Dindo grade I or II; Major complication: Clavien-Dindo grade III or IV; All complications: Clavien-Dindo grade I-V. Material from [220].

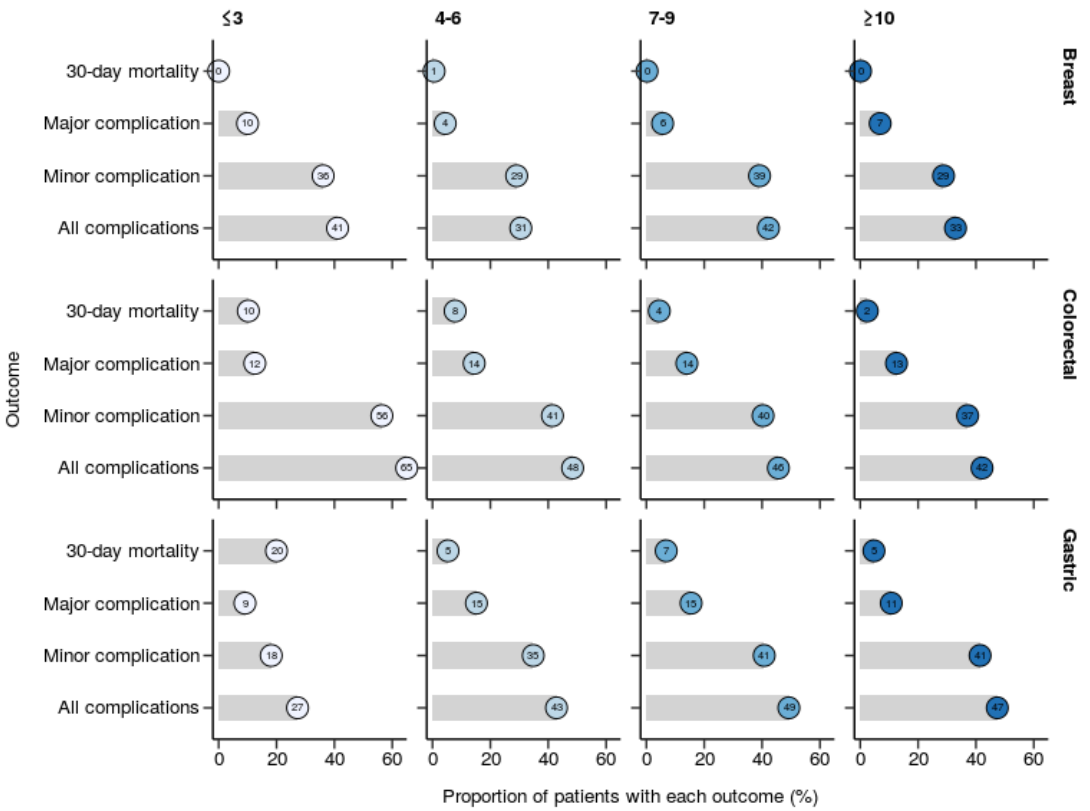


Table 6-2. Adjusted mortality rates stratified by hospital inclusion.

Adjusted mortality rates were calculated using generalised estimating equations (GEE) to account for potential confounders (WB tertile, age, sex, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with all confounders as covariates.

WB tertile	Hospital-level data available	Hospital number	Patient number	Adjusted mortality (95% CI)	Odds ratio	P
High	Yes	90	3202	1.4 (1.3 to 1.5)	Ref	
	No	150	5038	1.4 (1.3 to 1.5)	0.98 (0.67 to 1.42)	0.92
Upper middle	Yes	57	2011	2.2 (2 to 2.4)	Ref	
	No	24	563	2.2 (1.8 to 2.6)	0.97 (0.51 to 1.86)	1.00
Low/lower middle	Yes	91	3655	2.5 (2.3 to 2.7)	Ref	
	No	16	186	4.3 (3.3 to 5.4)	1.76 (0.84 to 3.68)	0.15

Table 6-3. Hospital facility selection using backward elimination.

Hospital facility	Coefficient	Standard error	Z value	P	Final model
Intercept	-1.79387	0.37231	-4.818	<0.001	-
MDT	0.16836	0.44184	0.381	0.7032	-
Oncologist	-0.30738	0.13607	-2.259	0.0239	Included
Palliative care	0.06800	0.17714	0.384	0.7011	-
Opioid analgesia	-0.53143	0.20977	-2.533	0.0113	Included
Ultrasound	-0.49329	0.24598	-2.005	0.0449	Included
CT scan	-0.70332	0.23303	-3.018	0.0025	Included
Recovery area	-0.30676	0.20158	-1.522	0.1281	-
Critical Care unit	-0.30738	0.13607	-2.259	0.0239	Included
Pathology	0.01728	0.25915	0.067	0.9468	-
Hospital type	-0.57405	0.30024	-1.912	0.0559	-
Oesophagectomy	-0.11290	0.16960	-0.666	0.5056	-

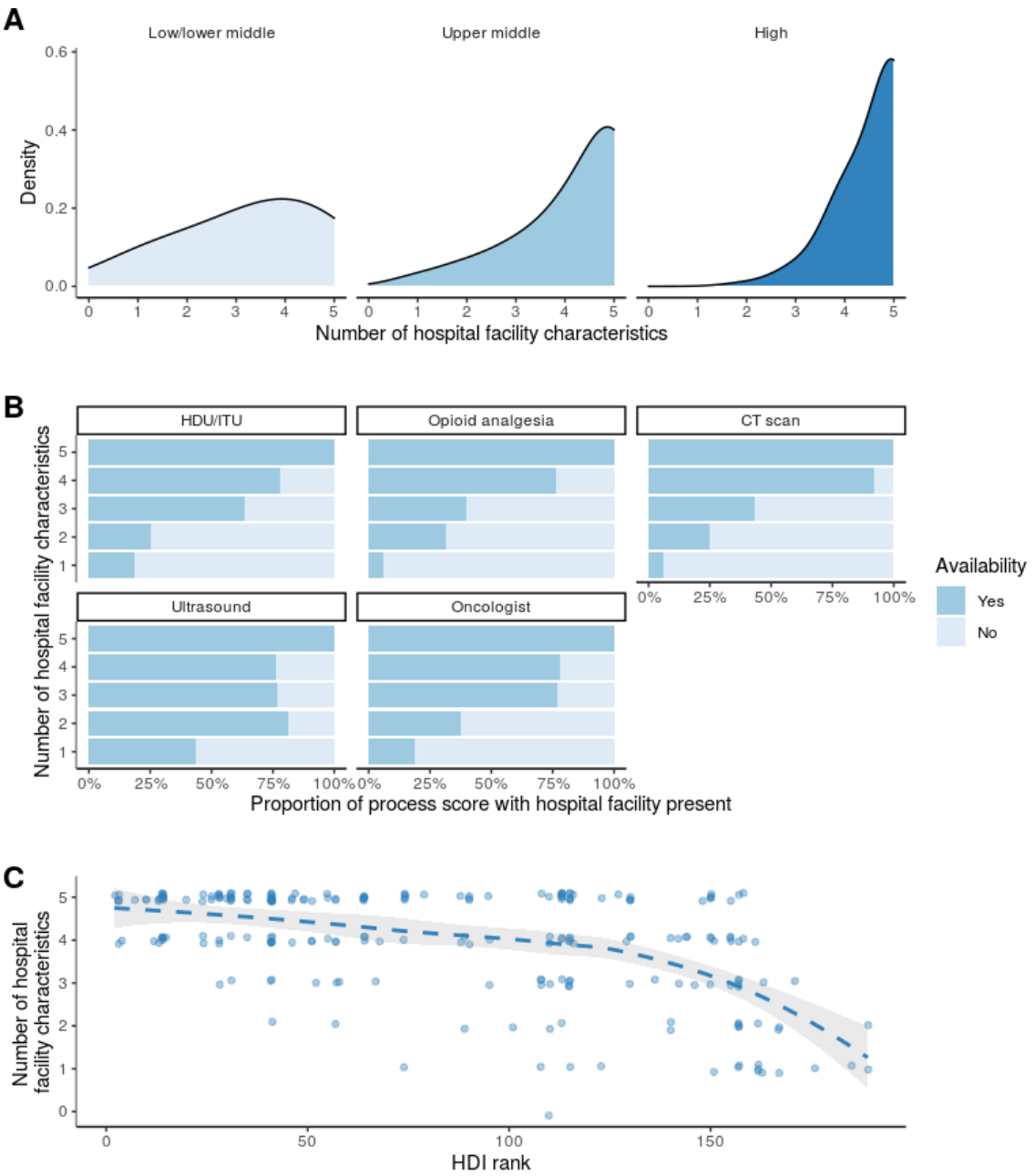
Table 6-4. Hospital facility selection sensitivity analysis.

Performed using bootstrap procedure (n=5000).

Hospital facility	Selected (%)	Deviance	Residual degrees of freedom	Residual deviation	AIC	Final model
CT scan	91.65	-	-	-	-	Included
Opioid analgesia	84.80	-	-	-	-	Included
Ultrasound	83.35	-	-	-	-	Included
Oncologist	71.80	-	-	-	-	Included
Critical Care unit	69.90	-	-	-	-	Included
Hospital type	38.35	0.001	9555	1843.525	1869.525	-
Recovery area	33.90	0.004	9556	1843.53	1867.530	-
Oesophagectomy	29.70	0.551	9560	1844.437	1860.437	-
Palliative care	26.60	0.145	9558	1843.679	1863.679	-
MDT	24.30	0.207	9559	1843.886	1861.886	-
Pathology	22.65	0.004	9557	1843.534	1865.534	-

Figure 6-4. Distribution of hospital facility characteristics worldwide.

By country income group (A), individual hospital facility (B), and Human Development Index (C). Material from [220].



Following categorisation by patient distribution, three hospital capability tertiles were identified (five facility capacities, 113 hospitals; four facility capacities, 63 hospitals; three or less capacities, 62 hospitals). Patient distribution across these three categorised hospital facility levels is shown in Table 6-5. Patients treated in hospitals with three or less facility characteristics were more likely to be from low-income settings and present with colorectal or gastric cancer. Also, these patients had poorer performance status, advanced disease and were more likely to require an emergency operation.

Hospitals with three or less facility characteristics were less likely to use the surgical safety checklist (73.6 vs. 83.7% for hospitals with more than three facilities; P<0.001), achieve a negative resection margin (87.5 vs. 90.8; P=0.001), review patients in clinic after discharge (45.6 vs. 75.9%; P<0.001), discuss patient management through a multidisciplinary tumour board (31.3 vs. 78.3%; P<0.001), and had longer in-patient stays (5 days [IQR 3-9] vs. 3 [1-7]; P<0.001), compared to hospitals with more facility characteristics (Table 6-6). The availability of surgical treatment for common cancer types was also reduced in hospitals with three or fewer facilities (Table 6-7).

6.3.3 Multilevel Logistic Regression Modelling

After adjusting for patient and disease factors, mortality rates were higher in hospitals with three or less facility characteristics across all cancers (3.7 vs. 1.0%, OR 3.85, 2.58-5.75; P<0.001; Table 6-8). No difference in adjusted mortality rates were seen in hospitals with four characteristics as compared to five. A sub-analysis showed a similar finding in patients with colorectal and gastric cancer patients (6.9 vs 4.1%; OR 1.73, 1.18-2.52; P=0.006; Table 6-8). Both effects were robust in sensitivity analysis (Table 6-9 and Table 10-30).

Table 6-5. Patient characteristics by hospital facility characteristic level.

Numbers are n (%) or mean (SD). High income included 20 countries and 91 hospitals. Upper-middle income included 19 countries and 57 hospitals. Lower-middle income or low income included 27 countries and 90 hospitals. The total column therefore includes 66 countries and 238 hospitals. ASA=American Society of Anesthesiologists. ECOG=Eastern Cooperative Oncology Group.

Hospital facility level		5 (n = 6378)	4 (n = 2013)	≤3 (n = 1294)	P
Distribution of patients across WB income (tertile)	High	2669 (41.8)	867 (43.1)	100 (7.7)	<0.001
	Upper middle	1375 (21.6)	251 (12.5)	493 (38.1)	
	Low/lower middle	2334 (36.6)	895 (44.5)	701 (54.2)	
Cancer type	Breast	3834 (60.1)	1192 (59.2)	625 (48.3)	<0.001
	Colorectal (colon or rectum)	2010 (31.5)	654 (32.5)	534 (41.3)	
	Gastric (stomach)	534 (8.4)	167 (8.3)	135 (10.4)	
Age (years)		57.9 (14.4)	58.5 (14.2)	56.2 (13.8)	<0.001
Sex (%)	Male	1489 (23.3)	465 (23.1)	379 (29.3)	<0.001
	Female	4886 (76.6)	1546 (76.8)	914 (70.6)	
	(Missing)	3 (0.0)	2 (0.1)	1 (0.1)	
ECOG performance status	0	3668 (57.5)	1007 (50.0)	612 (47.3)	<0.001
	1	1520 (23.8)	519 (25.8)	356 (27.5)	
	2	750 (11.8)	226 (11.2)	157 (12.1)	
	3/4	198 (3.1)	94 (4.7)	115 (8.9)	
	(Missing)	242 (3.8)	167 (8.3)	54 (4.2)	

ASA	I	1385 (21.7)	387 (19.2)	382 (29.5)	<0.001
	II	3469 (54.4)	1099 (54.6)	668 (51.6)	
	III	1191 (18.7)	359 (17.8)	148 (11.4)	
	IV	89 (1.4)	32 (1.6)	22 (1.7)	
	V	6 (0.1)	11 (0.5)	3 (0.2)	
	(Missing)	238 (3.7)	125 (6.2)	71 (5.5)	
Stage	0	192 (3.0)	51 (2.5)	11 (0.9)	<0.001
	I	2631 (41.3)	812 (40.3)	334 (25.8)	
	II	593 (9.3)	216 (10.7)	146 (11.3)	
	III	2456 (38.5)	777 (38.6)	608 (47.0)	
	IV	453 (7.1)	146 (7.3)	179 (13.8)	
	(Missing)	53 (0.8)	11 (0.5)	16 (1.2)	
Urgency	Elective	6081 (95.3)	1850 (91.9)	1180 (91.2)	<0.001
	Emergency	295 (4.6)	161 (8.0)	114 (8.8)	
	(Missing)	2 (0.0)	2 (0.1)	0 (0.0)	
30-day mortality	Alive	6210 (97.4)	1947 (96.7)	1216 (94.0)	<0.001
	Dead	97 (1.5)	42 (2.1)	56 (4.3)	
	(Missing)	71 (1.1)	24 (1.2)	22 (1.7)	
Major complication	Yes	603 (9.5)	192 (9.5)	143 (11.1)	0.178
	No	5744 (90.1)	1800 (89.4)	1136 (87.8)	
	(Missing)	31 (0.5)	21 (1.0)	15 (1.2)	

Table 6-6. Relationship between hospital facility level and patient safety and quality of cancer care metrics.

Numbers are n (%) or median (IQR). Negative resection margins were defined according to National Institute for Clinical Excellence Guidance and guidelines. MDT, multidisciplinary team.

Hospital facility level		5 (n = 6378)	4 (n = 2013)	≤3 (n = 1294)	P
Surgical safety checklist used		5160 (83.1)	1712 (85.4)	910 (73.6)	<0.001
Anastomosis performed		1949 (77.9)	604 (76.2)	467 (72.9)	0.024
Negative margin		5403 (90.9)	1612 (90.7)	948 (87.5)	0.002
Length of stay (days)		3.0 (1.0 to 7.0)	3.0 (1.0 to 7.0)	5.0 (3.0 to 9.0)	<0.001
Readmission		309 (4.9)	88 (4.5)	68 (5.4)	0.490
Method of follow-up at 30 days	Still inpatient or readmitted	168 (2.7)	82 (4.1)	79 (6.2)	<0.001
	Clinic review	4978 (79.4)	1295 (64.9)	584 (45.6)	
	Telephone review	882 (14.1)	532 (26.7)	578 (45.2)	
	Community/home review	21 (0.3)	6 (0.3)	1 (0.1)	
	Discharged before 30 days and not contacted again	219 (3.5)	79 (4.0)	38 (3.0)	
Radiotherapy available		5280 (82.8)	1340 (66.6)	588 (45.4)	<0.001
Chemotherapy available		6091 (95.5)	1717 (85.3)	958 (74.0)	<0.001

Multidisciplinary tumour board available for all cancers treated in hospital	5269 (82.6)	1299 (64.5)	405 (31.3)	<0.001

Table 6-7. Proportion of hospitals performing elective operations for each cancer across hospital facility level.

Operation	5 (n = 113)	4 (n = 63)	≤3 (n = 62)	P
Breast	101 (89.4)	53 (84.1)	55 (88.7)	0.575
Oesophagus	76 (67.3)	28 (44.4)	20 (32.3)	<0.001
Lung	73 (64.6)	24 (38.1)	13 (21.0)	<0.001
Gastric	104 (92.0)	52 (82.5)	46 (74.2)	0.006
Liver	80 (70.8)	30 (47.6)	17 (27.4)	<0.001
Pancreas	86 (76.1)	30 (47.6)	22 (35.5)	<0.001
Renal	98 (86.7)	43 (68.3)	41 (66.1)	0.002
Colorectal	111 (98.2)	59 (93.7)	58 (93.5)	0.206
Rectum	108 (95.6)	52 (82.5)	49 (79.0)	0.002
Cervical	93 (82.3)	44 (69.8)	43 (69.4)	0.074
Ovarian	97 (85.8)	44 (69.8)	44 (71.0)	0.017

Table 6-8. Adjusted mortality rate across hospital facility characteristic count.

Adjusted mortality rates were calculated using generalized estimating equations (GEE) to account for clustering of patients by hospital and potential confounders (WB tertile, age, sex, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with the number of hospital characteristics and all confounders as covariates.

	Hospital facility level	Hospital number (%)	Number of Patients (%)	Adjusted mortality (95% CI)	Odds ratio	P
All cancers	5	113 (47.7)	5912 (66.6)	1 (0.7 to 1.2)	Ref	
	4	63 (26.6)	1787 (20.2)	1.5 (0.9 to 2)	1.49 (0.94 to 2.37)	0.092
	≤3	61 (25.7)	1169 (13.2)	3.7 (2.6 to 4.8)	3.85 (2.58 to 5.75)	<0.001
Colorectal and gastric cancer	5	105 (48.0)	2388 (63.8)	4.1 (3.8 to 4.3)	Ref	
	4	57 (26.0)	753 (20.1)	5.2 (4.6 to 5.8)	1.29 (0.88 to 1.89)	0.217
	≤3	57 (26.0)	602 (16.1)	6.9 (6 to 7.8)	1.73 (1.18 to 2.52)	0.006

Table 6-9. Sensitivity analysis using imputed dataset for adjusted mortality.

Adjusted mortality rates were calculated using generalised estimating equations (GEE) to account for clustering of patients in hospital and for potential confounders (WB tertile, age, sex, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with the number of hospital facilities and all confounders as covariates.

	Hospital facility level	Hospital number	Patient number	Adjusted mortality rate (95% CI)	Odds ratio	P
All cancers	5	215	9617	1.5 (1.4 to 1.6)	Ref	
	4	140	3736	1.9 (1.8 to 2.1)	1.29 (0.97 to 1.72)	0.079
	≤3	72	1302	4.8 (4.2 to 5.3)	3.29 (2.43 to 4.46)	<0.001
Colorectal and gastric cancer	5	205	4407	3.0 (2.9 to 3.2)	Ref	
	4	127	1932	3.5 (3.2 to 3.8)	1.15 (0.86 to 1.56)	0.350
	≤3	66	670	9.1 (8 to 10.1)	3.22 (2.35 to 4.41)	<0.001

Table 6-10. Adjusted major complication rates across hospital facility characteristic count.

Adjusted major complication rates were calculated using generalized estimating equations (GEE) to account for clustering of patients by hospital and potential confounders (WB tertile, age, sex, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with the number of hospital characteristics and all confounders as covariates.

	Hospital facility level	Hospital number (%)	Number of Patients (%)	Adjusted major complication rate (95% CI)	Odds ratio	P
All cancers	5	113 (47.5)	5951 (66.7)	9.3 (9.1 to 9.5)	Ref	
	4	63 (26.5)	1789 (20.1)	9.6 (9.2 to 9.9)	1.03 (0.86 to 1.23)	0.746
	≤3	62 (26.0)	1175 (13.2)	11.8 (11.2 to 12.3)	1.30 (1.06 to 1.58)	0.011
Colorectal and gastric cancer	5	105 (47.7)	2405 (63.8)	13.5 (13.2 to 13.8)	Ref	
	4	57 (26.0)	755 (20.1)	15.9 (15.2 to 16.6)	1.21 (0.97 to 1.52)	0.105
	≤3	58 (26.3)	608 (16.1)	18.0 (17.1 to 18.8)	1.40 (1.11 to 1.78)	0.008

Table 6-11. Capacity to rescue patients following major complication following case-mix adjustment.

Adjusted mortality rates after major complication were calculated using generalized estimating equations (GEE) to account for clustering of patients by hospital and potential confounders (WB tertile, age, sex, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with the number of hospital characteristics and all confounders as covariates.

	Hospital facility level	Hospital number (%)	Number of Patients (%)	Adjusted capacity to rescue (95% CI)	Odds ratio	P
All cancers	5	86 (50.6)	569 (65.0)	82.7 (81.1 to 84.4)	Ref	
	4	43 (25.3)	173 (19.7)	77.9 (74.6 to 81.3)	0.74 (0.49 to 1.13)	0.184
	≤3	41 (24.1)	134 (15.3)	63.0 (58.4 to 67.6)	0.35 (0.23 to 0.53)	<0.001
Colorectal and gastric cancer	5	73 (49.3)	320 (58.3)	71.5 (69.3 to 73.7)	Ref	
	4	41 (27.7)	119 (21.7)	69.5 (65.5 to 73.5)	0.92 (0.58 to 1.45)	0.723
	≤3	34 (23.0)	110 (20.0)	56.4 (51.8 to 60.9)	0.51 (0.33 to 0.8)	0.004

Table 6-12. Sensitivity analysis using imputed dataset for capacity to rescue.

Adjusted mortality rates after major complication were calculated using generalised estimating equations (GEE) to account for clustering of patients in hospital and for potential confounders (WB tertile, age, sex, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with the number of hospital facilities and all confounders as covariates.

	Hospital facility level	Hospital number	Patient number	Adjusted capacity to rescue (95% CI)	Odds ratio	P
All cancers	5	175	940	84.7 (83.6 to 85.9)	Ref	
	4	97	377	81.0 (78.9 to 83.0)	0.77 (0.56 to 1.05)	0.100
	≤3	49	148	57.9 (53.3 to 62.5)	0.25 (0.17 to 0.36)	<0.001
Colorectal and gastric cancer	5	156	599	78.0 (76.5 to 79.5)	Ref	
	4	93	289	76.9 (74.6 to 79.2)	0.94 (0.67 to 1.31)	0.730
	≤3	40	122	50.0 (45.5 to 54.5)	0.28 (0.19 to 0.42)	<0.001

Adjusted 30-day major complication rates were higher in hospitals with three or less facility characteristics (11.8 vs 9.3%, OR 1.30, 1.06-1.58; P=0.011) and for patients following colorectal and gastric cancer surgery (18.0 vs. 13.5%, OR 1.40, 1.11-1.78; P=0.008; Table 6-10). After the development of a major complication, the capacity to rescue patients was significantly lower in hospitals with reduced infrastructure and processes (63.0 vs. 82.7%, OR 0.35, 0.23-0.53; P<0.001: Table 6-11). These effects persisted in sensitivity analysis (Table 6-12 and Table 10-32).

The absolute risk differences for 30-day mortality across hospital capability were examined for common patient covariates in patients with colorectal and gastric cancer (Figure 6-5). The presence of four or more hospital facility characteristics were associated with fewer deaths in both the low-income and lower-middle-income group (two to three fewer deaths per 100 operations, number needed to treat 33-50), upper-middle-income group (one to two fewer deaths per 100 operations, number needed to treat 50-100) and high-income groups (one fewer death per 100 operations, number needed to treat 100).

I determined the absolute risk for 30-day mortality for higher risk surgical patients, using common patient covariates for patients with an ASA grade of three or higher (Figure 6-6). An increase in absolute risk difference was found across different levels of hospital capability for all income groups; low-income and lower-middle-income group (four to five fewer deaths per 100 operations, number needed to treat 20-25), upper-middle-income group (two to three fewer deaths per 100 operations, number needed to treat 33-50) and high-income groups (one fewer death per 100 operations, number needed to treat 100).

Figure 6-5. Absolute risk for 30-day mortality associated with four or more hospital facility characteristics within each income group stratified by cancer type and sex.

Estimates for a patient of age 60 years, performance status 1, ASA grade 2, cancer stage III, and elective surgery. Material from [220].

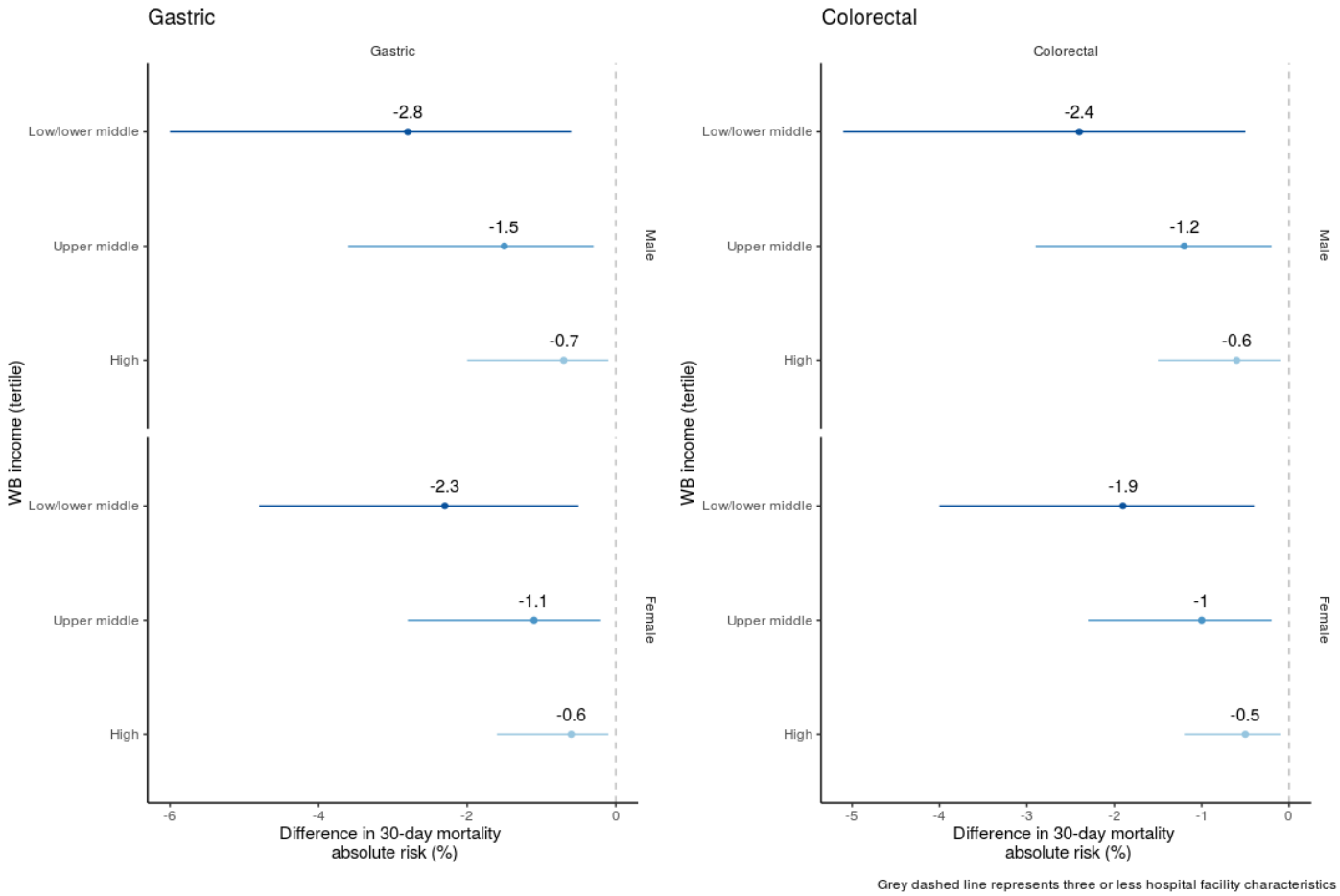
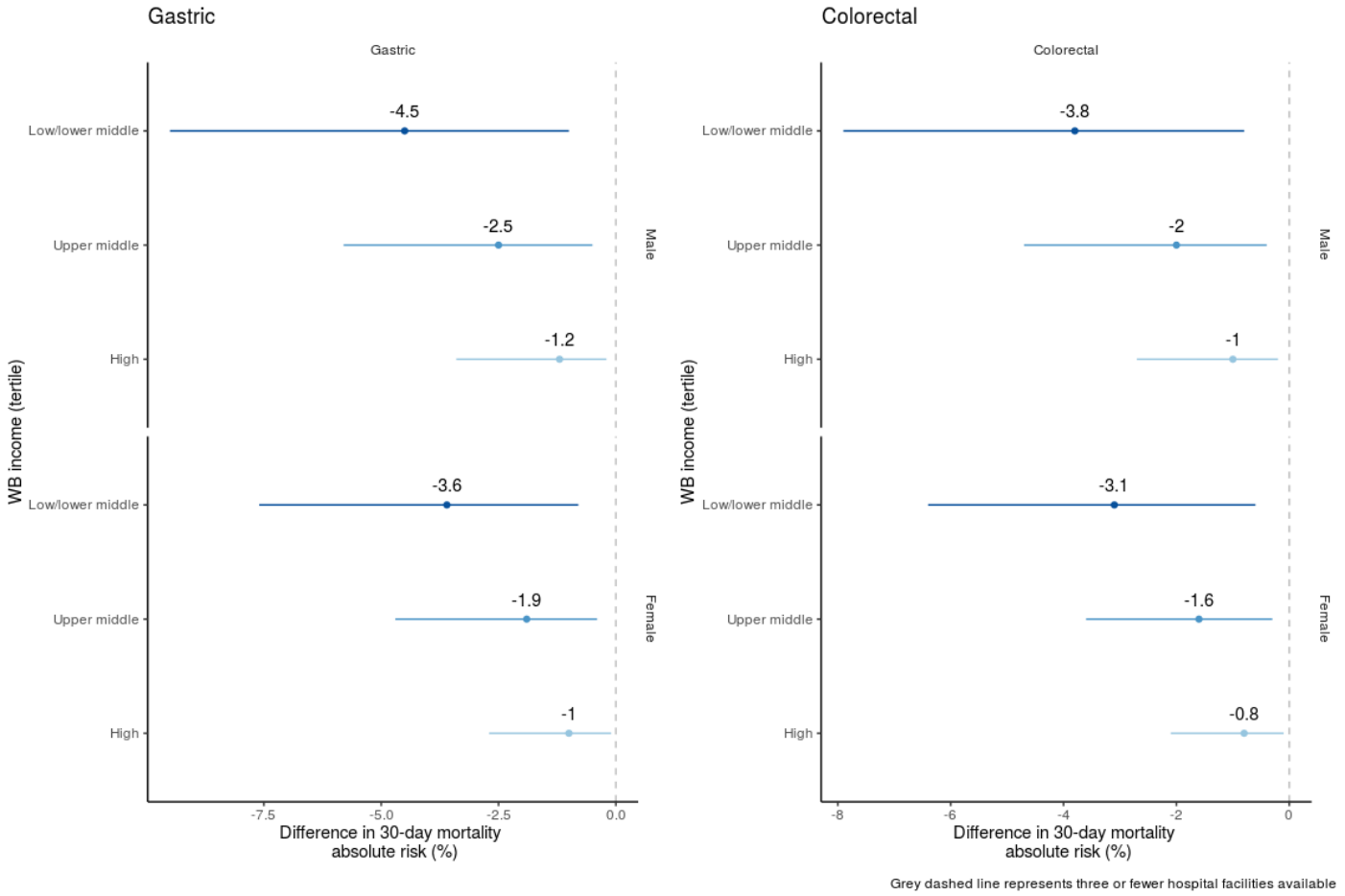


Figure 6-6. Absolute risk for 30-day mortality associated with four or more hospital facilities within each income group stratified by cancer type and sex for higher risk surgical patients.

Estimates for age 70 years, performance status 3 or 4, ASA grade ≥3, cancer stage III, and elective surgery. Material from [220].



6.4 Discussion

6.4.1 Summary of key findings in context of previous literature

In this prospective study of patients undergoing cancer surgery in 238 hospitals from 66 countries, higher availability of specific hospital infrastructure and resources were associated with improved outcomes. Well-resourced hospitals had less than half the postoperative mortality rate, demonstrating an improved ability to prevent death following the development of postoperative complications, with up to three fewer deaths per 100 operations performed. Importantly, these findings were independent of country income group. Improving hospital resources has long been thought to influence clinical outcomes in lower income settings; the magnitude of this effect is now clear.

Despite the overall mortality benefit seen in hospitals with more resources and strong processes, many patients do not have access to such hospital infrastructure, particularly in low income settings[221]. Improvements in hospital facilities are known to be cost-effective[181], however the absence of high-quality data limits interpretability, while the impact of specific hospital facilities on outcomes following cancer surgery worldwide were previously unclear. Strategic planning requires detailed and accurate information to allocate appropriate resources, prioritise quality improvement and evaluate their effects. Determining the effectiveness of hospital infrastructure can guide future investment and provide a platform for continued assessment of hospital performance.

6.4.2 Policy implications

My results offer a concrete approach by focusing on specific infrastructure and resources in hospitals worldwide. Such hospitals perform significantly better than others without them: in the 62 hospitals with three or fewer facilities, mortality rates were three times higher than in the 113 hospitals with all facilities present. This difference was explained by a 50% increase in the capacity to rescue patients following the development of a major complication. These relationships were robust in sensitivity analysis and a similar trend was identified when all eleven hospital facilities were included. This suggests that a strategy of expanding system capabilities at hospitals, particularly in low- and middle-income settings, could markedly improve outcomes and patient access to safe, effective surgical care.

Others have found similar relationships between key hospital facilities and mortality. Funk *et al* found that the presence of complex medical oncology services and specific radiology services were important to lowering mortality in oesophagectomy patients[182]. Similarly, Joseph *et al* found that several institutional characteristics had a stronger influence on operative mortality following pancreatic resection than hospital volume[222]. However, differences in major morbidity following surgery are often undescribed[182,184].

6.4.3 Strengths of this study

This study is the first global analysis to assess the impact of hospital facilities on short-term outcomes following cancer surgery. The synergistic effect of scaling up of imaging, treatments and quality in low-income settings on oncological outcomes has recently been

shown[181,223]. In particular, investments in imaging modality availability are a critical component for comprehensive improvement in global cancer survival[181].

However, caution must be taken when interpreting my results. I suspect that these facilities are markers for the expertise, resources, and complex processes of care required to facilitate surgery, including the optimisation of preoperative, intraoperative and postoperative care for patients undergoing surgery for cancer. It is unlikely that the presence of a CT scanner will directly improve patient outcomes without associated investment in additional supportive capacity, such as healthcare workers and technical support.

The five key facilities that were included in my multivariable models are likely indirect markers for other structural and process measures that are also closely related to outcomes following cancer surgery. For example, I found hospitals with more resources were more likely to use the WHO surgical safety checklist and achieve negative resection margins, potentially reflecting related organisational processes associated with these facilities. A similar pattern in outcomes was demonstrated in models including all eleven hospital facilities originally assessed, suggesting the five identified in my analysis may also reflect further development of additional hospital services.

Higher levels of hospital facilities were also associated with increased access to surgical care for a broad range of cancer types. The majority of hospitals with all five facilities present were able to perform elective operations for eleven different cancers, which represent 60% of all incident cancers and 70% cancer deaths worldwide over the next ten years[181]. Patients also presented with earlier stage disease, suggesting hospital facility improvement may be associated with concurrent investment in early detection programmes

and strengthening of healthcare systems. Similar outcomes were demonstrated between hospitals with four or five key facilities, which may suggest a ceiling effect between expanding system capabilities and outcome improvement.

Centres providing cancer care worldwide vary in size, scale and structure. Designated cancer centres, referral networks, and standardized cancer pathways are underdeveloped or absent in many LMICs[224]. The centralisation of services into comprehensive cancer centres, supported by my analysis, is likely to improve quality of care, particularly in resource-constrained environments. However, centralization can unintentionally reduce access to safe and effective cancer care, secondary to geographic and financial barriers for patients, particularly in the absence of robust referral mechanisms[173]. Therefore, selection of a geographical location to serve the greatest number of patients, whilst defining the minimum requirements of a comprehensive cancer centre, are crucial[224]. Efforts to improve the quality of cancer care must occur alongside efforts to increase access to care, in order to maximise health gains and develop equitable cancer systems.

6.4.4. Study limitations

My study has important limitations. I have detailed hospital-level data for 55% of hospitals included within the primary analysis, with responses lower from high-income hospitals. However, I covered 87% patients in LMIC settings, where the majority of all cancer deaths occur[225]. Furthermore, case volume and adjusted mortality rates of non-included hospitals were similar, while a sensitivity analysis demonstrated robust findings across all measured outcomes. Therefore, a relationship between missing responses and measured outcomes is unlikely. Meanwhile despite including validated measures of overall patient health, I was

unable to account for detailed patient comorbidity across income group within the adjusted models due to the burden of additional data collection, particularly in low resource settings.

The five hospital facilities identified could represent additional, unmeasured structural and complex care processes. Despite capturing a broad range of hospital infrastructure and resources, I was unable to extrapolate my results to all additional resources a hospital may contain. However, as the number of hospital facilities increased, a clear trend in the capacity to rescue patients was demonstrated. Therefore, investment and improvement in overall hospital capability is likely to greatly improve early patient outcomes following cancer surgery. In countries without universal healthcare however, additional investment in hospital facilities must avoid unaffordable increases in total costs to patients for safe surgical care. Further work validating my findings and exploring the effect of specific combinations, particularly in LMIC settings, is required.

I was also unable to follow up patients beyond 30-days after surgery. Little is known about longer-term outcomes such as cancer-free survival in resource-limited settings[52,181]. Nevertheless, postoperative complications following major surgery can influence longer-term outcomes, including patient survival and disability[185]. Longer-term disease and overall survival following surgery may be lower in LMICs, particularly as patients presented with later stage disease. The impact of delayed surgery in life-years lost for stage I to III disease is well described in high-income countries[226], however knowledge gaps exist globally. In addition, only patients undergoing primary surgery for breast, colorectal, or gastric cancers were included, and therefore my conclusions may not translate across other globally prevalent cancers.

Finally, I did not have information on surgeon volume or nurse to bed ratio, which are both known mediators in the relationship between hospital facilities and mortality[222]. Debate still exists whether hospital volume versus hospital process is the primary reason for lower perioperative mortality in cancer surgery[60,222], particularly as available clinical resources often increase with hospital volume[222]. Additional studies are required to determine their impact on hospital mortality globally.

6.4.5 Conclusion

The number of patients undergoing surgery in hospitals with reduced resources and weak processes of care is higher in low and middle-income settings, putting these patients at additional risk. Although early mortality following cancer surgery is known to be elevated in LMICs, the improvement of facilities, processes and quality of care can dramatically reduce perioperative mortality in these settings. A more comprehensive study of systems strengthening and improvement interventions to reduce postoperative mortality would provide important information on mechanisms to impact cancer surgery outcomes for the large numbers of patients who receive care at these institutions.

6.5 Contribution statement

The primary data for this chapter were collected during the GlobalSurg 3 observational study, an international collaborative led by Professor Ewen Harrison. I led the methodology and analyses presented in this chapter from conception to completion and dissemination.

6.6 Outputs relating to this chapter

This study is published in *The Lancet Global Health:*

NIHR Global Health Research Unit on Global Surgery [**Knight SR** first author in writing group] (2022). Effects of hospital facilities on patient outcomes after cancer surgery: an international, prospective, observational study. **Lancet Global Health.** 10, E1003-E1011.

https://doi.org/10.1016/S2214-109X(22)00168-1

I also presented this work as an oral presentation at the Association of Surgeons in Training (ASiT) Conference, March 2021 (virtual).

Chapter 7 The impact of malnutrition on early outcomes after cancer surgery

7.1 Introduction

Patients with cancer commonly suffer from malnutrition, which has been linked with elevated all-cause mortality[227] and worse postoperative outcomes[228]. Patients undergoing surgery for cancer often present with loss of weight, sarcopenia, and in some instances cachexia, which contribute to poorer postoperative outcomes for patients undergoing surgery[229].

A recently published series highlighted that the double burden of malnutrition[230], the simultaneous presence of undernutrition and overnutrition, is increasingly prevalent in LMICs. This burden is likely to have been exacerbated by the COVID-19 pandemic, secondary to delays in diagnosis and subsequent presentation with advanced disease[231]. Treating malnutrition in the perioperative period has been shown to improve outcomes following cancer surgery[232] and has been identified as an area of high research priority in LMICs[31].

Little high-quality data exists on the burden and impact of malnutrition in patients undergoing surgery for cancer worldwide. Retrospective designs, small study samples and inconsistent definitions currently limit global comparisons. I aimed to determine the effect of malnutrition on early postoperative outcomes, 30-day mortality and major

complications, in patients undergoing elective surgery for colorectal or gastric cancer using standardised malnutrition classification criteria.

7.2 Methods

7.2.1 Study Design and participants

For the purposes of this analysis, only colorectal or gastric cancer patients were included due to the known high burden of malnutrition in gastrointestinal cancers patients[227]. Patients who underwent emergency surgery, defined as occurring within 72 hours of admission, were also excluded as preoperative oral nutrition given for less than three days is often ineffective[233].

Nutritional status was defined using the Global Leadership Initiative on Malnutrition (GLIM) criteria[234], using either body mass index (BMI) and percentage weight loss within the preceding six months. Patients were defined as having severe malnutrition if presenting with a BMI <18.5kg/m^2 or >10% weight loss.

A sensitivity analysis using multiple imputations with chained equations was undertaken to account for missing values for all statistical models, under the missing at random assumption. Ten sets, each with ten iterations, were imputed using available patient-level explanatory variables, according to methodology described by Sterne et al[235]. The outcome variable was included as a predictor but excluded from imputation, with Rubin's rules used to combine results[236].

Additional data and analyses which support this Chapter are contained within Appendix 10.5.

7.3 Results

7.3.1 Patient cohort

A total of 5709 patients (colorectal cancer: 4593 patients, gastric cancer: 1116 patients), from 381 hospitals in 75 countries were included (Figure 7-1). Of all patients, 3612 (63.3%) were from high-income, 1135 patients (19.9%) from upper middle-income and 962 (16.8%) from low/lower middle-income countries. Patient characteristics grouped by country income group are shown in Table 7-1.

Overall, one third of patients were severely malnourished at the time of their elective surgery, with a disproportionate burden found in upper middle (44.4%) and low/lower-middle income (66.7%) settings. Severe malnutriton was more likely in patients from upper middle (aOR 2.50, 2.14-2.92; P<0.001) and lower/lower middle income countries (aOR 5.44, 4.54-6.54; P<0.001; Figure 7-2). In addition, gastric cancer, female sex, smoking, and disease stage were independently associated with the presence of severe malnutrition.

7.3.2 Malnutrition and post-operative outcomes

The distribution of unadjusted mortality and complications stratified by nutrition status across income group are shown in Figure 7-3. Severely malnourished patients experienced higher postoperative mortality across all income groups (high 3.2% vs 1.4%, upper middle 3.8 vs. 1.3%, low/lower middle 7.6% vs 2.8%).

Figure 7-1. Patient flowchart for malnutrition analysis.

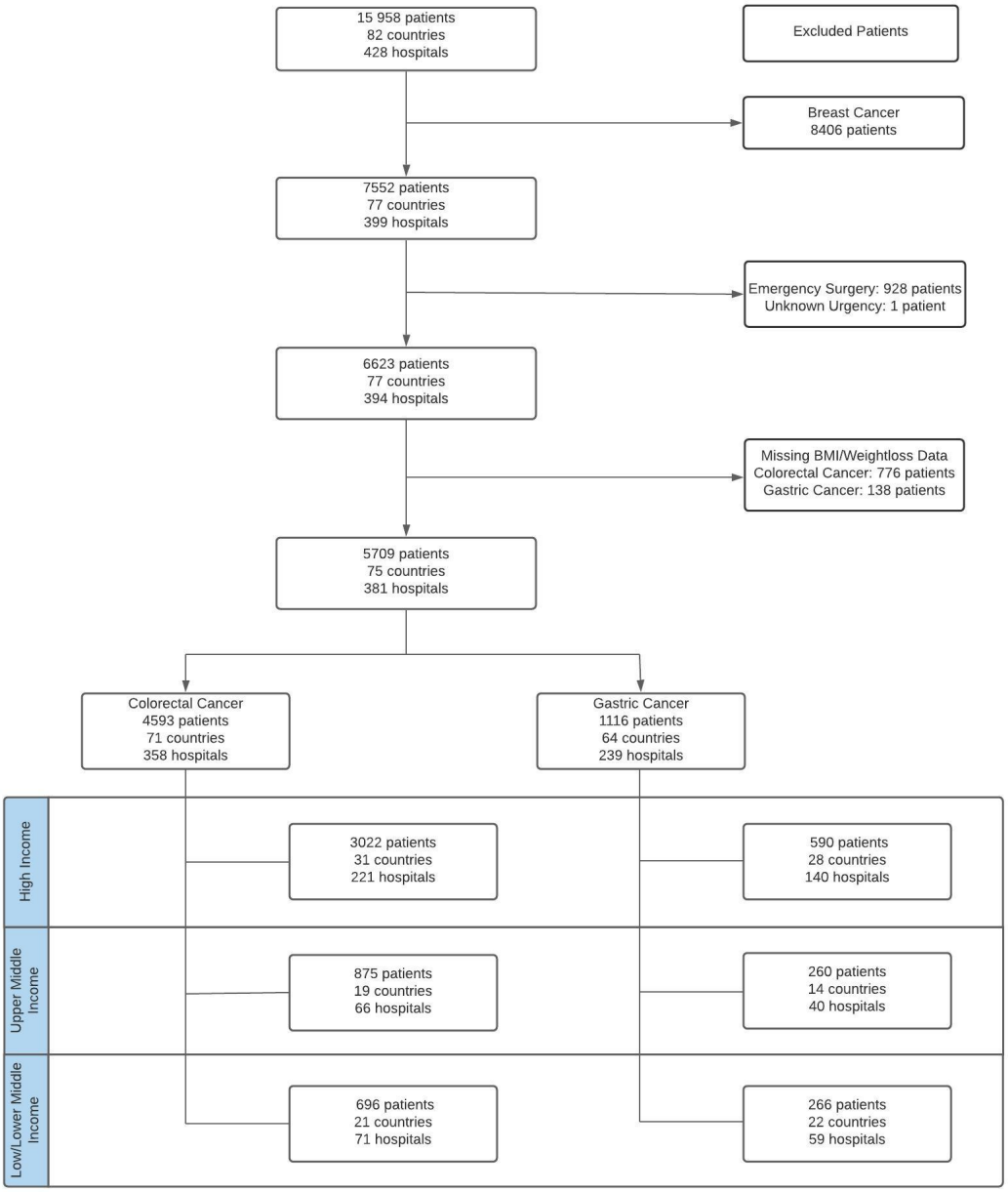


Table 7-1. Patient Characteristics by country income level.

ASA, American Society of Anaesthesiologists Score; ECOG, Eastern Cooperative Oncology Group Performance Status.

		High N = 3612	Upper middle N = 1135	Low/lower middle N = 962
Nutritional Status	No/moderate Malnutrition	2818 (78.0)	631 (55.6)	361 (37.5)
	Severe Malnutrition	794 (22.0)	504 (44.4)	601 (62.5)
Cancer Type	Colorectal (colon or rectum)	3022 (83.7)	875 (77.1)	696 (72.3)
	Gastric (stomach)	590 (16.3)	260 (22.9)	266 (27.7)
Age (years)	Mean (SD)	68.2 (12.3)	62.4 (12.4)	54.7 (13.6)
Sex	Female	1515 (41.9)	493 (43.4)	424 (44.1)
	Male	2093 (57.9)	642 (56.6)	538 (55.9)
	(Missing)	4 (0.1)	0 (0.0)	0 (0.0)
ASA	I	301 (8.3)	234 (20.6)	276 (28.7)
	II	1856 (51.4)	610 (53.7)	522 (54.3)
	III	1305 (36.1)	255 (22.5)	137 (14.2)
	IV	113 (3.1)	21 (1.9)	13 (1.4)
	V	2 (0.1)	0 (0.0)	5 (0.5)
	(Missing)	35 (1.0)	15 (1.3)	9 (0.9)
ECOG performance status	0	1894 (52.4)	642 (56.6)	380 (39.5)
	1	1018 (28.2)	326 (28.7)	357 (37.1)
	2	459 (12.7)	107 (9.4)	131 (13.6)

	3	139 (3.8)	49 (4.3)	72 (7.5)
	4	11 (0.3)	5 (0.4)	10 (1.0)
	(Missing)	91 (2.5)	6 (0.5)	12 (1.2)
Stage	I	1369 (37.9)	233 (20.5)	161 (16.7)
	II	733 (20.3)	280 (24.7)	199 (20.7)
	III	1183 (32.8)	451 (39.7)	456 (47.4)
	IV	318 (8.8)	161 (14.2)	125 (13.0)
	(Missing)	9 (0.2)	10 (0.9)	21 (2.2)
Smoking	No, never	1996 (55.3)	690 (60.8)	692 (71.9)
	Stopped >6 weeks ago	899 (24.9)	200 (17.6)	117 (12.2)
	Yes, current smoker	474 (13.1)	179 (15.8)	123 (12.8)
	(Missing)	243 (6.7)	66 (5.8)	30 (3.1)
Diabetes	No	2898 (80.2)	917 (80.8)	757 (78.7)
	Non-insulin dependent	555 (15.4)	157 (13.8)	104 (10.8)
	Insulin	136 (3.8)	54 (4.8)	46 (4.8)
	(Missing)	23 (0.6)	7 (0.6)	55 (5.7)
BMI	Normal (BMI 18.5 to 24.9)	1446 (40.0)	575 (50.7)	491 (51.0)
	Underweight (BMI <18.5)	115 (3.2)	69 (6.1)	123 (12.8)
	Overweight/Obese (BMI >24.9)	2051 (56.8)	491 (43.3)	348 (36.2)
>10% weight loss	No	2864 (79.3)	646 (56.9)	369 (38.4)
	Yes	748 (20.7)	489 (43.1)	593 (61.6)

Figure 7-2. Multivariable regression model for factors associated with presence of severe malnutrition.

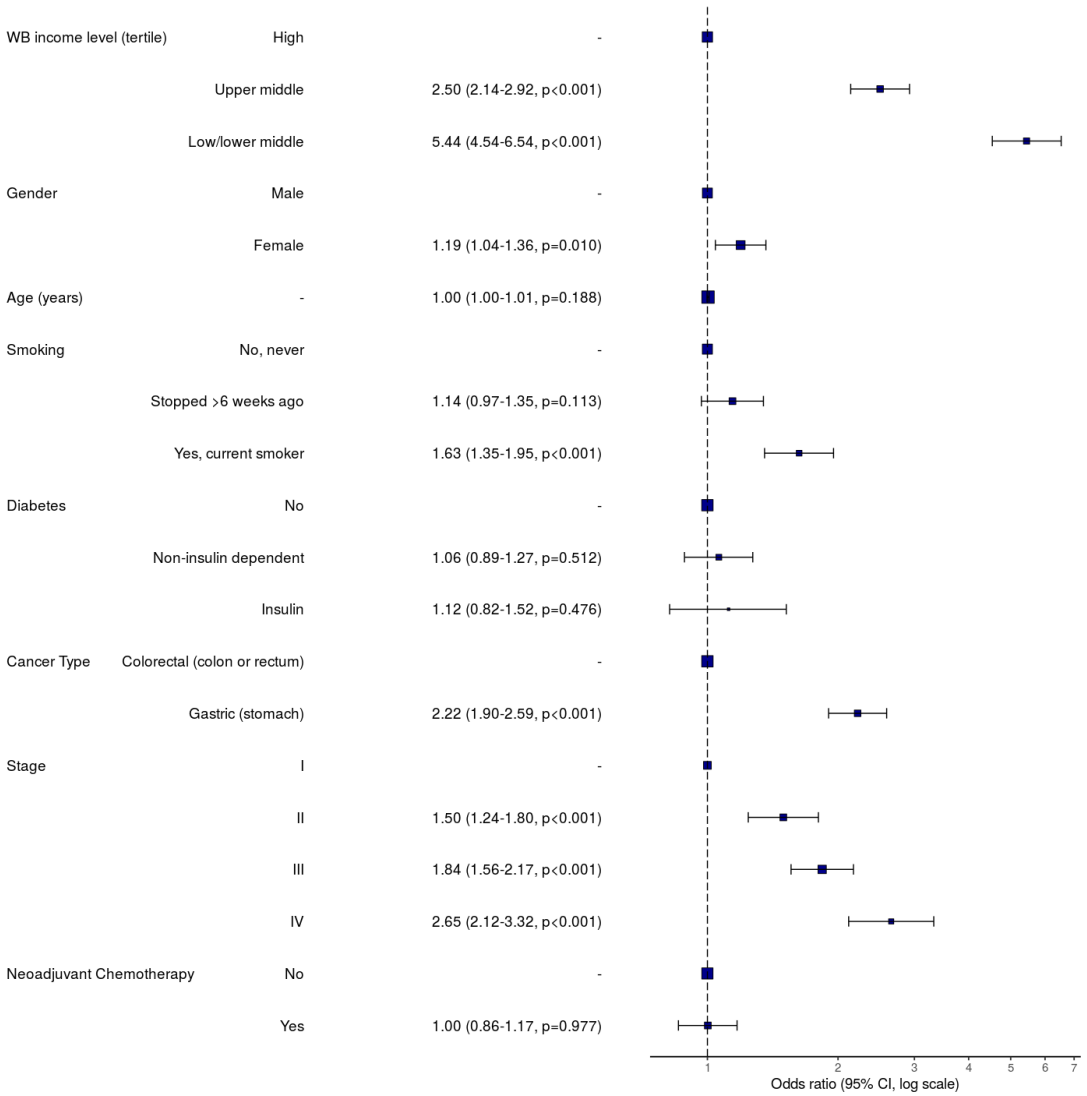
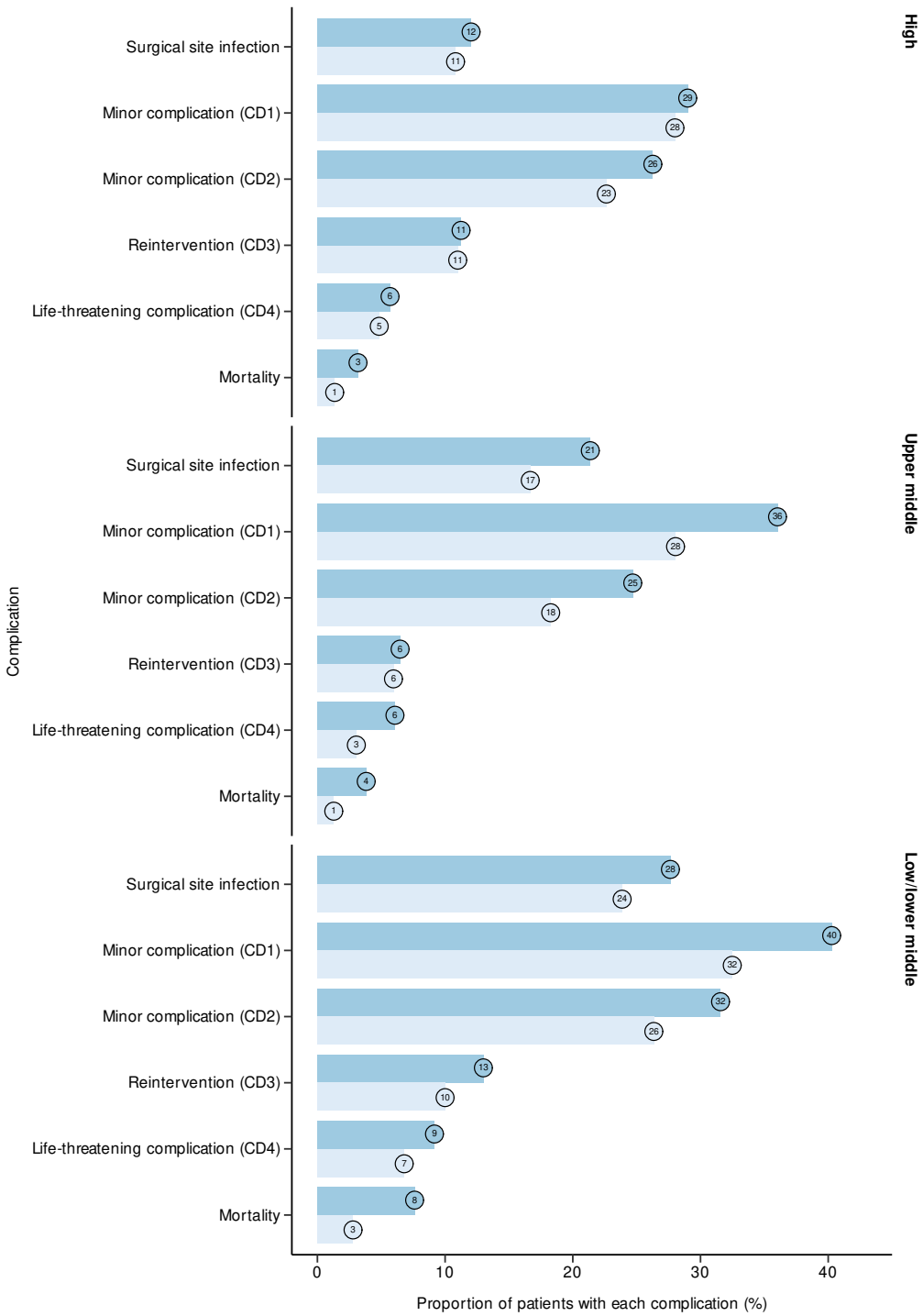


Figure 7-3. Distribution of complications by nutritional state and country income group.



The proportion of patients experiencing postoperative complications or surgical site infection was higher in patients with severe malnutrition, particularly in low/lower income countries. This relationship was similar across both colorectal and gastric cancer (Figure 7-4 and 7-5).

Outcomes were adjusted in three-level models accounting for patient and disease factors nested within hospitals and country of treatment (Figure 7-6). Severe malnutrition was associated with increased risk of 30-day mortality across all income groups (high: aOR 1.96, 95% confidence interval 1.14 to 3.37, p=0.015; upper middle: 3.05, 1.45 to 6.42, p=0.003; low/lower middle: 11.57, 5.87 to 22.80, P<0.001). In low/lower middle income countries, patients without severe malnutrition were also at an increased risk of mortality at 30 days (4.47, 1.81 to 11.03, p=0.001). Similar effects were seen across colorectal and gastric cancer individually (Table 7-2 and 7-3) and in a sensitivity analysis accounting for missing data (Table 7-4; Tables 10-43 to 10-60).

Patients losing >10% of their weight in the 6 months preceding their operation was associated with an increased 30-day mortality (aOR 2.02 1.36 to 2.99, P<0.001), as was being underweight (BMI < 18.5) at the point of undergoing their operation (aOR 2.59, 1.50 to 4.47, p=0.001). Overweight patients appeared to have a lower 30-day mortality, however this was not a significant association (aOR 0.80, 0.65 to 1.18, p=0.259; Figure 7-7).

The proportion of patients sustaining a major complication, any complication, or anastomotic leak in these adjusted analyses was similar across country income groups, except for weak evidence of fewer major complications in the absence of severe malnutrition in the upper middle income group. However, surgical site infection was more

common in patients with severe malnutriton in upper middle (aOR 2.30, 95% CI 1.46 to 3.62; P<0.001) and across all nutritional states in low/lower middle income country groups (no/moderate malnutrition 2.77, 1.70 to 4.51; P<0.001; severe malnutriton 3.00, 95% CI 1.90 to 4.74; P<0.001; Figure 7-8).

7.3.3 Impact of malnutrition in LMICs

The associations between country income group and 30-day mortality (Figure 7-9) and surgical site infection (Figure 7-10) were examined in a three-way decomposition mediation model of nutritional status. A significant proportion of the excess mortality was mediated by severe malnutrition in upper middle (1.18, 1.08 to 1.30, 40%) and low/lower middle countries (1.41, 1.22 to 1.64, 32%) income groups. Meanwhile, excess surgical site infections were also mediated by severe malnutrition in upper middle income (1.04, 1.01 to 1.07, 7%) and low/lower middle (1.08, 1.02 to 1.15, 11%) groups. All effects persisted in a sensitivity analysis (Tables 7-5 and 7-6; Tables 10-61 and 10-62).

Figure 7-4. Distribution of 30-day complications by nutritional state and country income group for colorectal cancer.

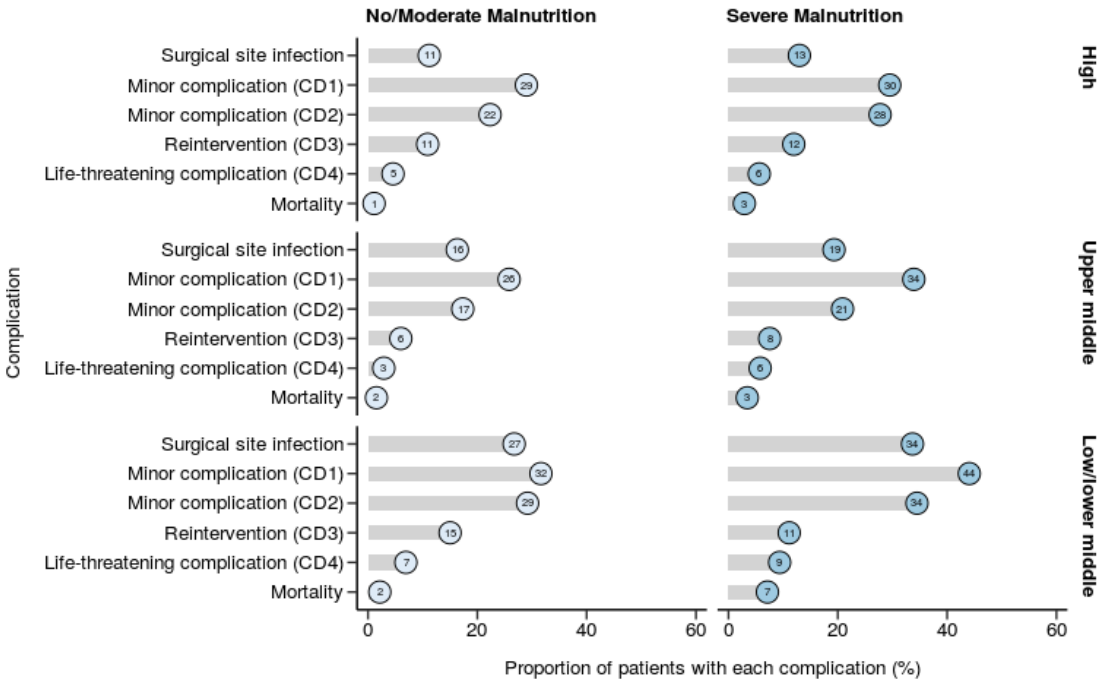


Figure 7-5. Distribution of 30-day complications by nutritional state and country income group for gastric cancer.

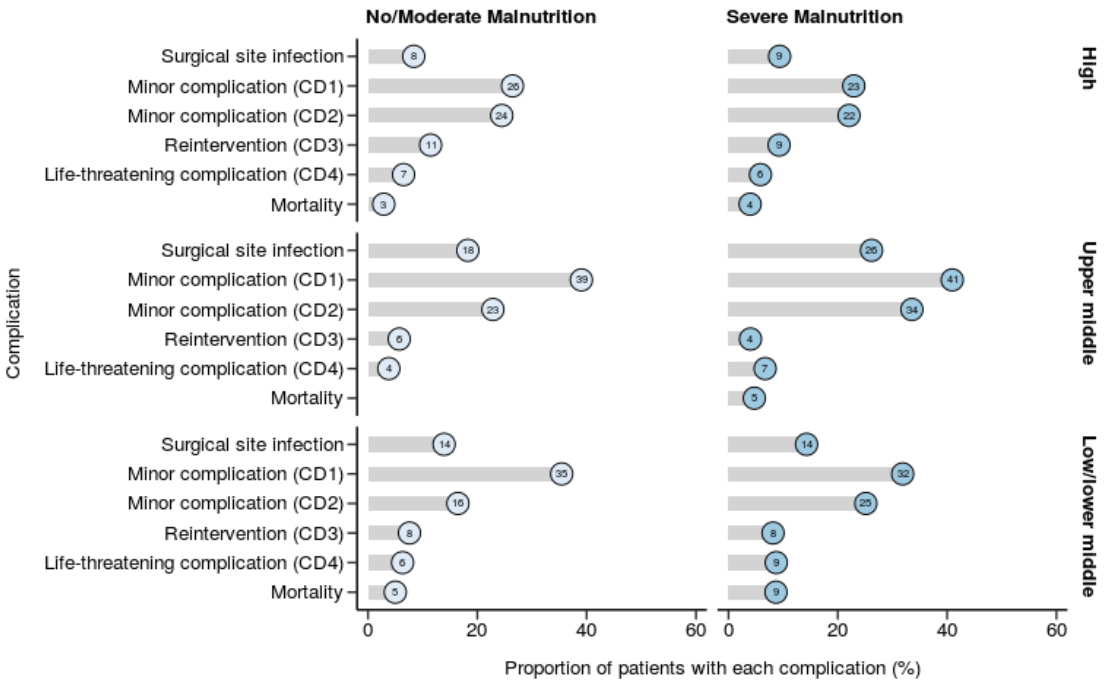


Figure 7-6. Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status.

Model adjusted for cancer type, age, sex, and disease stage, with population stratification by hospital and country of residence. Interaction term between World Bank income group and nutritional status, as defined by the GLIM criteria, included within model.

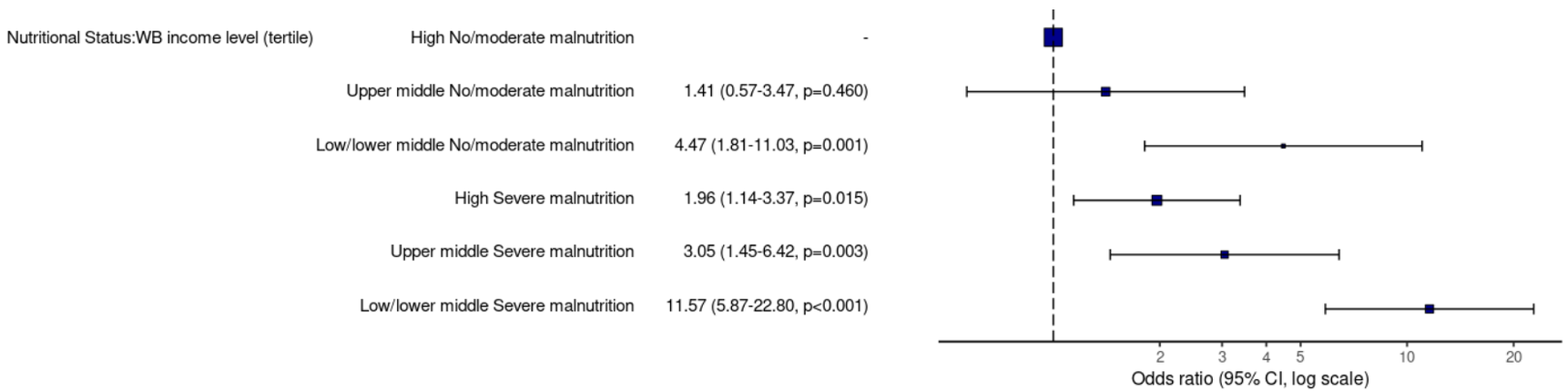


Table 7-2. Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status in patients undergoing surgery for colorectal cancer.

Model adjusted for cancer type, age, sex, and disease stage, with population stratification by hospital and country of residence. Interaction term between World Bank income group and nutritional status, as defined by the GLIM criteria, included within model.

		Alive	Dead	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	2396 (98.9)	27 (1.1)	-
	Upper middle No/moderate malnutrition	510 (98.5)	8 (1.5)	2.21 (0.82-6.02, p=0.119)
	Low/lower middle No/moderate malnutrition	272 (97.8)	6 (2.2)	6.09 (1.97-18.85, p=0.002)
	High Severe malnutrition	567 (97.1)	17 (2.9)	2.30 (1.19-4.41, p=0.013)
	Upper middle Severe malnutrition	337 (96.6)	12 (3.4)	3.52 (1.38-8.95, p=0.008)
	Low/lower middle Severe malnutrition	378 (92.9)	29 (7.1)	19.28 (8.18-45.44, P<0.001)
Age (years)	Mean (SD)	1943 (98.3)	34 (1.7)	-
Sex	Male	2513 (97.5)	65 (2.5)	1.55 (0.99-2.44, p=0.055)
	Female	1943 (98.3)	34 (1.7)	-
Stage	I	1356 (98.3)	23 (1.7)	-
	II	996 (98.0)	20 (2.0)	0.95 (0.50-1.83, p=0.888)

III	1615 (98.1)	31 (1.9)	0.94 (0.52-1.71, p=0.851)
IV	464 (94.9)	25 (5.1)	2.74 (1.42-5.26, p=0.003)

Table 7-3. Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status in patients undergoing surgery for gastric cancer.

Model adjusted for cancer type, age, sex, and disease stage, with population stratification by hospital and country of residence. Interaction term between World Bank income group and nutritional status, as defined by the GLIM criteria, included within model.

		Alive	Dead	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	370 (97.1)	11 (2.9)	-
	Upper middle No/moderate malnutrition	106 (100.0)	0 (0.0)	0.00 (0.00-Inf, p=0.995)
	Low/lower middle No/moderate malnutrition	76 (95.0)	4 (5.0)	2.37 (0.44-12.61, p=0.313)
	High Severe malnutrition	194 (96.0)	8 (4.0)	1.13 (0.37-3.47, p=0.828)
	Upper middle Severe malnutrition	141 (95.3)	7 (4.7)	1.57 (0.40-6.10, p=0.515)
	Low/lower middle Severe malnutrition	168 (91.3)	16 (8.7)	4.25 (1.24-14.57, p=0.021)
Age (years)	Mean (SD)	62.8 (13.6)	69.9 (13.1)	1.07 (1.03-1.11, P<0.001)
Sex	Male	424 (97.0)	13 (3.0)	-
	Female	631 (95.0)	33 (5.0)	1.78 (0.80-3.97, p=0.157)
Stage	I	0 (0.0)	0 (0.0)	-
	II	364 (97.1)	11 (2.9)	-
	III	184 (96.8)	6 (3.2)	1.08 (0.32-3.65, p=0.899)

	IV	410 (96.5)	15 (3.5)	1.18 (0.45-3.13, p=0.733)

Table 7-4. Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status after multiple imputation for missing data.

Model adjusted for cancer type, age, sex, and disease stage, with population stratification by hospital and country of residence. Interaction term between World Bank income group and nutritional status, as defined by the GLIM criteria, included within model. Multiple imputation performed using multiple chain equations using ten sets, each with ten iterations, with results combined using Rubin's rules.

		OR (multivariable imputation)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	-
	Upper middle No/moderate malnutrition	1.34 (0.62-2.88, p=0.459)
	Low/lower middle No/moderate malnutrition	4.17 (1.94-8.98, P<0.001)
	High Severe malnutrition	2.10 (0.76-5.81, p=0.142)
	Upper middle Severe malnutrition	3.30 (1.61-6.76, p=0.001)
	Low/lower middle Severe malnutrition	10.61 (5.66-19.89, P<0.001)
Cancer Type	Colorectal (colon or rectum)	-
	Gastric (stomach)	1.50 (1.05-2.14, p=0.027)
Age (years)	Mean (SD)	1.06 (1.05-1.08, P<0.001)
Sex	Male	-
	Female	0.70 (0.50-0.97, p=0.032)
Stage	I	-
	II	0.69 (0.42-1.14, p=0.148)

III	0.86 (0.56-1.31, p=0.482)
IV	2.41 (1.50-3.85, P<0.001)

Figure 7-7. Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status.

Interaction term included between income group and nutritional status, as defined by GLIM criteria (A), >10% weight loss (B) and BMI (C). Model adjusted for cancer type, age, sex, and disease stage, with population stratification by hospital and country of residence.

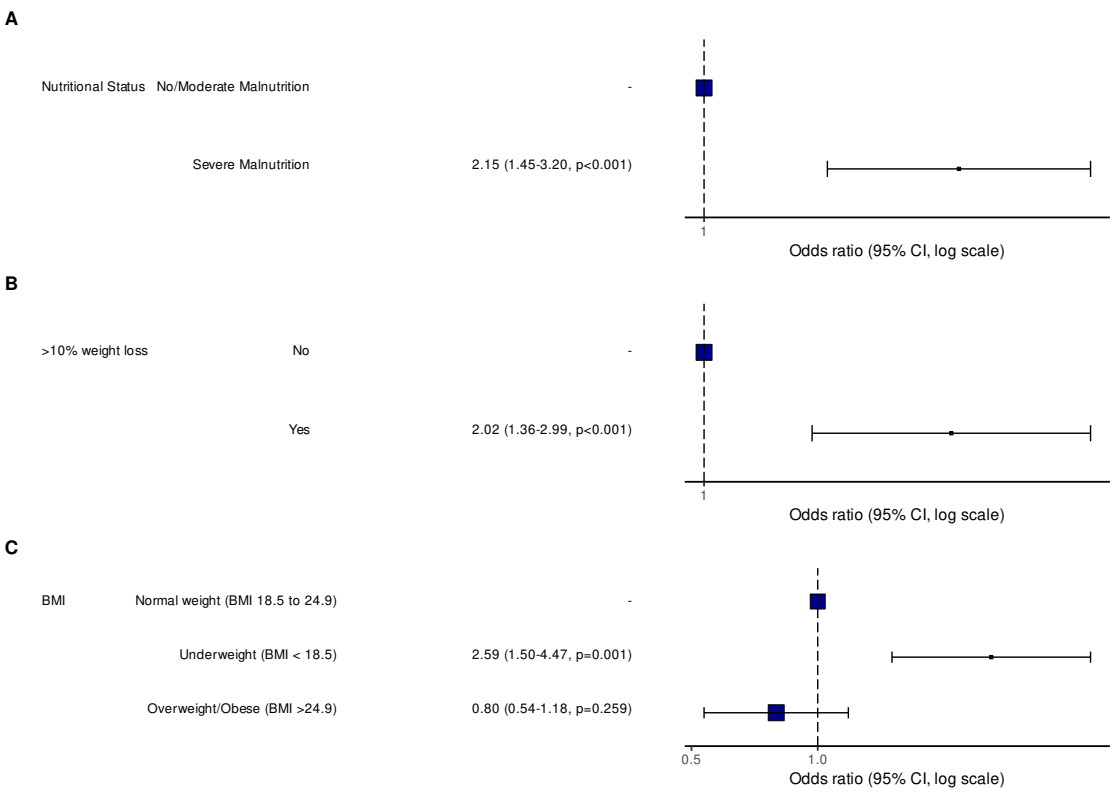


Figure 7-8. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status.

Major complication (A), all complications (B), anastomotic leak (C), and surgical site infection (D). All models were adjusted for World Bank income group, cancer type, age, sex, and disease stage.

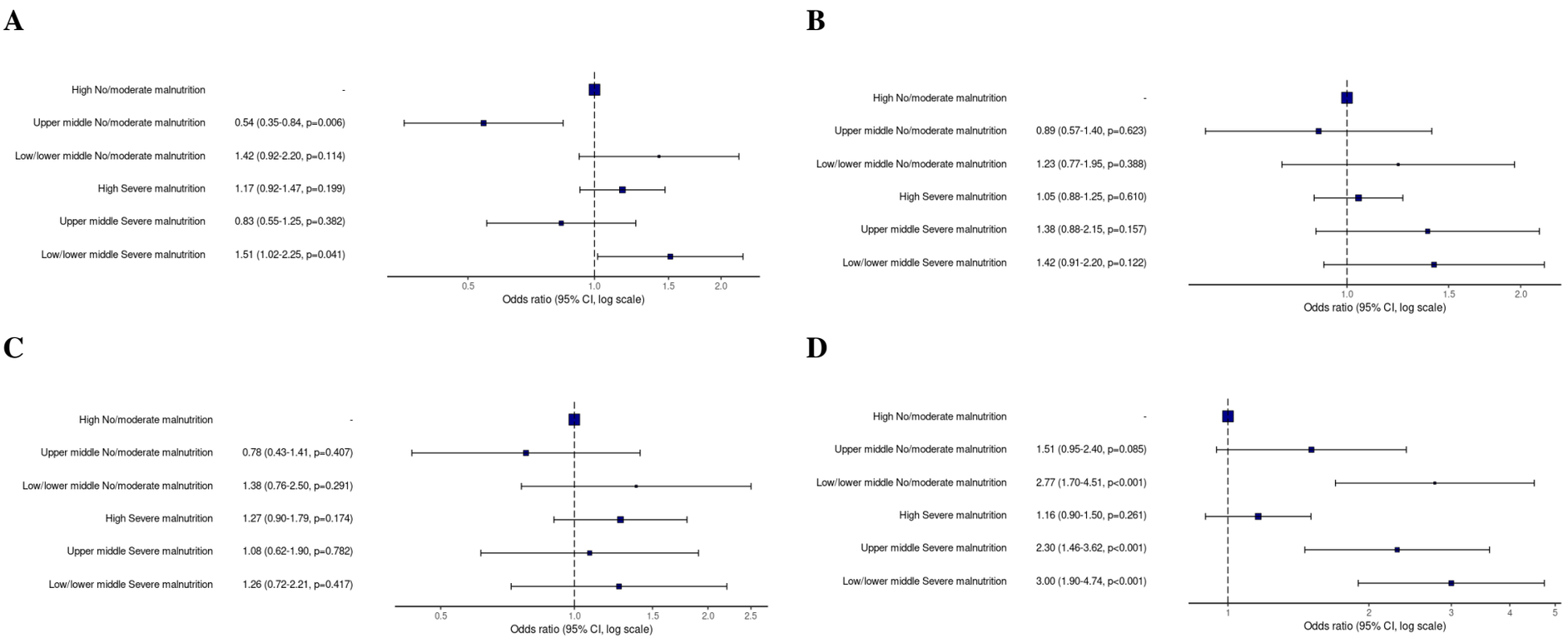


Figure 7-9. Three-way decomposition mediation model of the effect of country income group on 30-day mortality mediated by nutritional state.

Model adjusted for patient, cancer and disease covariates. Uncertainty determined using bootstrap resampling (5000 draws) and confidence intervals constructed using percentiles.

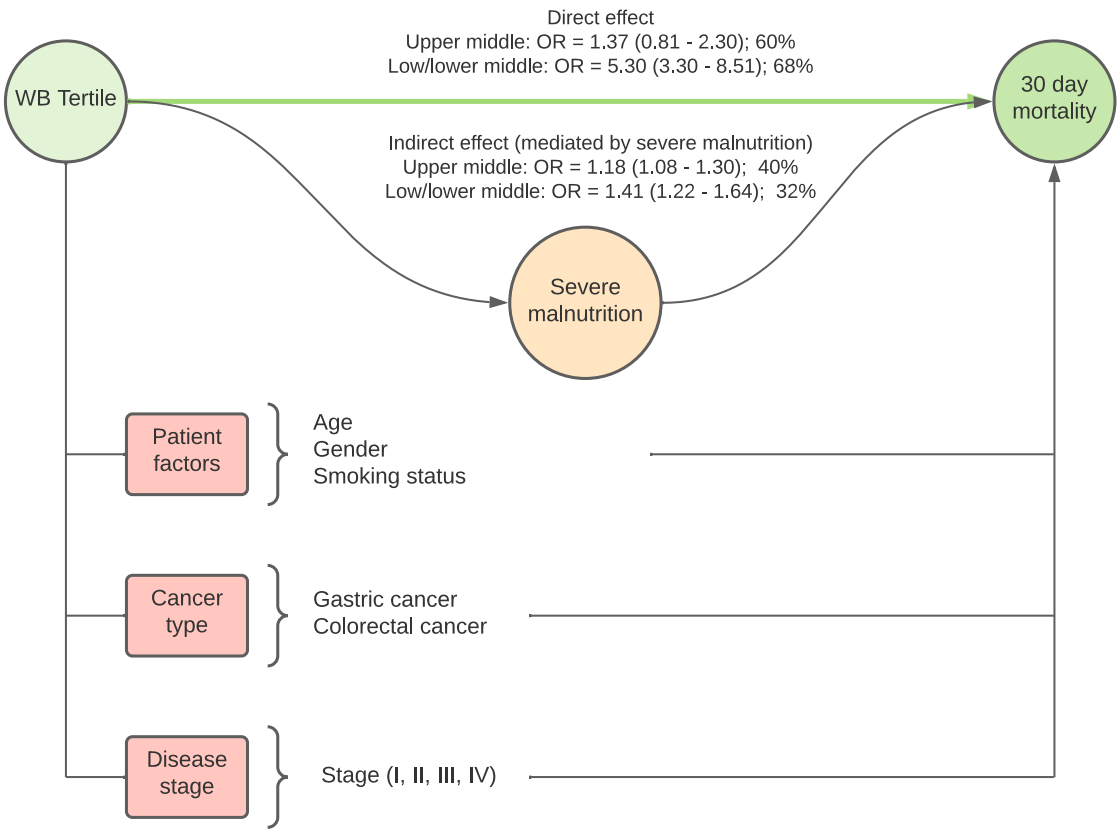


Figure 7-10. Three-way decomposition mediation model of the effect of country income group on 30-day surgical site infection rates mediated by nutritional state.

Model adjusted for patient, cancer and disease covariates. Uncertainty determined using bootstrap resampling (5000 draws) and confidence intervals constructed using percentiles.

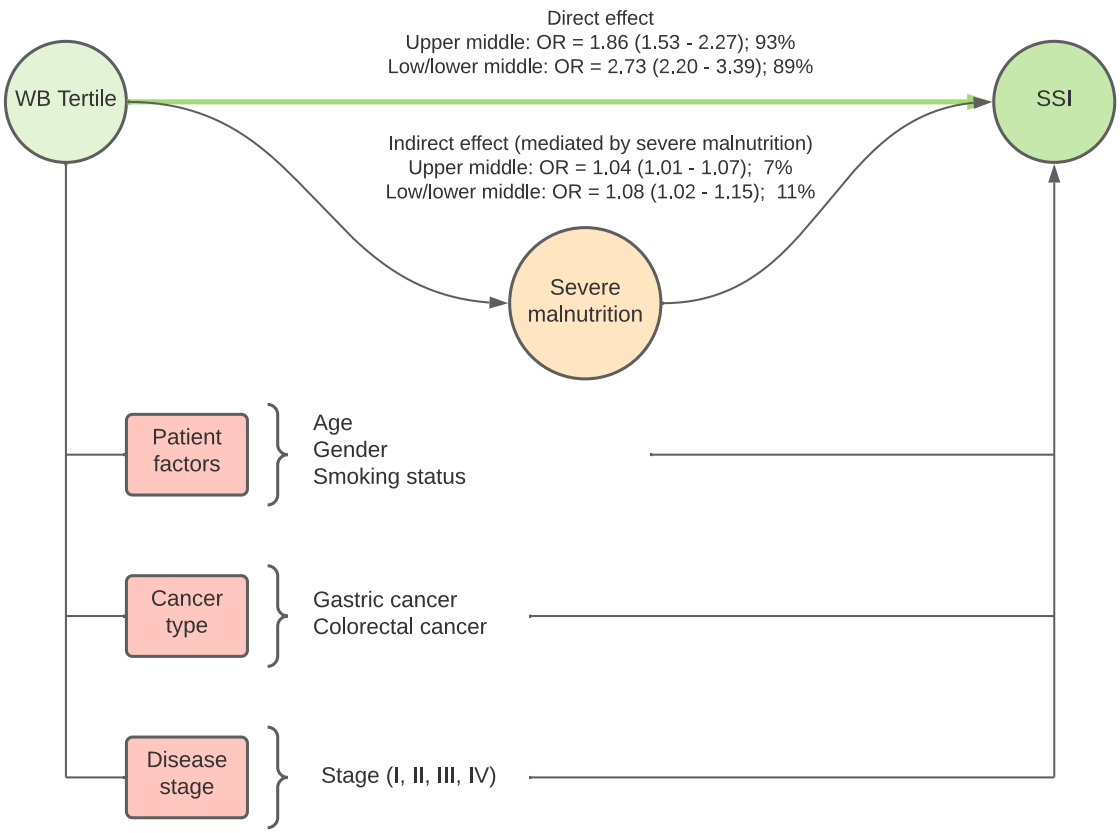


Table 7-5. Three-way decomposition mediation model of the effect of country income group on 30-day mortality mediated by nutritional state after multiple imputation for missing data.

	Pathway	OR	95% CI	Percentage mediated
Upper middle	Direct	1.40	0.90-2.18	61
	Indirect	1.17	1.08-1.26	39
Low/lower middle	Direct	4.45	2.94-6.74	69
	Indirect	1.36	1.18-1.56	31

Table 7-6. Three-way decomposition mediation model of the effect of country income group on surgical site infection mediated by nutritional state after multiple imputation for missing data.

	Pathway	OR	95% CI	Percentage mediated
Upper middle	Direct	1.72	1.43-2.05	90
	Indirect	1.04	1.01-1.07	10
Low/lower middle	Direct	2.60	2.14-3.15	90
	Indirect	1.08	1.02-1.14	10

7.4 Discussion

7.4.1 Summary of key findings in context of previous literature

In this prospective study of patients undergoing cancer surgery in 381 hospitals from 75 countries, severe malnutrition was present across all income levels, with a disproportionate burden in low-income settings. Severe malnutrition in LMICs was associated with an increased risk of surgical site infection and 30-day mortality, mediating around one third of early deaths following surgery for cancer.

Provision of safe and equitable surgical care is increasingly recognised as an essential part of cancer care, while improving nutrition forms part of the United Nations Sustainable Development Goal 2[12]. As delays in presentation result in poorer survival secondary to cancer cachexia[237], early cancer detection programmes and improved access to surgical care are likely to reduce malnutrition rates in LMICs. However, patients often present with malnutrition despite good access to cancer care services[237]. Whilst associated with poorer outcomes, malnutrition represents a potentially modifiable risk factor to reduce the effects of cancer cachexia within the early postoperative period[238]. Randomised control trials conducted in LMICs have demonstrated perioperative nutritional supplementation can reduce early morbidity and mortality[239,240], potentially representing a low-cost and sustainable intervention in LMICs to improve surgical outcomes.

7.4.2 Policy implications

Severe malnutrition rates reported in my study were higher than previous estimates across LMICs for patients undergoing surgery for cancer[241]. We found unadjusted postoperative complication rates were higher in malnourished patients, however these differences

disappeared after case-mix adjustment. Within LMICs, increased complication rates in malnourished patients have previously been reported[242], however the use non-standardised outcome definitions limit interpretation. Across high-income settings, similar relationships between malnutrition and poor early postoperative outcomes have been demonstrated[227,243].

Malnutrition reduces a patient's ability to compensate for traumatic events, including major surgery[242], with the negative impact of malnutrition on the anabolic process of wound healing and postoperative recovery well described[244]. Excess mortality in malnourished patients is likely to occur secondary to the inability to recover from the associated physiological stress associated with complications[244]. This highlights the importance of recognising nutritionally vulnerable patients early to allow additional support and escalation of care if appropriate.

Several nutritional assessment tools are often used within surgical populations to identify patients at higher risk of surgical complications, however these are often time consuming to complete[234]. Despite high levels of awareness around the importance of nutritional assessment few doctors or nurses routinely screen patients[245], emphasising the importance of simple and efficient assessment tools. Recently, the Global Leadership Initiative on Malnutrition gathered together major clinical nutrition societies to reach a global consensus on the identification of criteria for the diagnosis of malnutrition in clinical settings[234]. I demonstrate the GLIM criteria can be applied to a global patient cohort and is an independent risk factor for 30-day mortality and surgical site infection following surgery for cancer. Furthermore, >10% weight loss and low BMI (18.5), both diagnostic of cancer cachexia, were also independent predictors of early mortality following cancer surgery in

this cohort. This suggests that these criteria have promise as a simple preoperative screening tool to identify nutritionally vulnerable patients, however further comparison to existing nutritional assessment tools in LMICs is required.

7.4.3 Strengths of this study

A major strength of this study is its prospective design and standardised criteria to assess nutritional status and postoperative outcomes across a wide breadth of global settings. Data quality was ensured though collaborator-facing web applications and real-time data entry quality assurance, with independent validation study verifying data accuracy and case ascertainment. Assessment of nutrition status and outcome was standardised, and training provided through an online platform. The quantification of surgical cancer care in resource-limited settings has been hindered by an insufficient amount of high-quality data. This study therefore contributes to closing this knowledge gap and allows meaningful comparison from multiple income settings following case-mix adjustment.

7.4.4 Study limitations

My study has important limitations. I was only able to identify the presence of severely malnourished patients prior to surgery, using percentage weight loss and *a priori* categorised body mass index, to ensure a high percentage of data completeness. Therefore, the comparison group contained both well-nourished patients and those with moderate malnutrition. As a result, my analysis is likely to have underestimated the true effect of severe malnutrition on postoperative outcomes.

Furthermore, other globally prevalent cancers associated with malnutrition, such as gynaecological and oral cancer, were not included[227]. To maximise case ascertainment and

ensure data quality, a pragmatic decision was made to collect data on cancer types commonly treated across the collaborative network. My results may only be generalisable to patients presenting with colorectal and gastric cancer, with additional studies required to determine the impact of nutritional status on early postoperative outcomes globally across different cancers.

Finally, the combined impact of patient comorbidity on early postoperative outcomes following cancer surgery in this cohort remains unknown. Preoperative comorbidity is known to correlate with poorer nutritional state, with potential confounding possible despite model adjustment for important patient and disease factors. However, these included factors are likely to be colinear with overall measures of patient comorbidity and my results remained consistent across sensitivity analysis.

7.4.5 Conclusion

Severe malnutrition is common and an independent risk factor for increased 30-day mortality and surgical site infection in elective cancer surgery patients worldwide. This suggests perioperative nutritional intervention may be effective in improving outcomes after cancer surgery, with excess deaths in LMICs mediated by the presence of severe malnutrition. Therefore, the identification and treatment of malnutrition perioperatively represents a potential low-cost, sustainable intervention in LMICs to reduce postoperative mortality. If research gaps are addressed, preoperative oral nutrition is likely to form part of future global surgical guidelines as a simple measure that can improve outcomes after surgery for cancer. An international randomised control trial investigating the feasibility

and effectiveness of perioperative nutritional intervention for elective cancer surgery is currently underway[246].

Severe malnutrition represents a high global burden in cancer surgery and is an independent risk-factor for 30-day mortality and surgical site infection following elective surgery for colorectal and gastric cancer worldwide. Perioperative nutritional interventions may improve outcomes after cancer surgery, with future research particularly focused across lower income settings.

7.5 Contribution statement

The primary data for this chapter were collected during the GlobalSurg 3 observational study, an international collaborative led by Professor Ewen Harrison. I co-led the methodology and analyses presented in this chapter from conception to completion and dissemination whilst supervising Miss Aya Riad during her BMedSci student project.

7.6 Outputs relating to this chapter

This study is published in *The Lancet Global Health.*

NIHR Global Health Research Unit on Global Surgery [**Knight SR** second author in writing group] (2021). The impact of malnutrition on early outcomes after cancer surgery: an international, prospective cohort study. **Lancet Global Health.** 11, E341-E349.

This research was also selected for the March 2023 edition of *In conversation with the Lancet Global Health* podcast following publication, exploring the analysis further and its likely impact on patient care and health policy.

It received the University of Edinburgh BMedSci Best Student Prize (Miss Aya Riad) and an Royal College of Surgeons Intercalated Bachelor of Science Degree in Surgery Award.

This work was presented as an oral presentation at the Association of Surgeons in Training (ASiT) International Surgical Summit Virtual Conference 2020 and Surgical Research Society Virtual Online Meeting 2020 by Miss Riad. The Global Anaesthesia, Surgery and Obstetric Collaboration (GASOC) Research Prize and SRS Medical Student Prize were awarded at these meetings, respectively.

In addition, I led a follow-up study from conception to completion which evaluated the impact of preoperative oral nutritional supplementation in patients undergoing surgery for cancer in LMICs and is published in *Scientific Reports*:

Knight SR, Qureshi AU, Drake TM, Lapitan MCM, Maimbo M, Yenli E, *et al*. The impact of preoperative oral nutrition supplementation on outcomes in patients undergoing gastrointestinal surgery for cancer in low- and middle-income countries: a systematic review and meta-analysis. **Sci Rep**. 2022; 12:12456.

Chapter 8 Discussion

8.1 Summary of key findings in context of wider literature

In this thesis, I determined the rate of early mortality after cancer surgery is higher in LMICs, which can be explained by a number of perioperative factors. The key findings are summarised in the paragraphs below. Detailed critique of the strengths and limitations of these analyses were discussed in the relevant chapters.

8.1.1 Excess mortality in LMICs following surgery for cancer

In Chapters 5 and 6, I demonstrated excess mortality in LMICs can be partly explained by the reduced ability to rescue a patient following surgery. The proportion of patients who died after a major complication was three to six times higher in LMICs following case-mix adjustment. Postoperative death following the development of a complication was explained by patient, hospital, and country factors, with cancer stage alone explaining little of the early variation in mortality (Chapters 4 and 5). This finding contrasts with previous data, which suggests earlier stage diagnosis and treatment of cancer is associated with improved survival[247,248].

It is widely accepted that surgical outcomes following surgery are worse in LMICs (Chapter 1), however quantification of surgical cancer care in resource-limited settings has been hindered by an insufficient amount of high-quality data (Chapter 1 and 2). For the first time, I provide comprehensive and high-quality data across income settings for patients undergoing surgery for three globally common cancers (Chapter 4). This study

therefore contributes to closing this knowledge gap and allows meaningful comparison across multiple income settings.

8.1.2 Influence of hospital facilities on early postoperative outcomes

The importance of rescuing patients from common complications is now well established, with variation described globally[249]. Yet, for the first time, I identify capacity to rescue as an important early determinant of outcomes following cancer surgery in resource-restricted settings (Chapter 5). The capacity to rescue patients from death after the development of common postoperative complications explains a significant part of the disproportionate mortality burden in LMICs. Overall, the absence of consistently available postoperative care facilities was associated with seven to ten more deaths for every 100 major complications in LMICs.

My work also provides comprehensive data across income settings on the effect of hospital facility availability on early patient outcomes following surgery for cancer (Chapter 6). Even after case-mix adjustment, patients treated in hospitals with lower levels of hospital infrastructure and resources had higher postoperative mortality, despite similar complication rates. Across LMICs, improvements in hospital facilities would prevent one to three deaths for every 100 patients undergoing surgery for cancer.

These findings are consistent with previous research in high-income settings[182,183] and previous estimates have suggested similar effects in LMICs[28]. Improved availability of hospital facilities is likely to aid the early identification and treatment of postoperative complications, but also reflects a hospital's ability to perform elective operations safely for

a wide range of cancers, highlighting their importance worldwide for access to high-quality, effective surgical cancer care (Chapter 6.3.2).

8.1.3 Impact of malnutrition on early outcomes after surgery for cancer

In Chapter 7, consistent with findings from previous studies[241,250], I found that malnutrition is common in patients requiring elective surgery for colorectal and gastric cancers worldwide. By utilizing a global consensus definition of malnutrition, I was able to demonstrate the presence of malnutrition is higher than previous estimates across LMICs[241,251], which contributes to significantly worse postoperative surgical site infection and mortality rates. Overall, one third of the excess early mortality in LMICs following surgery was mediated by the presence of severe malnutrition.

Despite using standardised and validated methods, my findings are likely to underestimate the true effect of malnutrition on postoperative outcomes. I was only able to identify the presence of severely malnourished patients prior to surgery, while extending the follow-up period to 90 days would have improved capture of delayed postoperative complications, given the impact of nutritional status was likely to persist beyond 30 days[252]. However, the shorter follow-up period was chosen for pragmatic reasons to facilitate data completeness, particularly across resource limited settings.

8.1.4 Implications for global surgical cancer care

My findings further highlight that patients undergoing surgery in lower-resourced settings have worse early postoperative outcomes. I have shown large scale, high-quality granular data collection across lower-resourced settings is possible, co-designed with LMIC surgical experts and using readily available open-source software (Chapter 4). Poorer

outcomes in LMICs were well described[12,52], however conclusions were limited by the absence of co-ordinated prospective data collection using standardised definitions (Chapter 1 and 2).

My analyses in Chapter 5 suggest that presentation with later stage disease, which is more common in LMICs, does not explain the poorer early outcomes experienced by patients undergoing surgery for cancer in these settings. This finding was possible through the use of a standardised classification system[197], which allowed for meaningful comparisons of cancer stage in settings with limited access to imaging and pathological services (demonstrated in Chapter 6). I found the Essential TNM stage classification system showed good correlation with gold-standard pathological staging (Chapter 4.3.2). This suggests that future research should utilise this pragmatic, user-friendly classification system which allows for comparisons across income settings without significantly limiting analyses.

Current research must also consider its application and impact in relation to the COVID-19 pandemic. Importantly, the methodology described in Chapter 3 enabled the rapid quantification of the impact of COVID-19 on postoperative recovery[217] and the ability of surgical systems to recover from the pandemic[253]. As an external system stressor, significant disruption in surgical cancer services were identified, particularly within hospitals with less infrastructure[254]. I highlight in Chapter 6 the impact of hospitals with fewer available resources on patient care, including a reduction in the quality of surgical treatment provided and elevated mortality rate, suggesting these effects were exacerbated during the COVID-19 pandemic across all income groups. However, the greatest burden is most likely to have occurred in lower-resourced settings (Chapter 6.3.3). Further work is

clearly required to understand the relevant importance of particular system structures within lower-resource environments to strengthen surgical cancer services.

Adequate access to surgical care and treatment delays also came into focus during the COVID-19 pandemic. Even short delays in surgery for breast and colorectal cancer have been shown to increase mortality by more than 5%[255]. As a result, many advocate the prioritisation and organisation of health systems to improve access and reduce delays to surgical cancer treatment. However, my analysis suggests that without concomitant strengthening of hospital infrastructure and patient care pathways, the reductions in cancer-associated mortality secondary to improved access will not be realised in LMICs.

8.2 Future research priorities

My findings give rise to a number of subsequent research questions that are summarised by the hypotheses below.

8.2.1 Hypothesis 1: Isolated improvements in global access to surgical cancer care will paradoxically increase perioperative mortality rates

Estimates suggest 45 million surgical procedures are needed worldwide each year to treat cancer (Chapter 1), yet fewer than 25% of patients with cancer have access to safe, affordable, and timely surgery. Accordingly, there has been focus to expand access to surgical services within underserved populations and has been prioritised by funders and policy makers.

In Chapter 5, I show that perioperative mortality is disproportionately greater in LMICs, resulting in up to ten additional deaths for every 100 patients developing a postoperative

complication. Importantly, I also show that major complication rates are similar across all income settings. This suggests expanding access to surgical cancer services in order to address unmet needs, without concomitant investment to improve perioperative surgical cancer care, would result in a significant increase in deaths globally within 30 days of surgery[24]. Despite estimates available across all procedures, future studies are required to determine the specific impact of scaling access to surgical cancer care across LMICs.

In addition, improved access provides further opportunities for optimisation of individual patients through, for instance, nutritional interventions and neoadjuvant therapies. Addressing these factors with high-quality interventional trials to build a global evidence base for the delivery of safe cancer surgery is likely to have significant impact and improve cancer survival.

8.2.2 Hypothesis 2: Improvement in hospital facilities will result in higher quality care across the entire surgical cancer care pathway

High-quality health systems adaptable to changing population health needs, growing public expectations, and novel treatments are now required to improve health outcomes and provide greater societal value globally[28]. The key foundations of high-quality surgical care are present across the entire cancer care pathway[52], but little was known about the influence of such factors on surgical outcomes. As demonstrated in Chapter 6, I quantify the impact of particular hospital facilities on early postoperative outcomes, which represent markers for the expertise, resources, and complex processes of care required to facilitate high-quality surgical care. Future studies could measure these indicators to define the current

state of surgical cancer care systems, before more comprehensive studies examine the mechanisms through which system strengthening can reduce postoperative mortality.

8.2.3 Hypothesis 3: The preoperative treatment of malnutrition will improve early outcomes after cancer surgery in LMICs

Throughout my thesis, I have identified a number of factors which influence early outcomes after cancer surgery worldwide. However, it remains unknown whether possible interventions to address these will result in measurable reductions in postoperative mortality.

There is an urgent need to determine whether perioperative nutritional interventions can improve early outcomes following gastrointestinal cancer surgery worldwide. Meta-analyses of randomised control trials conducted in both high-income[256] and LMICs[251] have demonstrated simple perioperative oral nutritional supplementation can reduce early morbidity and mortality following surgery, potentially representing a low-cost and sustainable intervention in LMICs to improve surgical outcomes. This important question will be addressed by an underway randomised trial that seeks to determine the impact of perioperative nutrition on early outcomes following surgery in LMICs (NCT 04448041), as an extension of my work in Chapter 7.

Yet it is important to acknowledge that in environments with limited resources, the effectiveness of simple, pragmatic perioperative interventions may not deliver expected improvements in postoperative outcomes[257]. System-level factors, diversion away from routine clinical care, required behaviour change, and communication barriers can all negatively impact the implementation of interventions[187,257,258]. Therefore, this trial is

being carefully co-designed with local teams of healthcare professionals within LMICs to enable the sustainable adoption of this nutritional intervention into routine clinical care.

8.2.4 Hypothesis 4: The availability of high-quality surgical cancer care influences longer term survival in LMICs

As shown in Chapter 5 and 6, improvements in perioperative care pathways and hospital facilities can dramatically reduce perioperative mortality in LMICs and improve the quality of surgical care provided to patients. This is particularly evident in colorectal and gastric cancer, where major complication and mortality rates are higher following surgery. However, early outcomes in breast cancer surgery, where surgical risk is much lower, are similar across different income settings.

Yet disparities in longer-term breast cancer outcomes are linked to income group, suggesting these relate to differences in the delivery of effective cancer care[259]. A number of LMIC-focused guidelines for the management of breast cancer exist[260–262], however the relationship between resource availability and the quality of surgical care provided is unknown. Currently, to address this knowledge gap, further work is underway to determine the extent to which particular resources and guidelines impact the care quality for patients undergoing surgery for breast cancer worldwide.

8.3 Wider relevance and applications of methodology used in this thesis

In this thesis, I have used a range of methodological approaches and data science techniques – spanning the principles of large prospective cohort design, the monitoring and measurement of data quality, multiple imputation, multilevel logistic regression, mediation

analysis, and generalised estimating equations. These principles and methods are transferrable to the study of many diseases, as demonstrated in the examples below.

8.3.1 Use of big data to measure surgical outcomes

In Chapters 3 and 4, I designed and delivered a large, prospective observational study across 428 hospitals worldwide. This included leading data analysis and interpretation (Chapters 5 to 7). I have subsequently applied similar methods to three large multinational observational studies exploring early outcomes in patients presenting with an acute surgical abdomen[263], acute pancreatitis[264], and inguinal hernias[265]. These analyses are ongoing, however the data science skills developed and demonstrated throughout my thesis have enabled additional opportunities through these studies. As one example, I have been invited to perform additional research using the National Emergency Laparotomy Audit (NELA) database, which holds records on more than 100 000 patients and usually only available to NELA research fellows.

8.3.2 Prediction model development and validation

Prognostic models attempt to transform complex clinical pictures into tangible numerical values. Across my thesis, as I developed a range of data science skills, I sought to align these with best standards throughout. This included: adherence to gold-standard reporting guidelines; using multiple imputation to adequately deal with missing data; and advanced regression modelling.

I have subsequently applied these methods in response to the COVID-19 pandemic by leading development and validation of the International Severe Acute Respiratory and Emerging Infections Consortium Coronavirus Clinical Characterisation Consortium

(ISARIC4C) Mortality model (4C Mortality) for adults hospitalised with COVID-19. In this work, I sought to develop an easy-to-use risk stratification score based on commonly available parameters at hospital presentation addressing the weaknesses of existing prognostic models in clinical use for COVID-19 patients[266]. Previously, most risk stratification models had shown moderate performance at best and provided no overall benefit to clinical decision making in COVID-19 patients[267,268]. I used data from more than 55 000 patients across 260 hospitals to develop and validate a prognostic model for mortality following admission to hospital with COVID-19[269].

This outperformed existing scores, demonstrated utility to directly inform clinical decision making, and could be used to stratify patients with COVID-19 into different management groups, including those potentially appropriate for community management or requiring urgent treatment escalation. Subsequently, the 4C Mortality Score was the most commonly used risk stratification score in the United Kingdom,[270] informed government policy,[271] and has been validated across 28 countries worldwide.

As a result of this work, I have been also involved in further studies assessing the performance of prognostic scores in COVID-19[272,273] and postoperative pulmonary complications[274]; delivered the introductory lecture on 'Prognostic Studies and Clinical Prediction Rules' for the Research and Evidence Based Medicine module (1st Year MB ChB); and reviewed submitted manuscripts for the *British Medical Journal*, *Lancet Digital Health*, and *eClinicalMedicine*.

8.4 Conclusion

In this thesis, I have designed, delivered and analysed a large prospective cohort study to determine early global outcomes following cancer surgery.

8.5 Outputs relating to this chapter

I applied the principles and methodology used in this thesis in the following publications to study COVID-19:

Knight SR, *et al*, on behalf of the ISARIC4C Investigators (2020). Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. **BMJ**. 370; m3339.

https://doi.org/10.1136/bmj.m3339

Gupta RK, Harrison EM, Ho A, Docherty AB, **Knight SR**, …, *et al*, on behalf of the ISARIC4C Investigators (2021). Development and validation of the ISARIC 4C Deterioration model for adults hospitalised with COVID-19: a prospective cohort study. **Lancet Respiratory Medicine.** 9; 349–59.

https://doi.org/10.1016/S2213-2600(20)30559-2

Knight SR, *et al*, on behalf of the ISARIC4C Investigators (2022). Prospective validation of the 4C prognostic models for adults hospitalised with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. **Thorax.** 77; 606–15.

http://dx.doi.org/10.1136/thoraxjnl-2021-217629

Knight SR, Harrison EM (2022). Risk stratification of patients with COVID-19 in the community. **Lancet Digital Health.** 4; e628–9.

https://doi.org.10.1016/S2589-7500(22)00146-7

In addition, the work included within this thesis received the Syme Medal from the Royal College of Surgeons of Edinburgh (2022), acknowledging the likely impact of this work on future research or clinical practice.

Chapter 9 References

1. Bath M, Bashford T, Fitzgerald JE. What is 'global surgery'? Defining the multidisciplinary interface between surgery, anaesthesia and public health. BMJ Global Health. 2019 Oct 1;4(5):e001808.

2. World Health Organization. Medical devices: managing the mismatch: an outcome of the priority medical devices project: methodology briefing paper [Internet]. World Health Organization; 2010 [cited 2022 Sep 27]. Report No.: WHO/HSS/EHT/DIM/10.10. Available from: https://apps.who.int/iris/handle/10665/70491

3. World Health Organization. Barriers to innovation in the field of medical devices: background paper 6, August 2010 [Internet]. World Health Organization; 2010 [cited 2022 Sep 27]. Report No.: WHO/HSS/EHT/DIM/10.6. Available from: https://apps.who.int/iris/handle/10665/70457

4. Halfdan Mahler. Surgery and Health For All. 1980 Jun 29; XXII Biennial World Congress of the International College of Surgeons, Mexico City.

5. Bae JY, Groen RS, Kushner AL. Surgery as a public health intervention: common misconceptions versus the truth. Bull World Health Organ. 2011 Jun 1;89(6):394.

6. United Nations Millennium Development Goals [Internet]. United Nations; [cited 2022 Sep 25]. Available from: https://www.un.org/millenniumgoals/?

7. Greenberg SLM, Maine R, Gillies R, Hagander L, Meara JG. Surgery: A post-2015 Millennium Development Goal priority. The World We Want 2015. [Internet]. [cited 2022 Sep 25]. Available from: http://www.worldwewant2015.org/node/298620

8. Farmer PE, Kim JY. Surgery and Global Health: A View from Beyond the OR. World J Surg. 2008 Apr;32(4):533–6.

9. The Lancet Commission on Global Surgery [Internet]. [cited 2021 Feb 2]. Available from: https://www.thelancet.com/commissions/global-surgery

10. Meara JG, Leather AJM, Hagander L, Alkire BC, Alonso N, Ameh EA, et al. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. Lancet. 2015 Aug 8;386(9993):569–624.

11. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012 Dec 15;380(9859):2224–60.

12. Meara JG, Hagander L, Leather AJM. Surgery and global health: a Lancet Commission. Lancet. 2014 Jan 4;383(9911):12–3.

13. Shrime MG, Bickler SW, Alkire BC, Mock C. Global burden of surgical disease: an estimation from the provider perspective. Lancet Glob Health. 2015 Apr 27;3 Suppl 2:S8-9.

14. Global health estimates: Leading causes of DALYs [Internet]. [cited 2022 Oct 24]. Available from: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/global-health-estimates-leading-causes-of-dalys

15. Global Burden of Disease Study 2016 (GBD 2016) All-cause Under-5 Mortality, Adult Mortality, and Life Expectancy 1970-2016 | GHDx [Internet]. [cited 2022 Jul 25]. Available from: http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-all-cause-under-5-mortality-adult-mortality-and

16. Life expectancy and health life expectancy. Global Health Observatory, World Health Organisation. [Internet]. [cited 2022 Sep 25]. Available from: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-life-expectancy-and-healthy-life-expectancy

17. Chao TE, Sharma K, Mandigo M, Hagander L, Resch SC, Weiser TG, et al. Cost-effectiveness of surgery and its policy implications for global health: a systematic review and analysis. The Lancet Global Health. 2014 Jun 1;2(6):e334–45.

18. Holmer H, Bekele A, Hagander L, Harrison EM, Kamali P, Ng-Kamstra JS, et al. Evaluating the collection, comparability and findings of six global surgery indicators. Br J Surg. 2019 Jan;106(2):e138–50.

19. Weiser TG, Regenbogen SE, Thompson KD, Haynes AB, Lipsitz SR, Berry WR, et al. An estimation of the global volume of surgery: a modelling strategy based on available data. Lancet. 2008 Jul 12;372(9633):139–44.

20. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012 Dec 15;380(9859):2095–128.

21. Alkire BC, Shrime MG, Dare AJ, Vincent JR, Meara JG. Global economic consequences of selected surgical diseases: a modelling study. Lancet Glob Health. 2015 Apr 27;3 Suppl 2:S21-27.

22. Weiser TG, Haynes AB, Molina G, Lipsitz SR, Esquivel MM, Uribe-Leitz T, et al. Estimate of the global volume of surgery in 2012: an assessment supporting improved health outcomes. Lancet. 2015 Apr 27;385 Suppl 2:S11.

23. Sobhy S, Arroyo-Manzano D, Murugesu N, Karthikeyan G, Kumar V, Kaur I, et al. Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: a systematic review and meta-analysis. The Lancet. 2019 May 11;393(10184):1973–82.

24. Nepogodiev D, Martin J, Biccard B, Makupe A, Bhangu A, National Institute for Health Research Global Health Research Unit on Global Surgery. Global burden of postoperative death. Lancet. 2019 Feb 2;393(10170):401.

25. Biccard BM, Madiba TE, Kluyts HL, Munlemvo DM, Madzimbamuto FD, Basenero A, et al. Perioperative patient outcomes in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. Lancet. 2018 Apr 21;391(10130):1589–98.

26. GlobalSurg Collaborative. Mortality of emergency abdominal surgery in high-, middle- and low-income countries. Br J Surg. 2016 Jul;103(8):971–88.

27. GlobalSurg Collaborative. Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: a prospective, international, multicentre cohort study. Lancet Infect Dis. 2018;18(5):516–25.

28. Kruk ME, Gage AD, Arsenault C, Jordan K, Leslie HH, Roder-DeWan S, et al. High-quality health systems in the Sustainable Development Goals era: time for a revolution. The Lancet Global Health. 2018 Nov 1;6(11):e1196–252.

29. Røttingen JA, Regmi S, Eide M, Young AJ, Viergever RF, Ardal C, et al. Mapping of available health research and development data: what's there, what's missing, and what role is there for a global observatory? Lancet. 2013 Oct 12;382(9900):1286–307.

30. WHO Research and development to meet health needs in developing countries: strengthening global financing and coordination: Report of the Consultative Expert Working Group on Research and Development: Financing and Coordination. [Internet]. WHO: Research and development to meet health needs in developing countries. [cited 2018 Sep 15]. Available from: http://www.who.int/phi/cewg_report/en/

31. National Institute for Health Research Global Health Research Unit on Global Surgery. Prioritizing research for patients requiring surgery in low- and middle-income countries. Br J Surg. 2019 Jan;106(2):e113–20.

32. Alkire BC, Raykar NP, Shrime MG, Weiser TG, Bickler SW, Rose JA, et al. Global access to surgical care: a modelling study. Lancet Glob Health. 2015 Jun;3(6):e316-323.

33. Fitzmaurice C, Akinyemiju TF, Al Lami FH, Alam T, Alizadeh-Navaei R, Allen C, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer

Groups, 1990 to 2016: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol. 2018;1(4):1553–68.

34. United Nations. Sustainable Development Goals Report [Internet]. United Nations Sustainable Development. [cited 2022 Sep 27]. Available from: https://www.un.org/sustainabledevelopment/progress-report/

35. Groot Koerkamp B, Wang YC, Hunink MGM. Cost-effectiveness analysis for surgeons. Surgery. 2009 Jun;145(6):616–22.

36. World Health Organization Cost effectiveness thresholds [Internet]. [cited 2021 Sep 25]. Available from: http://www.who.int/choice/costs/CER_thresholds/en

37. Haynes AB, Weiser TG, Berry WR, Lipsitz SR, Breizat AHS, Dellinger EP, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. N Engl J Med. 2009 Jan 29;360(5):491–9.

38. GlobalSurg Collaborative. Pooled analysis of WHO Surgical Safety Checklist use and mortality after emergency laparotomy. Br J Surg. 2019 Jan;106(2):e103–12.

39. Daniels KM, Riesel JN, Meara JG. The scale-up of the surgical workforce. Lancet. 2015 Apr 27;385 Suppl 2:S41.

40. Federspiel F, Mukhopadhyay S, Milsom PJ, Scott JW, Riesel JN, Meara JG. Global surgical, obstetric, and anesthetic task shifting: A systematic literature review. Surgery. 2018 Sep;164(3):553–8.

41. Atiyeh BS, Gunn SWA, Hayek SN. Provision of essential surgery in remote and rural areas of developed as well as low and middle income countries. Int J Surg. 2010;8(8):581–5.

42. Ng-Kamstra JS, Greenberg SLM, Abdullah F, Amado V, Anderson GA, Cossa M, et al. Global Surgery 2030: a roadmap for high income country actors. BMJ Global Health. 2016 Apr 1;1(1):e000011.

43. McGlynn EA. Six challenges in measuring the quality of health care. Health Aff (Millwood). 1997 Jun;16(3):7–21.

44. Citron I, Saluja S, Amundson J, Ferreira RV, Ljungman D, Alonso N, et al. Surgical quality indicators in low-resource settings: A new evidence-based tool. Surgery. 2018 Nov;164(5):946–52.

45. About ACS NSQIP [Internet]. ACS. [cited 2022 Oct 5]. Available from: https://www.facs.org/quality-programs/data-and-registries/acs-nsqip/about-acs-nsqip/

46. AHRQ Quality Indicators [Internet]. [cited 2022 Oct 5]. Available from: https://qualityindicators.ahrq.gov/

47. Ng-Kamstra JS, Arya S, Greenberg SLM, Kotagal M, Arsenault C, Ljungman D, et al. Perioperative mortality rates in low-income and middle-income countries: a systematic review and meta-analysis. BMJ Glob Health. 2018;3(3):e000810.

48. Bainbridge D, Martin J, Arango M, Cheng D, Evidence-based Peri-operative Clinical Outcomes Research (EPiCOR) Group. Perioperative and anaesthetic-related mortality in developed and developing countries: a systematic review and meta-analysis. Lancet. 2012 Sep 22;380(9847):1075–81.

49. Uribe-Leitz T, Jaramillo J, Maurer L, Fu R, Esquivel MM, Gawande AA, et al. Variability in mortality following caesarean delivery, appendectomy, and groin hernia repair in low-income and middle-income countries: a systematic review and analysis of published data. Lancet Glob Health. 2016;4(3):e165-74.

50. Watters DA, Hollands MJ, Gruen RL, Maoate K, Perndt H, McDougall RJ, et al. Perioperative mortality rate (POMR): a global indicator of access to safe surgery and anaesthesia. World J Surg. 2015 Apr;39(4):856–64.

51. Weiser TG, Makary MA, Haynes AB, Dziekan G, Berry WR, Gawande AA, et al. Standardised metrics for global surgical surveillance. Lancet. 2009 Sep 26;374(9695):1113–7.

52. Sullivan R, Alatise OI, Anderson BO, Audisio R, Autier P, Aggarwal A, et al. Global cancer surgery: delivering safe, affordable, and timely cancer surgery. Lancet Oncol. 2015;16(11):1193–224.

53. Roser M, Ritchie H. Cancer. Our World in Data [Internet]. 2015 Jul 3 [cited 2022 Oct 11]; Available from: https://ourworldindata.org/cancer

54. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2018;68(6):394–424.

55. AERB. Home [Internet]. Government of India Atomic Energy Regulatory Board. [cited 2022 Aug 13]. Available from: https://www.aerb.gov.in/english/

56. ACTION Study Group, Jan S, Kimman M, Peters SAE, Woodward M. Financial catastrophe, treatment discontinuation and death associated with surgically operable cancer in South-East Asia: Results from the ACTION Study. Surgery. 2015;157(6):971–82.

57. Kapiteijn E, Marijnen CA, Nagtegaal ID, Putter H, Steup WH, Wiggers T, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. N Engl J Med. 2001 Aug 30;345(9):638–46.

58. Songun I, Putter H, Kranenbarg EMK, Sasako M, van de Velde CJH. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. Lancet Oncol. 2010 May;11(5):439–49.

59. Bilimoria KY, Phillips JD, Rock CE, Hayman A, Prystowsky JB, Bentrem DJ. Effect of surgeon training, specialization, and experience on outcomes for cancer surgery: a systematic review of the literature. Ann Surg Oncol. 2009 Jul;16(7):1799–808.

60. Birkmeyer JD, Stukel TA, Siewers AE, Goodney PP, Wennberg DE, Lucas FL. Surgeon Volume and Operative Mortality in the United States. New England Journal of Medicine. 2003;349(22):2117–27.

61. Reames BN, Ghaferi AA, Birkmeyer JD, Dimick JB. Hospital volume and operative mortality in the modern era. Ann Surg. 2014;260(2):244–51.

62. Van Leersum NJ, Snijders HS, Henneman D, Kolfschoten NE, Gooiker GA, ten Berge MG, et al. The Dutch surgical colorectal audit. Eur J Surg Oncol. 2013 Oct;39(10):1063–70.

63. Birgisson H, Talbäck M, Gunnarsson U, Påhlman L, Glimelius B. Improved survival in cancer of the colon and rectum in Sweden. Eur J Surg Oncol. 2005 Oct;31(8):845–53.

64. von Meyenfeldt EM, Gooiker GA, van Gijn W, Post PN, van de Velde CJH, Tollenaar RAEM, et al. The relationship between volume or surgeon specialty and outcome in the surgical treatment of lung cancer: a systematic review and meta-analysis. J Thorac Oncol. 2012 Jul;7(7):1170–8.

65. Foreman KJ, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016-40 for 195 countries and territories. Lancet. 2018 Nov 10;392(10159):2052–90.

66. World Health Organisation. WHO report on cancer: setting priorities, investing wisely and providing care for all [Internet]. [cited 2022 Aug 12]. Available from: https://www.who.int/publications-detail-redirect/9789240001299

67. National Cancer Control Programmes [Internet]. [cited 2022 Aug 12]. Available from: https://www.who.int/publications-detail-redirect/national-cancer-control-programmes

68. Meara JG, Leather AJM, Hagander L, Alkire BC, Alonso N, Ameh EA, et al. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. The Lancet. 2015 Aug 14;386(9993):569–624.

69. Ademuyiwa AO, Hardy P, Runigamugabo E, Sodonougbo P, Behanzin H, Kangni S, et al. Reducing surgical site infections in low-income and middle-income countries

(FALCON): a pragmatic, multicentre, stratified, randomised controlled trial. The Lancet. 2021 Nov 6;398(10312):1687–99.

70. NIHR Global Health Research Unit on Global Surgery. Study protocol for a cluster randomised trial of sterile glove and instrument change at the time of wound closure to reduce surgical site infection in low- and middle-income countries (CHEETAH). Trials. 2022 Apr 15;23(1):320.

71. Vedula SS, Hager GD. Surgical data science: the new knowledge domain. Innovative Surgical Sciences. 2017;2(3):109–21.

72. Pence HE. What is Big Data and Why is it Important? Journal of Educational Technology Systems. 2014 Dec 1;43(2):159–71.

73. McCue ME, McCoy AM. The Scope of Big Data in One Medicine: Unprecedented Opportunities and Challenges. Front Vet Sci [Internet]. 2017 Nov 16 [cited 2018 Sep 26];4. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5696324/

74. Bloomrosen M, Detmer DE. Informatics, evidence-based care, and research; implications for national policy: a report of an American Medical Informatics Association health policy conference. J Am Med Inform Assoc. 2010;17(2):115–23.

75. Targarona EM, Balla A, Batista G. Big data and surgery: The digital revolution continues. Cir Esp. 2018;96(5):247–9.

76. Khuri SF, Daley J, Henderson W, Hur K, Demakis J, Aust JB, et al. The Department of Veterans Affairs' NSQIP: the first national, validated, outcome-based, risk-adjusted, and peer-controlled program for the measurement and enhancement of the quality of surgical care. National VA Surgical Quality Improvement Program. Ann Surg. 1998 Oct;228(4):491–507.

77. Curado MP, Voti L, Sortino-Rachou AM. Cancer registration data and quality indicators in low and middle income countries: their interpretation and potential use for the improvement of cancer care. Cancer Causes Control. 2009 Jul 1;20(5):751–6.

78. Taylor L, Schroeder R. Is bigger better? The emergence of big data as a tool for international development policy. GeoJournal. 2015 Aug 1;80(4):503–18.

79. Jerven M. Poor Numbers: How We Are Misled by African Development Statistics and What to Do about It. Cornell University Press; 2013. 209 p.

80. Drake TM, Knight SR, Harrison EM, Søreide K. Global Inequities in Precision Medicine and Molecular Cancer Research. Front Oncol. 2018;8:346.

81. Knight SR, Ots R, Maimbo M, Drake TM, Fairfield CJ, Harrison EM. Systematic review of the use of big data to improve surgery in low- and middle-income countries. Br J Surg. 2019;106(2):e62–72.

82. PROSPERO: International prospective register of systematic reviews [Internet]. [cited 2022 Jul 22]. Available from: https://www.crd.york.ac.uk/prospero/

83. Cochrane LMIC Filters for PubMed (NLM), MEDLINE (Ovid), Embase (Ovid), and CENTRAL (Cochrane Library) to help identify studies relevant to LMIC [Internet]. [cited 2022 Jul 22]. Available from: https://epoc.cochrane.org/lmic-filters

84. World Bank Country and Lending Groups – World Bank Data Help Desk [Internet]. [cited 2022 Jul 22]. Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519

85. Core Team R. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/. 2022.

86. Wickham H. Tidyverse: Easily Install and Load the 'Tidyverse'. R package version 1.2.1. https://CRAN.R-project.org/package=tidyverse. 2022.

87. Moghimi-Dehkordi B, Safaee A, Zali MR. Survival rates and prognosis of gastric cancer using an actuarial life-table method. Asian Pac J Cancer Prev. 2008 Jun;9(2):317–21.

88. Zhaohui S, Shuxia Z, Xinghua F, Shujun L, Yanpu L, Bin B, et al. The design and implementation of chinese maxillofacial trauma registry, analysis and injury severity score system. J Trauma. 2008 Apr;64(4):1024–33.

89. Mariano MB, Tefilli MV, Fonseca GN, Goldraich IH. Laparoscopic radical prostatectomy: 10 years experience. Int Braz J Urol. 2009 Oct;35(5):565–71; discussion 571-572.

90. Rezaianzadeh A, Peacock J, Reidpath D, Talei A, Hosseini SV, Mehrabani D. Survival analysis of 1148 women diagnosed with breast cancer in Southern Iran. BMC Cancer. 2009 Jun 5;9:168.

91. Campos FG, Valarini R. Evolution of laparoscopic colorectal surgery in Brazil: results of 4744 patients from the national registry. Surg Laparosc Endosc Percutan Tech. 2009 Jun;19(3):249–54.

92. Elbasmi AA, Fayaz MS, Al-Mohanadi S, Al-Nesf Y, Al-Awadi A. Reliability of the Kuwait Cancer Registry: a comparison between breast cancer data collected by clinical oncologists and registry staff. Asian Pac J Cancer Prev. 2010;11(3):735–8.

93. Biglarian A, Hajizadeh E, Kazemnejad A, Zayeri F. Determining of prognostic factors in gastric cancer patients using artificial neural networks. Asian Pac J Cancer Prev. 2010;11(2):533–6.

94. Moghimi-Dehkordi B, Safaee A, Fatemi R, Ghiasi S, Zali MR. Impact of age on prognosis in Iranian patients with gastric carcinoma: review of 742 cases. Asian Pac J Cancer Prev. 2010;11(2):335–8.

95. Chen CQ, Fang LK, Cai SR, Ma JP, Yang GX, Yang W, et al. Effects of diabetes mellitus on prognosis of the patients with colorectal cancer undergoing resection: a cohort study with 945 patients. Chin Med J. 2010 Nov;123(21):3084–8.

96. Gupta NP, Ishwar R, Kumar A, Dogra PN, Seth A. Renal tumors presentation: changing trends over two decades. Indian J Cancer. 2010 Sep;47(3):287–91.

97. Latin American Pediatric Nephrology Association, Latin American Pediatric Renal Transplant Cooperative Study. Latin American Registry of Pediatric Renal Transplantation 2004-2008. Pediatr Transplant. 2010 Sep 1;14(6):701–8.

98. Muleta M, Rasmussen S, Kiserud T. Obstetric fistula in 14,928 Ethiopian women. Acta Obstet Gynecol Scand. 2010 Jul;89(7):945–51.

99. Ercole FF, Franco LMC, Macieira TGR, Wenceslau LCC, de Resende HIN, Chianca TCM. Risk of surgical site infection in patients undergoing orthopedic surgery. Rev Lat Am Enfermagem. 2011 Dec;19(6):1362–8.

100. Brisebois RJ, Tien HC. Surgical experience at the Canadian-led Role 3 Multinational Medical Unit in Kandahar, Afghanistan. J Trauma. 2011 Nov;71(5 Suppl 1):S397-400.

101. Ranasinghe WKB, Sibanda T, de Silva MVC, Ranasinghe TIJ, Persad R. Incidence of prostate cancer in Sri Lanka using cancer registry data and comparisons with the incidence in South Asian men in England. BJU Int. 2011 Oct;108(8 Pt 2):E184-189.

102. Nechuta S, Lu W, Chen Z, Zheng Y, Gu K, Cai H, et al. Vitamin supplement use during breast cancer treatment and survival: a prospective cohort study. Cancer Epidemiol Biomarkers Prev. 2011 Feb;20(2):262–71.

103. Elias ACGP, Matsuo T, Grion CMC, Cardoso LTQ, Verri PH. Incidence and risk factors for sepsis in surgical patients: a cohort study. J Crit Care. 2012 Apr;27(2):159–66.

104. Frajzyngier V, Ruminjo J, Asiimwe F, Barry T, Bello A, Danladi D, et al. Factors influencing choice of surgical route of repair of genitourinary fistula, and the influence of route of repair on surgical outcomes: findings from a prospective cohort study. BJOG. 2012 Oct;119(11):1344–53.

105. Piotto RF, Ferreira FB, Colósimo FC, Silva GS da, Sousa AG de, Braile DM. Independent predictors of prolonged mechanical ventilation after coronary artery bypass surgery. Rev Bras Cir Cardiovasc. 2012 Dec;27(4):520–8.

106. Löfgren J, Makumbi F, Galiwango E, Nordin P, Ibingira C, Forsberg BC, et al. Prevalence of treated and untreated groin hernia in eastern Uganda. Br J Surg. 2014 May;101(6):728–34.

107. Tollefson TT, Shaye D, Durbin-Johnson B, Mehdezadeh O, Mahomva L, Chidzonga M. Cleft lip-cleft palate in Zimbabwe: estimating the distribution of the surgical burden of disease using geographic information systems. Laryngoscope. 2015 Feb;125 Suppl 1:S1-14.

108. Mejía OAV, Matrangolo BLR, Titinger DP, de Faria LB, Dallan LRP, Galas FRB, et al. Age, Creatinine and Ejection Fraction Score in Brazil: Comparison with InsCor and the EuroSCORE. Arq Bras Cardiol. 2015 Nov;105(5):450–6.

109. Sivasubramaniam PG, Zhang BL, Zhang Q, Smith JS, Zhang B, Tang ZH, et al. Breast Cancer Disparities: A Multicenter Comparison of Tumor Diagnosis, Characteristics, and Surgical Treatment in China and the U.S. Oncologist. 2015 Sep;20(9):1044–50.

110. Noppakun K, Ingsathit A, Pongskul C, Premasthian N, Avihingsanon Y, Lumpaopong A, et al. A 25-year experience of kidney transplantation in Thailand: report from the Thai Transplant Registry. Nephrology (Carlton). 2015 Mar;20(3):177–83.

111. Biccard BM, Madiba TE, South African Surgical Outcomes Study Investigators. The South African Surgical Outcomes Study: A 7-day prospective observational cohort study. S Afr Med J. 2015;105(6):465–75.

112. Moodley Y, Biccard BM. Predictors of in-hospital mortality following non-cardiac surgery: Findings from an analysis of a South African hospital administrative database. S Afr Med J. 2015 Jan 3;105(2):126–9.

113. Zablotska LB, Nadyrov EA, Rozhko AV, Gong Z, Polyanskaya ON, McConnell RJ, et al. Analysis of thyroid malignant pathologic findings identified during 3 rounds of screening (1997-2008) of a cohort of children and adolescents from belarus exposed to radioiodines after the Chernobyl accident. Cancer. 2015 Feb 1;121(3):457–66.

114. Saifuddin A, Shahabuddin S, Perveen S, Furnaz S, Sharif H. Towards excellence in cardiac surgery: experience from a developing country. Int J Qual Health Care. 2015 Aug;27(4):255–9.

115. Filippi V, Ganaba R, Calvert C, Murray SF, Storeng KT. After surgery: the effects of life-saving caesarean sections in Burkina Faso. BMC Pregnancy Childbirth [Internet]. 2015 Dec 23 [cited 2018 Aug 30];15. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4688946/

116. Sangkittipaiboon S, Leklob A, Sriplung H, Bilheem S. Breast Cancer in Lopburi, a Province in Central Thailand: Analysis of 2001-2010 Incidence and Future Trends. Asian Pac J Cancer Prev. 2015;16(18):8359–64.

117. Lalitwongsa S, Pongnikorn D, Daoprasert K, Sriplung H, Bilheem S. Breast Cancer in Lampang, a Province in Northern Thailand: Analysis of 1993-2012 Incidence Data and Future Trends. Asian Pac J Cancer Prev. 2015;16(18):8327–33.

118. Tassanasunthornwong S, Chansaard W, Sriplung H, Bilheem S. Breast Cancer in Surat Thani, a Province in Southern Thailand: Analysis of 2004-2012 Incidence and Future Trends. Asian Pac J Cancer Prev. 2015;16(15):6735–40.

119. Paula F de L, da Cunha GM, Leite I da C, Pinheiro RS, Valente JG. Elderly readmission and death after discharge from treatment of hip fracture, occurred in public hospitals from 2008 to 2010, Rio de Janeiro. Rev Bras Epidemiol. 2015 Jun;18(2):439–53.

120. Islam MT, Yoshimura Y. Rate of cesarean delivery at hospitals providing emergency obstetric care in Bangladesh. Int J Gynaecol Obstet. 2015 Jan;128(1):40–3.

121. Moreno RP, Pearse R, Rhodes A. American Society of Anesthesiologists Score: still useful after 60 years? Results of the EuSOS Study. Rev Bras Ter Intensiva. 2015;27(2):105–12.

122. International Surgical Outcomes Study group. Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle- and high-income countries. Br J Anaesth. 2016 Oct 31;117(5):601–9.

123. Nagoshi N, Tetreault LA, Nakashima H, Nouri A, Arnold P, Zileli M, et al. Do Caucasians and East Asians have Different Outcomes Following Surgery for the Treatment of Degenerative Cervical Myelopathy?: Results From the Prospective Multicenter AOSpine International Study. Spine. 2016 Sep 15;41(18):1428–35.

124. Tostes MF do P, Covre ER, Fernandes CAM. Access to surgical assistance: challenges and perspectives. Rev Lat Am Enfermagem. 2016 Mar 28;24:e2677.

125. Wang P, Huang G, Tam N, Wu C, Fu S, Hughes BP, et al. Influence of preoperative sodium concentration on outcome of patients with hepatitis B virus cirrhosis after liver transplantation. Eur J Gastroenterol Hepatol. 2016 Oct;28(10):1210–5.

126. Garcia LP, Huang A, Corlew DS, Aeron K, Aeron Y, Rai SM, et al. Factors Affecting Burn Contracture Outcome in Developing Countries: A Review of 2506 Patients. Ann Plast Surg. 2016 Sep;77(3):290–6.

127. Xiang L, Li J, Chen J, Wang X, Guo P, Fan Y, et al. Prospective cohort study of laparoscopic and open hepatectomy for hepatocellular carcinoma. Br J Surg. 2016 Dec;103(13):1895–901.

128. Nandakumar A, Nandakumar A. Survival in Head and Neck Cancers - Results of A Multi- Institution Study. Asian Pac J Cancer Prev. 2016;17(4):1745–54.

129. Reyes PAC, Gabriel E.A. Incidence, prevalence, mortality, risks, and survival of colorectal carcinoma in metro Cebu from 2002 to 2012: A 10-year analysis. In Journal of Gastroenterology and Hepatology (Australia); 2016. p. 192.

130. Lei Z, Li J, Wu D, Xia Y, Wang Q, Si A, et al. Nomogram for Preoperative Estimation of Microvascular Invasion Risk in Hepatitis B Virus-Related Hepatocellular Carcinoma Within the Milan Criteria. JAMA Surg. 2016 Apr;151(4):356–63.

131. Bhandare MS, An NK, Batra S, Chaudhari V, Shrikh SV. Radical gastrectomy for gastric cancer at Tata Memorial Hospital. Indian J Cancer. 2017 Dec;54(4):605–8.

132. Acaroglu E, Guler UO, Cetinyurek-Yavuz A, Yuksel S, Yavuz Y, Ayhan S, et al. Decision analysis to identify the ideal treatment for adult spinal deformity: What is the impact of complications on treatment outcomes? Acta Orthop Traumatol Turc. 2017 May;51(3):181–90.

133. Fang C, Wang W, Zhang Y, Feng X, Sun J, Zeng Y, et al. Clinicopathologic characteristics and prognosis of gastroenteropancreatic neuroendocrine neoplasms: a multicenter study in South China. Chin J Cancer. 2017 Jun 21;36:51.

134. Figueiredo AE, de Mattos C, Saraiva C, Olandoski M, Barretti P, Pecoits Filho R, et al. Comparison between types of dressing following catheter insertion and early exit-site infection in peritoneal dialysis. J Clin Nurs. 2017 Nov;26(21–22):3658–63.

135. Zheng Z, Zhang H, Yuan X, Rao C, Zhao Y, Wang Y, et al. Comparing Outcomes of Coronary Artery Bypass Grafting Among Large Teaching and Urban Hospitals in China and the United States. Circ Cardiovasc Qual Outcomes. 2017 Jun;10(6).

136. Yousefzadeh Chabok S, Ranjbar Taklimie F, Malekpouri R, Razzaghi A. Predicting mortality, hospital length of stay and need for surgery in pediatric trauma patients. Chin J Traumatol. 2017 Dec;20(6):339–42.

137. Gajewski J, Dharamshi R, Strader M, Kachimba J, Borgstein E, Mwapasa G, et al. Who accesses surgery at district level in sub-Saharan Africa? Evidence from Malawi and Zambia. Trop Med Int Health. 2017;22(12):1533–41.

138. Shah S, Ross O, Pickering S, Knoble S, Rai I. Tablet e-Logbooks: Four Thousand Clinical Cases and Complications e-Logged by 14 Nondoctor Anesthesia Providers in Nepal. Anesth Analg. 2017;125(4):1337–41.

139. Hu Y, Huang K, Sun Y, Wang J, Xu Y, Yan S, et al. Placenta response of inflammation and oxidative stress in low-risk term childbirth: the implication of delivery mode. BMC Pregnancy Childbirth. 2017 Dec 6;17(1):407.

140. Arthur CPS, Mejia OAV, Osternack D, Nakazone MA, Goncharov M, Lisboa LAF, et al. Do We Need to Personalize Renal Function Assessment in the Stratification of Patients Undergoing Cardiac Surgery? Arq Bras Cardiol. 2017 Oct;109(4):290–8.

141. Hernandez MC, Kong VY, Aho JM, Bruce JL, Polites SF, Laing GL, et al. Increased anatomic severity in appendicitis is associated with outcomes in a South African population. J Trauma Acute Care Surg. 2017 Jul;83(1):175–81.

142. ACTION Study Group. Policy and priorities for national cancer control planning in low- and middle-income countries: Lessons from the Association of Southeast Asian Nations (ASEAN) Costs in Oncology prospective cohort study. Eur J Cancer. 2017;74:26–37.

143. Doshi P, Gopalan H, Sprague S, Pradhan C, Kulkarni S, Bhandari M. Incidence of infection following internal fixation of open and closed tibia fractures in India (INFINITI): a multi-centre observational cohort study. BMC Musculoskelet Disord. 2017 Apr 14;18(1):156.

144. Kopp DM, Bengtson AM, Tang JH, Chipungu E, Moyo M, Wilkinson J. Use of a postoperative pad test to identify continence status in women after obstetric vesicovaginal fistula repair: a prospective cohort study. BJOG. 2017 May;124(6):966–72.

145. Treeprasertsuk S, Poovorawan K, Soonthornworasiri N, Chaiteerakij R, Thanapirom K, Mairiang P, et al. A significant cancer burden and high mortality of intrahepatic cholangiocarcinoma in Thailand: a nationwide database study. BMC Gastroenterol. 2017 Jan 5;17(1):3.

146. Carvalho RLR de, Campos CC, Franco LM de C, Rocha ADM, Ercole FF, Carvalho RLR de, et al. Incidence and risk factors for surgical site infection in general surgeries. Rev Lat Am Enfermagem. 2017;25:e2848.

147. Wang K, Zhang X, Zheng K, Yin XD, Xing L, Zhang AJ, et al. Predictors of internal mammary lymph nodes (IMLN) metastasis and disease-free survival comparison

between IMLN-positive and IMLN-negative breast cancer patients: Results from Western China Clinical Cooperation Group (WCCCG) database (CONSORT). Medicine (Baltimore). 2018 Jul;97(28):e11296.

148. Van der Spuy K, Crowther M, Nejthardt M, Roodt F, Davids J, Roos J, et al. A multicentre, cross-sectional study investigating the prevalence of hypertensive disease in patients presenting for elective surgery in the Western Cape Province, South Africa. S Afr Med J. 2018 Jun 26;108(7):590–5.

149. George R, Menon VP, Edathadathil F, Balachandran S, Moni M, Sathyapalan D, et al. Myocardial injury after noncardiac surgery-incidence and predictors from a prospective observational cohort study at an Indian tertiary care centre. Medicine (Baltimore). 2018 May;97(19):e0402.

150. Augusto KL, Brilhante AVM, Modesto GCD, Saboia DM, Rocha CFC, Karbage SAL, et al. Costs and mortality rates of surgical approaches to hysterectomy in Brazil. Rev Saude Publica. 2018 Mar 12;52:25.

151. Brand M, Gaylard P, Ramos J. Colorectal cancer in South Africa: An assessment of disease presentation, treatment pathways and 5-year survival. S Afr Med J. 2018 Feb 1;108(2):118–22.

152. Global Burden of Disease Study 2016 (GBD 2016) Data Resources | GHDx [Internet]. [cited 2022 Jul 25]. Available from: http://ghdx.healthdata.org/gbd-2016

153. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1211–59.

154. GBD 2016 Alcohol Collaborators. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2018 Aug 23;

155. Lin JH, Jiang CQ, Ho SY, Zhang WS, Mai ZM, Xu L, et al. Smoking and nasopharyngeal carcinoma mortality: a cohort study of 101,823 adults in Guangzhou, China. BMC Cancer. 2015 Nov 16;15:906.

156. Reisman M. EHRs: The Challenge of Making Electronic Data Usable and Interoperable. P T. 2017 Sep;42(9):572–5.

157. Syzdykova A, Malta A, Zolfo M, Diro E, Oliveira JL. Open-Source Electronic Health Record Systems for Low-Resource Settings: Systematic Review. JMIR Med Inform. 2017 Nov 13;5(4):e44.

158. Rwanda PIH - MoH Collaboration - Projects - OpenMRS Wiki [Internet]. [cited 2022 Jul 25]. Available from: https://wiki.openmrs.org/display/projects/Rwanda+PIH+-+MoH+Collaboration

159. GSMA Mobile Economy 2018 [Internet]. Mobile Economy 2018. [cited 2022 Jul 25]. Available from: https://www.gsma.com/mobileeconomy/

160. Maruthappu M, Watkins J, Noor AM, Williams C, Ali R, Sullivan R, et al. Economic downturns, universal health coverage, and cancer mortality in high-income and middle-income countries, 1990-2010: a longitudinal analysis. Lancet. 2016 Aug 13;388(10045):684–95.

161. GlobalSurg Collaborative. Mortality of emergency abdominal surgery in high-, middle- and low-income countries. British Journal of Surgery. 2016 Jul 1;103(8):971–88.

162. Shrime MG, Dare A, Alkire BC, Meara JG. A global country-level comparison of the financial burden of surgery. Br J Surg. 2016 Oct;103(11):1453–61.

163. NICE | The National Institute for Health and Care Excellence [Internet]. NICE. NICE; [cited 2022 Jul 20]. Available from: https://www.nice.org.uk/

164. American College of Surgeons, 2019. CoC Quality of Care Measures [Internet]. American College of Surgeons. [cited 2022 Jul 20]. Available from: http://www.facs.org/quality-programs/cancer/ncdb/qualitymeasures

165. NIHR Global Health Research Unit on Global Surgery. Quality and outcomes in global cancer surgery: protocol for a multicentre, international, prospective cohort study (GlobalSurg 3). BMJ Open. 2019 May 1;9(5):e026646.

166. GlobalSurg C. GlobalSurg 3 Study documentation [Internet]. [cited 2022 Nov 20]. Available from: https://globalsurg.org/projects/cohort-studies/globalsurg-3/

167. GlobalSurg Collaborative. Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: a prospective, international, multicentre cohort study. Lancet Infect Dis. 2018 Feb 13;

168. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007 Oct 20;370(9596):1453–7.

169. Lang TA, Altman DG. Basic statistical reporting for articles published in biomedical journals: the "Statistical Analyses and Methods in the Published Literature" or the SAMPL guidelines. Science Editors' Handbook, European Association of Science Editors [Internet]. 2013 [cited 2013 Nov 4]; Available from: http://www.public.iastate.edu/~pdixon/stat511/resources/SAMPL%20guidelines.pdf

170. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009 Apr;42(2):377–81.

171. Piñeros M, Parkin DM, Ward K, Chokunonga E, Ervik M, Farrugia H, et al. Essential TNM: a registry tool to reduce gaps in cancer staging information. Lancet Oncol. 2019;20(2):e103–11.

172. Brierley JD, Gospodarowicz M, Wittekind C. Union for International Cancer Control TNM Classification of Malignant Tumours [Internet]. 8th ed. Chichester: John Wiley & Sons, Inc.; 2017 [cited 2022 Jul 27]. 272 p. Available from: https://www.wiley.com/en-gb/TNM+Classification+of+Malignant+Tumours%2C+8th+Edition-p-9781119263579

173. Gospodarowicz M, Trypuc J, Cruz AD, Khader J, Omar S, Knaul F. Chapter 11. Cancer services and the comprehensive cancer center. Third. Vol. 3.

174. World Health Organisation. Health topics [Internet]. [cited 2021 Mar 24]. Available from: https://www.who.int/health-topics

175. NHS England. NHS Data Model and Dictionary [Internet]. [cited 2022 Nov 24]. Available from: https://datadictionary.nhs.uk/

176. Types of Oncologists | Cancer.Net [Internet]. [cited 2019 Jan 10]. Available from: https://www.cancer.net/navigating-cancer-care/cancer-basics/cancer-care-team/types-oncologists

177. Oesophago-gastric cancer | Guidance and guidelines | NICE [Internet]. [cited 2019 Jan 10]. Available from: https://www.nice.org.uk/guidance/qs176/chapter/Quality-statement-2-Multidisciplinary-review

178. Dindo D, Demartines N, Clavien PA. Classification of Surgical Complications. Annals of Surgery. 2004 Aug;240(2):205–13.

179. Nakagawa S, Schielzeth H. A general and simple method for obtaining R2 from generalized linear mixed-effects models. Methods in Ecology and Evolution. 2013;4(2):133–42.

180. VanderWeele TJ. A Three-way Decomposition of a Total Effect into Direct, Indirect, and Interactive Effects. Epidemiology. 2013 Mar;24(2):224–32.

181. Ward ZJ, Scott AM, Hricak H, Atun R. Global costs, health benefits, and economic benefits of scaling up treatment and imaging modalities for survival of 11 cancers: a simulation-based analysis. The Lancet Oncology. 2021 Mar 1;22(3):341–50.

182. Funk LM, Gawande AA, Semel ME, Lipsitz SR, Berry WR, Zinner MJ, et al. Esophagectomy outcomes at low-volume hospitals: the association between systems characteristics and mortality. Ann Surg. 2011 May;253(5):912–7.

183. Sheetz KH, Dimick JB, Ghaferi AA. Impact of Hospital Characteristics on Failure to Rescue Following Major Surgery. Ann Surg. 2016 Apr;263(4):692–7.

184. McCrum ML, Lipsitz SR, Berry WR, Jha AK, Gawande AA. Beyond volume: does hospital complexity matter?: an analysis of inpatient surgical mortality in the United States. Med Care. 2014 Mar;52(3):235–42.

185. Khuri SF, Henderson WG, DePalma RG, Mosca C, Healey NA, Kumbhani DJ, et al. Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. Ann Surg. 2005 Sep;242(3):326–41; discussion 341-343.

186. Moons KGM, Altman DG, Reitsma JB, Ioannidis JPA, Macaskill P, Steyerberg EW, et al. Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD): explanation and elaboration. Ann Intern Med. 2015 Jan 6;162(1):W1-73.

187. National Institute for Health Research Global Health Research Unit on Global Surgery. Global variation in postoperative mortality and complications after cancer surgery: a multicentre, prospective cohort study in 82 countries. Lancet. 2021 Jan 30;397(10272):387–97.

188. NIHR Global Health Research Unit on Global Surgery. Quality and outcomes in global cancer surgery: protocol for a multicentre, international, prospective cohort study (GlobalSurg 3). BMJ Open. 2019;9(5):e026646.

189. Bass GA, Kaplan LJ, Ryan ÉJ, Cao Y, Lane-Fall M, Duffy CC, et al. The snapshot audit methodology: design, implementation and analysis of prospective observational cohort studies in surgery. Eur J Trauma Emerg Surg. 2022 Jul 15;

190. Altman DG. Practical Statistics for Medical Research. Chapman and Hall; 2020. 650 p44-50.

191. Grimes CE, Bowman KG, Dodgion CM, Lavy CBD. Systematic review of barriers to surgical care in low-income and middle-income countries. World J Surg. 2011 May;35(5):941–50.

192. Jocelyn D. Traditional medicine in sub-Saharan Africa : its importance and potential policy options [Internet]. World Bank. [cited 2022 Jul 28]. Available from: https://documents.worldbank.org/en/publication/documents-reports/documentdetail/251121468742850751/Traditional-medicine-in-sub-Saharan-Africa-its-importance-and-potential-policy-options

193. Thaddeus S, Maine D. Too far to walk: maternal mortality in context. Soc Sci Med. 1994 Apr;38(8):1091–110.

194. Mollura DJ, Shah N, Mazal J, RAD-AID Conference Writing Group. White paper report of the 2013 RAD-AID Conference: improving radiology in resource-limited regions and developing countries. J Am Coll Radiol. 2014 Sep;11(9):913–9.

195. Perry L, Malkin R. Effectiveness of medical equipment donations to improve health systems: how much medical equipment is broken in the developing world? Med Biol Eng Comput. 2011 Jul;49(7):719–22.

196. Funk LM, Weiser TG, Berry WR, Lipsitz SR, Merry AF, Enright AC, et al. Global operating theatre distribution and pulse oximetry supply: an estimation from reported data. Lancet. 2010 Sep 25;376(9746):1055–61.

197. Piñeros M, Parkin DM, Ward K, Chokunonga E, Ervik M, Farrugia H, et al. Essential TNM: a registry tool to reduce gaps in cancer staging information. The Lancet Oncology. 2019;20(2):e103–11.

198. Minicozzi P, Innos K, Sánchez MJ, Trama A, Walsh PM, Marcos-Gragera R, et al. Quality analysis of population-based information on cancer stage at diagnosis across Europe, with presentation of stage-specific cancer survival estimates: A EUROCARE-5 study. Eur J Cancer. 2017 Oct;84:335–53.

199. Walters S, Maringe C, Butler J, Brierley JD, Rachet B, Coleman MP. Comparability of stage data in cancer registries in six countries: lessons from the International Cancer Benchmarking Partnership. Int J Cancer. 2013 Feb 1;132(3):676–85.

200. Essential TNM | UICC [Internet]. [cited 2022 Jul 27]. Available from: https://www.uicc.org/resources/access-all-resources/tnm-classification-malignant-tumours/essential-tnm

201. Wright NJ, Leather AJM, Ade-Ajayi N, Sevdalis N, Davies J, Poenaru D, et al. Mortality from gastrointestinal congenital anomalies at 264 hospitals in 74 low-income, middle-income, and high-income countries: a multicentre, international, prospective cohort study. The Lancet. 2021 Jul 24;398(10297):325–39.

202. STARSurg Collaborative. Prognostic model to predict postoperative acute kidney injury in patients undergoing major gastrointestinal surgery based on a national prospective observational cohort study. BJS Open. 2018 Dec;2(6):400–10.

203. STARSurg Collaborative. Impact of postoperative non-steroidal anti-inflammatory drugs on adverse events after gastrointestinal surgery. Br J Surg. 2014 Oct;101(11):1413–23.

204. Alkire BC, Shrime MG, Dare AJ, Vincent JR, Meara JG. Global economic consequences of selected surgical diseases: a modelling study. Lancet Glob Health. 2015 Apr 27;3 Suppl 2:S21-27.

205. Ghaferi AA, Birkmeyer JD, Dimick JB. Variation in hospital mortality associated with inpatient surgery. New England Journal of Medicine. 2009;361(14):1368.

206. Global Cancer Observatory [Internet]. [cited 2020 Sep 15]. Available from: https://gco.iarc.fr/

207. Chaker L, Falla A, van der Lee SJ, Muka T, Imo D, Jaspers L, et al. The global impact of non-communicable diseases on macro-economic productivity: a systematic review. Eur J Epidemiol. 2015 May;30(5):357–95.

208. Ng-Kamstra JS, Arya S, Greenberg SLM, Kotagal M, Arsenault C, Ljungman D, et al. Perioperative mortality rates in low-income and middle-income countries: a systematic review and meta-analysis. BMJ Global Health. 2018 Jun 1;3(3):e000810.

209. McPhail S, Johnson S, Greenberg D, Peake M, Rous B. Stage at diagnosis and early mortality from cancer in England. British Journal of Cancer. 2015 Mar;112(1):S108–15.

210. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. The Lancet Oncology. 2011 May 1;12(5):489–95.

211. Gyawali B, Bouche G, Crisp N, André N. Challenges and opportunities for cancer clinical trials in low- and middle-income countries. Nature Cancer. 2020 Feb;1(2):142–5.

212. Ahmad T, Bouwman RA, Grigoras I, Aldecoa C, Hofer C, Hoeft A, et al. Use of failure-to-rescue to identify international variation in postoperative care in low-, middle- and high-income countries: a 7-day cohort study of elective surgery. Br J Anaesth. 2017 Aug 1;119(2):258–66.

213. Ward ZJ, Scott AM, Hricak H, Abdel-Wahab M, Paez D, Lette MM, et al. Estimating the impact of treatment and imaging modalities on 5-year net survival of 11 cancers in 200 countries: a simulation-based analysis. The Lancet Oncology. 2020 Aug 1;21(8):1077–88.

214. Santhirapala V, Peden CJ, Meara JG, Biccard BM, Gelb AW, Johnson WD, et al. Towards high-quality peri-operative care: a global perspective. Anaesthesia. 2020;75(S1):e18–27.

215. Sud A, Jones ME, Broggio J, Loveday C, Torr B, Garrett A, et al. Collateral damage: the impact on outcomes from cancer surgery of the COVID-19 pandemic. Annals of Oncology. 2020 Aug 1;31(8):1065–74.

216. Sustainable Development Goals [Internet]. UNDP. [cited 2020 Nov 20]. Available from: https://www.undp.org/content/undp/en/home/sustainable-development-goals.html

217. COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. Lancet. 2020 Jul 4;396(10243):27–38.

218. World Health Assembly 70. Cancer prevention and control in the context of an integrated approach. 2017 [cited 2020 Sep 15]; Available from: https://apps.who.int/iris/handle/10665/275676

219. Donabedian A. The quality of care. How can it be assessed? JAMA. 1988 Sep 23;260(12):1743–8.

220. NIHR Global Health Research Unit on Global Surgery. Effects of hospital facilities on patient outcomes after cancer surgery: an international, prospective, observational study. Lancet Glob Health. 2022 Jul;10(7):e1003–11.

221. Allemani C, Matsuda T, Carlo VD, Harewood R, Matz M, Nikšić M, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. The Lancet. 2018 Mar 17;391(10125):1023–75.

222. Joseph B, Morton JM, Hernandez-Boussard T, Rubinfeld I, Faraj C, Velanovich V. Relationship between hospital volume, system clinical resources, and mortality in pancreatic resection. J Am Coll Surg. 2009 Apr;208(4):520–7.

223. Hricak H, Abdel-Wahab M, Atun R, Lette MM, Paez D, Brink JA, et al. Medical imaging and nuclear medicine: a Lancet Oncology Commission. Lancet Oncol. 2021 Mar 3;

224. Sirohi B, Chalkidou K, Pramesh CS, Anderson BO, Loeher P, El Dewachi O, et al. Developing institutions for cancer care in low-income and middle-income countries: from cancer units to comprehensive cancer centres. The Lancet Oncology. 2018 Aug 1;19(8):e395–406.

225. Cancer | WHO Factsheet [Internet]. [cited 2022 Dec 24]. Available from: https://www.who.int/news-room/fact-sheets/detail/cancer

226. Sud A, Jones ME, Broggio J, Loveday C, Torr B, Garrett A, et al. Collateral damage: the impact on outcomes from cancer surgery of the COVID-19 pandemic. Ann Oncol. 2020 Aug;31(8):1065–74.

227. Pressoir M, Desné S, Berchery D, Rossignol G, Poiree B, Meslier M, et al. Prevalence, risk factors and clinical implications of malnutrition in French Comprehensive Cancer Centres. Br J Cancer. 2010 Mar 16;102(6):966–71.

228. Ho JWC, Wu AHW, Lee MWK, Lau S ying, Lam P shan, Lau W shan, et al. Malnutrition risk predicts surgical outcomes in patients undergoing gastrointestinal operations: Results of a prospective study. Clin Nutr. 2015 Aug;34(4):679–84.

229. Shen Y, Hao Q, Zhou J, Dong B. The impact of frailty and sarcopenia on postoperative outcomes in older patients undergoing gastrectomy surgery: a systematic review and meta-analysis. BMC Geriatr. 2017 Aug 21;17(1):188.

230. Popkin BM, Corvalan C, Grummer-Strawn LM. Dynamics of the double burden of malnutrition and the changing nutrition reality. Lancet. 2020 Jan 4;395(10217):65–74.

231. Maringe C, Spicer J, Morris M, Purushotham A, Nolte E, Sullivan R, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. Lancet Oncol. 2020 Aug;21(8):1023–34.

232. Burden ST, Gibson DJ, Lal S, Hill J, Pilling M, Soop M, et al. Pre-operative oral nutritional supplementation with dietary advice versus dietary advice alone in weight-losing patients with colorectal cancer: single-blind randomized controlled trial. J Cachexia Sarcopenia Muscle. 2017 Jun;8(3):437–46.

233. Miller KR, Wischmeyer PE, Taylor B, McClave SA. An evidence-based approach to perioperative nutrition support in the elective surgery patient. JPEN J Parenter Enteral Nutr. 2013 Sep;37(5 Suppl):39S-50S.

234. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. J Cachexia Sarcopenia Muscle. 2019 Feb;10(1):207–17.

235. Sterne JAC, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ. 2009 Jun 29;338:b2393.

236. Rubin DB, editor. Multiple Imputation for Nonresponse in Surveys [Internet]. Hoboken, NJ, USA: John Wiley & Sons, Inc.; 1987 [cited 2020 Jul 18]. (Wiley Series in Probability and Statistics). Available from: http://doi.wiley.com/10.1002/9780470316696

237. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol. 2011 May;12(5):489–95.

238. Allison SP. Malnutrition, disease, and outcome. Nutrition. 2000 Aug;16(7–8):590–3.

239. Wu GH, Liu ZH, Wu ZH, Wu ZG. Perioperative artificial nutrition in malnourished gastrointestinal cancer patients. World Journal of Gastroenterology. 2006 Apr 21;12(15):2441–4.

240. Sagar RC, Kumar KVV, Ramachandra C, Arjunan R, Althaf S, Srinivas C. Perioperative Artificial Enteral Nutrition in Malnourished Esophageal and Stomach

Cancer Patients and Its Impact on Postoperative Complications. Indian J Surg Oncol. 2019 Sep 1;10(3):460–4.

241. Nakahara S, Nguyen DH, Bui AT, Sugiyama M, Ichikawa M, Sakamoto T, et al. Perioperative nutrition management as an important component of surgical capacity in low- and middle-income countries. Trop Med Int Health. 2017;22(7):784–96.

242. Sungurtekin H, Sungurtekin U, Balci C, Zencir M, Erdem E. The influence of nutritional status on complications after major intraabdominal surgery. J Am Coll Nutr. 2004 Jun;23(3):227–32.

243. Antoun S, Rey A, Béal J, Montange F, Pressoir M, Vasson MP, et al. Nutritional risk factors in planned oncologic surgery: what clinical and biological parameters should be routinely used? World J Surg. 2009 Aug;33(8):1633–40.

244. Demling RH. Nutrition, anabolism, and the wound healing process: an overview. Eplasty. 2009;9:e9.

245. Rasmussen HH, Kondrup J, Ladefoged K, Staun M. Clinical nutrition in danish hospitals: a questionnaire-based investigation among doctors and nurses. Clin Nutr. 1999 Jun;18(3):153–8.

246. Knight S. CRANE Feasibility Study: Nutritional Intervention for Patients Undergoing Cancer Surgery in Low- and Middle-Income Countries [Internet]. [cited 2022 Oct 2]. Available from: https://clinicaltrials.gov/ct2/show/NCT04448041

247. Unger-Saldaña K. Challenges to the early diagnosis and treatment of breast cancer in developing countries. World J Clin Oncol. 2014 Aug 10;5(3):465–77.

248. Neal RD, Tharmanathan P, France B, Din NU, Cotton S, Fallon-Ferguson J, et al. Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review. Br J Cancer. 2015 Mar 31;112 Suppl 1(Suppl 1):S92-107.

249. Ahmad T, Bouwman RA, Grigoras I, Aldecoa C, Hofer C, Hoeft A, et al. Use of failure-to-rescue to identify international variation in postoperative care in low-, middle- and high-income countries: a 7-day cohort study of elective surgery. Br J Anaesth. 2017 Aug 1;119(2):258–66.

250. Waitzberg DL, Caiaffa WT, Correia MI. Hospital malnutrition: the Brazilian national survey (IBRANUTRI): a study of 4000 patients. Nutrition. 2001 Aug;17(7–8):573–80.

251. Knight SR, Qureshi AU, Drake TM, Lapitan MCM, Maimbo M, Yenli E, et al. The impact of preoperative oral nutrition supplementation on outcomes in patients undergoing gastrointestinal surgery for cancer in low- and middle-income countries: a systematic review and meta-analysis. Sci Rep. 2022 Jul 21;12(1):12456.

252. Schuetz P, Seres D, Lobo DN, Gomes F, Kaegi-Braun N, Stanga Z. Management of disease-related malnutrition for patients being treated in hospital. Lancet. 2021 Nov 20;398(10314):1927–38.

253. NIHR Global Health Unit on Global Surgery, COVIDSurg Collaborative. Elective surgery system strengthening: development, measurement, and validation of the surgical preparedness index across 1632 hospitals in 119 countries. Lancet. 2022 Nov 5;400(10363):1607–17.

254. COVIDSurg Collaborative. Effect of COVID-19 pandemic lockdowns on planned cancer surgery for 15 tumour types in 61 countries: an international, prospective, cohort study. Lancet Oncol. 2021 Nov;22(11):1507–17.

255. Hanna TP, King WD, Thibodeau S, Jalink M, Paulin GA, Harvey-Jones E, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. BMJ. 2020 Nov 4;371:m4087.

256. Burden S, Todd C, Hill J, Lal S. Pre-operative nutrition support in patients undergoing gastrointestinal surgery. Cochrane Database Syst Rev. 2012 Nov 14;11:CD008879.

257. ASOS-2 Investigators. Enhanced postoperative surveillance versus standard of care to reduce mortality among adult surgical patients in Africa (ASOS-2): a cluster-randomised controlled trial. Lancet Glob Health. 2021 Oct;9(10):e1391–401.

258. Blencowe NS, Brown JM, Cook JA, Metcalfe C, Morton DG, Nicholl J, et al. Interventions in randomised controlled trials in surgery: issues to consider during trial design. Trials. 2015 Sep 4;16:392.

259. Soerjomataram I, Cabasag C, Bardot A, Fidler-Benaoudia MM, Miranda-Filho A, Ferlay J, et al. Cancer survival in Africa, central and south America, and Asia (SURVCAN-3): a population-based benchmarking study in 32 countries. Lancet Oncol. 2023 Jan;24(1):22–32.

260. Carlson RW, Scavone JL, Koh WJ, McClure JS, Greer BE, Kumar R, et al. NCCN Framework for Resource Stratification: A Framework for Providing and Improving Global Quality Oncology Care. J Natl Compr Canc Netw. 2016 Aug;14(8):961–9.

261. Anderson BO, Shyyan R, Eniu A, Smith RA, Yip CH, Bese NS, et al. Breast cancer in limited-resource countries: an overview of the Breast Health Global Initiative 2005 guidelines. Breast J. 2006;12 Suppl 1:S3-15.

262. Hunter N, Dempsey N, Tbaishat F, Jahanzeb M, Al-Sukhun S, Gralow JR. Resource-Stratified Guideline-Based Cancer Care Should Be a Priority: Historical Context and Examples of Success. Am Soc Clin Oncol Educ Book. 2020 Mar;40:1–10.

263. Reeves N, Chandler S, McLennan E, Price A, Boyle J, Knight S, et al. Defining the older patient population that require, but do not undergo emergency laparotomy: an observational cohort study protocol. International Journal of Clinical Trials. 2021 Apr 22;8(2):138–44.

264. Study management group. Protocol letter: multicentre prospective cohort study of the early management of acute pancreatitis in Great Britain and Ireland: PANC Study (Pancreatitis: A National Cohort Study). Br J Surg. 2021 Jul 23;108(7):e243–4.

265. Project Hippo – Global Surgery Research [Internet]. [cited 2023 Jan 10]. Available from: https://www.globalsurgeryunit.org/clinical-trials-holding-page/hippo/

266. Wynants L, Calster BV, Bonten MMJ, Collins GS, Debray TPA, Vos MD, et al. Prediction models for diagnosis and prognosis of covid-19 infection: systematic review and critical appraisal. BMJ. 2020 Apr 7;369(m1328).

267. Chen JH, Chang SS, Liu JJ, Chan RC, Wu JY, Wang WC, et al. Comparison of clinical characteristics and performance of pneumonia severity score and CURB-65 among younger adults, elderly and very old subjects. Thorax. 2010 Nov;65(11):971–7.

268. Gupta RK, Marks M, Samuels THA, Luintel A, Rampling T, Chowdhury H, et al. Systematic evaluation and external validation of 22 prognostic models among hospitalised adults with COVID-19: an observational cohort study. Eur Respir J. 2020 Dec;56(6):2003498.

269. Knight SR, Ho A, Pius R, Buchan I, Carson G, Drake TM, et al. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. BMJ. 2020 Sep 9;370:m3339.

270. Blunsum AE, Perkins JS, Arshad A, Bajpai S, Barclay-Elliott K, Brito-Mutunayagam S, et al. Evaluation of the Implementation of the 4C Mortality Score in United Kingdom hospitals during the second pandemic wave [Internet]. medRxiv; 2022 [cited 2022 Jun 8]. p. 2021.12.18.21268003. Available from: https://www.medrxiv.org/content/10.1101/2021.12.18.21268003v2

271. NHS England. NHS England [Internet]. NHS England guidelines for Remdesivir therapy in COVID-19 patients. Available from: https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/07/C1322-interim-cc-policy-remdesivir-for-people-hospitalised-with-covid-19-v3.pdf

272. Knight SR, Gupta RK, Ho A, Pius R, Buchan I, Carson G, et al. Prospective validation of the 4C prognostic models for adults hospitalised with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. Thorax. 2022 Jun;77(6):606–15.

273. Gupta RK, Harrison EM, Ho A, Docherty AB, Knight SR, van Smeden M, et al. Development and validation of the ISARIC 4C Deterioration model for adults hospitalised with COVID-19: a prospective cohort study. Lancet Respir Med. 2021 Apr;9(4):349–59.

274. STARSurg Collaborative and TASMAN Collaborative. Evaluation of prognostic risk models for postoperative pulmonary complications in adult patients undergoing major abdominal surgery: a systematic review and international external validation cohort study. Lancet Digit Health. 2022 Jul;4(7):e520–31.

Chapter 10 Appendix: Supplementary material

10.1 Supplementary material for Chapter 2

Systematic review literature search terms

EMBASE/Medline

1. Developing Countries**.sh,kf.**

2. (Africa or Asia or Caribbean or West Indies or South America or Latin America or Central America)**.hw,kf,ti,ab,cp.**

3. (Afghanistan or Albania or Algeria or Angola or Armenia or Armenian or Azerbaijan or Bangladesh or Benin or Byelarus or Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or Herzegovina or Hercegovina or Botswana or Brasil or Brazil or Bulgaria or Burkina Faso or Burkina Fasso or Upper Volta or Burundi or Urundi or Cambodia or Khmer Republic or Kampuchea or Cameroon or Cameroons or Cameron or Camerons or Cape Verde or Central African Republic or Chad or China or Colombia or Comoros or Comoro Islands or Comores or Mayotte or Congo or Zaire or Costa Rica or Cote d'Ivoire or Ivory Coast or Croatia or Cuba or Cyprus or Djibouti or French Somaliland or Dominica or Dominican Republic or East Timor or East Timur or Timor Leste or Ecuador or Egypt or United Arab Republic or El Salvador or Eritrea or Ethiopia or Fiji or Gabon or Gabonese Republic or Gambia or Gaza or Georgia Republic or Georgian Republic or Ghana or Gold Coast or Greece or Grenada or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti or Honduras or India or Maldives or Indonesia or Iran or Iraq or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Kosovo or Kyrgyzstan or Kirghizia or Kyrgyz Republic or Kirghiz or Kirgizstan or Lao PDR or Laos or Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania or Macedonia or Madagascar or Malagasy Republic or Sabah or Sarawak or Malawi or Nyasaland or Mali or Marshall Islands or Mauritania or Mauritius or Agalega Islands or Mexico or Micronesia or Middle East or Moldova or Moldovia or Moldovian or Mongolia or Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal or Netherlands Antilles or New Caledonia or Nicaragua or Niger or Nigeria or Northern Mariana Islands or Oman or Muscat or Pakistan or Palau or Palestine or Paraguay or Peru or Philippines or Philipines or Phillipines or Phillippines or Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or Saint Kitts or St Kitts or Nevis or Saint Lucia or St Lucia or Saint Vincent or St Vincent or Grenadines or Samoa or Samoan Islands or Navigator Island or

Navigator Islands or Sao Tome or Senegal or Serbia or Montenegro or Seychelles or Sierra Leone or Slovenia or Sri Lanka or Ceylon or Solomon Islands or Somalia or South Africa or Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadzhikistan or Tadjikistan or Tadzhik or Tanzania or Thailand or Togo or Togolese Republic or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or USSR or Soviet Union or Union of Soviet Socialist Republics or Uzbekistan or Uzbek or Vanuatu or New Hebrides or Venezuela or Vietnam or Viet Nam or West Bank or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia)**.hw,ti,ab,cp.**

4. ((developing or less* developed or under developed or underdeveloped or middle income or low* income or underserved or under served or deprived or poor*) adj (countr* or nation? or population? or world))**.ti,ab.**

5. ((developing or less* developed or under developed or underdeveloped or middle income or low* income) adj (economy or economies))**.ti,ab.**

6. (low* adj (gdp or gnp or gross domestic or gross national))**.ti,ab.**

7. (low adj3 middle adj3 countr*)**.ti,ab.**

8. (lmic or lmics or third world or lami countr*)**.ti,ab.**

9. transitional countr***.ti,ab.**

10. or/1-9

11. surgery or surg* not precision medicine

12. big data or large data or informatics or database or cohort or registry

13. Limits: Full text, English language, Humans, 2008 – present

10.2 Supplementary material for Chapter 3

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10.3 Supplementary material for Chapter 5

Table 10-1. Patient and operative characteristics by country income group stratified by cancer type, including missing data.

		Breast High	Breast Upper middle	Breast Low/lower middle	Colorectal High	Colorectal Upper middle	Colorectal Low/lower middle	Gastric High	Gastric Upper middle	Gastric Low/lower middle
Total N		4220	1319	2867	4174	1113	928	712	289	336
Age (years)	Mean (SD)	61.0 (13.4)	53.4 (13.1)	50.7 (11.9)	68.6 (12.4)	62.4 (12.3)	54.5 (14.4)	67.4 (12.8)	62.5 (13.2)	55.4 (12.9)
Sex	Male	43 (1.0)	13 (1.0)	32 (1.1)	2394 (57.4)	596 (53.5)	485 (52.3)	427 (60.0)	182 (63.0)	206 (61.3)
	Female	4172 (98.9)	1306 (99.0)	2833 (98.8)	1774 (42.5)	515 (46.3)	443 (47.7)	285 (40.0)	107 (37.0)	130 (38.7)
	(Missing)	5 (0.1)	0 (0.0)	2 (0.1)	6 (0.1)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ASA	I	767 (18.2)	462 (35.0)	937 (32.7)	319 (7.6)	219 (19.7)	238 (25.6)	62 (8.7)	58 (20.1)	110 (32.7)
	II	2383 (56.5)	726 (55.0)	1576 (55.0)	2042 (48.9)	612 (55.0)	506 (54.5)	344 (48.3)	136 (47.1)	160 (47.6)
	III	744 (17.6)	83 (6.3)	223 (7.8)	1545 (37.0)	227 (20.4)	141 (15.2)	269 (37.8)	81 (28.0)	48 (14.3)
	IV	28 (0.7)	11 (0.8)	10 (0.3)	166 (4.0)	23 (2.1)	18 (1.9)	23 (3.2)	8 (2.8)	8 (2.4)
	V	2 (0.0)	0 (0.0)	0 (0.0)	15 (0.4)	1 (0.1)	6 (0.6)	0 (0.0)	0 (0.0)	4 (1.2)
	(Missing)	296 (7.0)	37 (2.8)	121 (4.2)	87 (2.1)	31 (2.8)	19 (2.0)	14 (2.0)	6 (2.1)	6 (1.8)
BMI	Normal weight (BMI 18.5 to 24.9)	1443 (34.2)	462 (35.0)	887 (30.9)	1510 (36.2)	521 (46.8)	456 (49.1)	314 (44.1)	165 (57.1)	168 (50.0)
	Underweight (BMI < 18.5)	74 (1.8)	23 (1.7)	62 (2.2)	119 (2.9)	63 (5.7)	111 (12.0)	38 (5.3)	25 (8.7)	61 (18.2)
	Overweight (BMI 25 to 30)	1341 (31.8)	458 (34.7)	1077 (37.6)	1517 (36.3)	348 (31.3)	206 (22.2)	221 (31.0)	76 (26.3)	71 (21.1)
	Obese (BMI >30)	928 (22.0)	308 (23.4)	736 (25.7)	749 (17.9)	145 (13.0)	115 (12.4)	96 (13.5)	17 (5.9)	16 (4.8)
	(Missing)	434 (10.3)	68 (5.2)	105 (3.7)	279 (6.7)	36 (3.2)	40 (4.3)	43 (6.0)	6 (2.1)	20 (6.0)
>10% weight loss	No	3321 (78.7)	1091 (82.7)	2468 (86.1)	2817 (67.5)	606 (54.4)	337 (36.3)	422 (59.3)	116 (40.1)	91 (27.1)
	Yes	98 (2.3)	84 (6.4)	187 (6.5)	732 (17.5)	427 (38.4)	514 (55.4)	219 (30.8)	162 (56.1)	216 (64.3)
	(Missing)	801 (19.0)	144 (10.9)	212 (7.4)	625 (15.0)	80 (7.2)	77 (8.3)	71 (10.0)	11 (3.8)	29 (8.6)
ECOG performance status	0	2688 (63.7)	984 (74.6)	1657 (57.8)	2056 (49.3)	583 (52.4)	379 (40.8)	346 (48.6)	165 (57.1)	100 (29.8)
	1	838 (19.9)	242 (18.3)	621 (21.7)	1116 (26.7)	319 (28.7)	318 (34.3)	198 (27.8)	78 (27.0)	146 (43.5)
	2	311 (7.4)	48 (3.6)	400 (14.0)	557 (13.3)	125 (11.2)	117 (12.6)	93 (13.1)	28 (9.7)	53 (15.8)

	3	73 (1.7)	17 (1.3)	68 (2.4)	188 (4.5)	63 (5.7)	81 (8.7)	38 (5.3)	14 (4.8)	27 (8.0)
	4	6 (0.1)	1 (0.1)	14 (0.5)	22 (0.5)	6 (0.5)	12 (1.3)	4 (0.6)	2 (0.7)	5 (1.5)
	(Missing)	304 (7.2)	27 (2.0)	107 (3.7)	235 (5.6)	17 (1.5)	21 (2.3)	33 (4.6)	2 (0.7)	5 (1.5)
Smoking	No, never	2800 (66.4)	1056 (80.1)	2728 (95.2)	2236 (53.6)	688 (61.8)	684 (73.7)	327 (45.9)	158 (54.7)	219 (65.2)
	Stopped >6 weeks ago	517 (12.3)	86 (6.5)	34 (1.2)	965 (23.1)	170 (15.3)	103 (11.1)	168 (23.6)	66 (22.8)	44 (13.1)
	Yes, current smoker	562 (13.3)	133 (10.1)	27 (0.9)	496 (11.9)	173 (15.5)	100 (10.8)	116 (16.3)	41 (14.2)	43 (12.8)
	(Missing)	341 (8.1)	44 (3.3)	78 (2.7)	477 (11.4)	82 (7.4)	41 (4.4)	101 (14.2)	24 (8.3)	30 (8.9)
Diabetes	No	3696 (87.6)	1074 (81.4)	2107 (73.5)	3311 (79.3)	859 (77.2)	720 (77.6)	587 (82.4)	246 (85.1)	273 (81.2)
	Diet	71 (1.7)	16 (1.2)	27 (0.9)	125 (3.0)	20 (1.8)	14 (1.5)	13 (1.8)	6 (2.1)	4 (1.2)
	Medication (non-insulin)	307 (7.3)	139 (10.5)	312 (10.9)	510 (12.2)	161 (14.5)	84 (9.1)	78 (11.0)	24 (8.3)	26 (7.7)
	Insulin	92 (2.2)	55 (4.2)	136 (4.7)	160 (3.8)	52 (4.7)	43 (4.6)	27 (3.8)	13 (4.5)	12 (3.6)
	(Missing)	54 (1.3)	35 (2.7)	285 (9.9)	68 (1.6)	21 (1.9)	67 (7.2)	7 (1.0)	0 (0.0)	21 (6.2)
HIV tested	No	3995 (94.7)	779 (59.1)	1349 (47.1)	3984 (95.4)	689 (61.9)	616 (66.4)	671 (94.2)	158 (54.7)	153 (45.5)
	Yes - Negative	179 (4.2)	524 (39.7)	1511 (52.7)	186 (4.5)	413 (37.1)	308 (33.2)	39 (5.5)	130 (45.0)	182 (54.2)
	Yes - Positive	6 (0.1)	16 (1.2)	7 (0.2)	2 (0.0)	9 (0.8)	4 (0.4)	1 (0.1)	1 (0.3)	1 (0.3)
	(Missing)	40 (0.9)	0 (0.0)	0 (0.0)	2 (0.0)	2 (0.2)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
Distance to home (km)	< 10 km	1637 (38.8)	340 (25.8)	352 (12.3)	1630 (39.1)	270 (24.3)	179 (19.3)	230 (32.3)	67 (23.2)	44 (13.1)
	10-20 km	859 (20.4)	272 (20.6)	460 (16.0)	814 (19.5)	266 (23.9)	170 (18.3)	125 (17.6)	79 (27.3)	43 (12.8)
	20-50 km	809 (19.2)	241 (18.3)	511 (17.8)	791 (19.0)	206 (18.5)	200 (21.6)	156 (21.9)	32 (11.1)	57 (17.0)
	50-100 km	346 (8.2)	78 (5.9)	385 (13.4)	324 (7.8)	89 (8.0)	97 (10.5)	68 (9.6)	28 (9.7)	32 (9.5)
	>100 km	219 (5.2)	199 (15.1)	1039 (36.2)	279 (6.7)	176 (15.8)	235 (25.3)	78 (11.0)	64 (22.1)	135 (40.2)
	(Missing)	350 (8.3)	189 (14.3)	120 (4.2)	336 (8.0)	106 (9.5)	47 (5.1)	55 (7.7)	19 (6.6)	25 (7.4)

Numbers are n (%), unless otherwise indicated.

Figure 10-1. Stage of presentation, 30-day mortality, and 30-day complications by cancer and country income group.

Panels A, B and C are replicated from Figure 5-2 to aid comparisons. A, proportion of patients enrolled by cancer stage by country income group. B, proportion of patients dying or sustaining a major complication or any complication by day 30 after surgery stratified by country income group. C, proportion of patients sustaining a major complication who died within 30 days. D, E, F, 30-day mortality (D), major complication (E), and any complication (F) stratified by cancer type, cancer stage, and country income group.

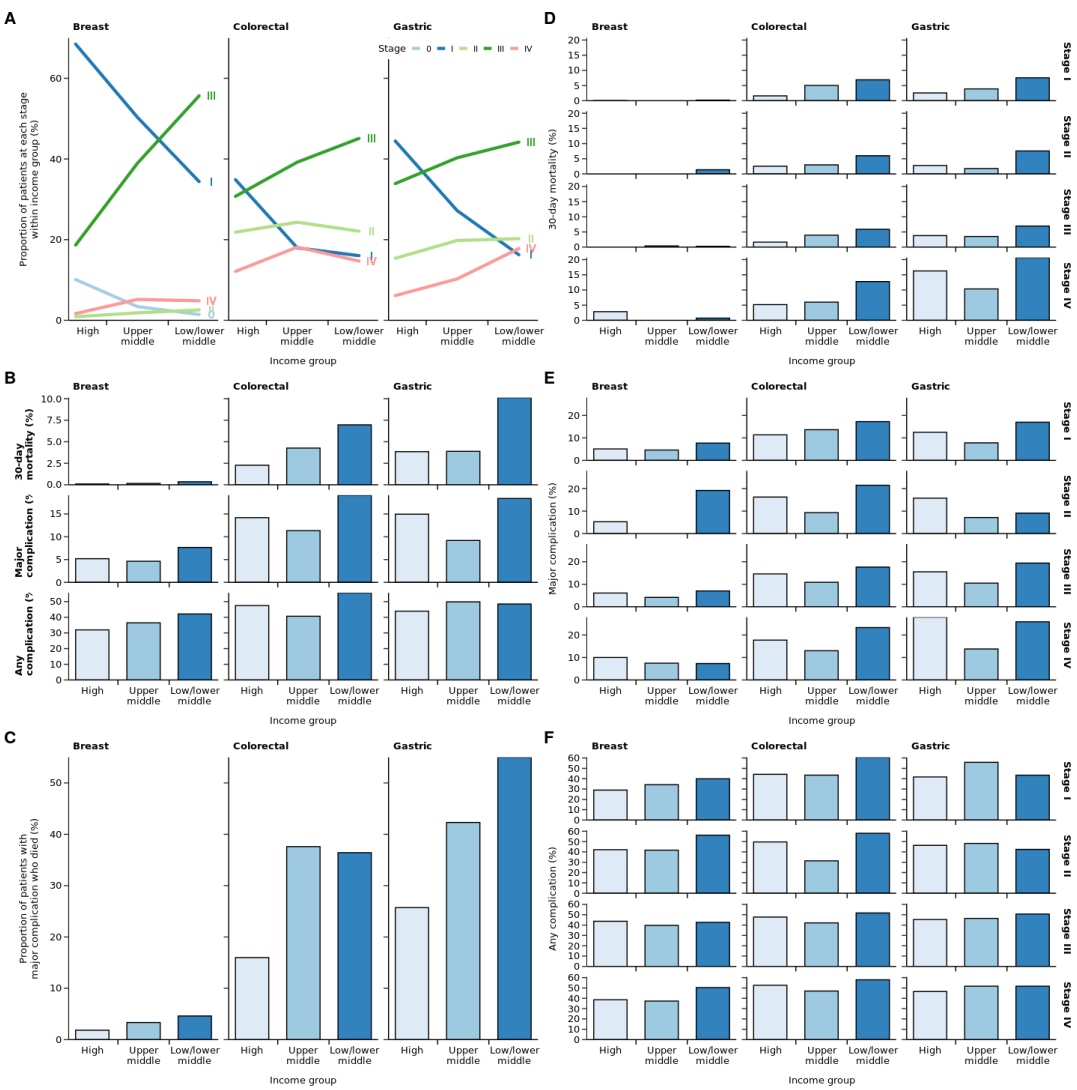


Figure 10-2. Adjusted rates of 30-day complication rates after surgery for cancer

Adjusted proportion of patients dying or sustaining a major complication or any complication by day 30 after surgery stratified by country income group (A). Proportion of patients sustaining a major complication who died within 30 days (B).

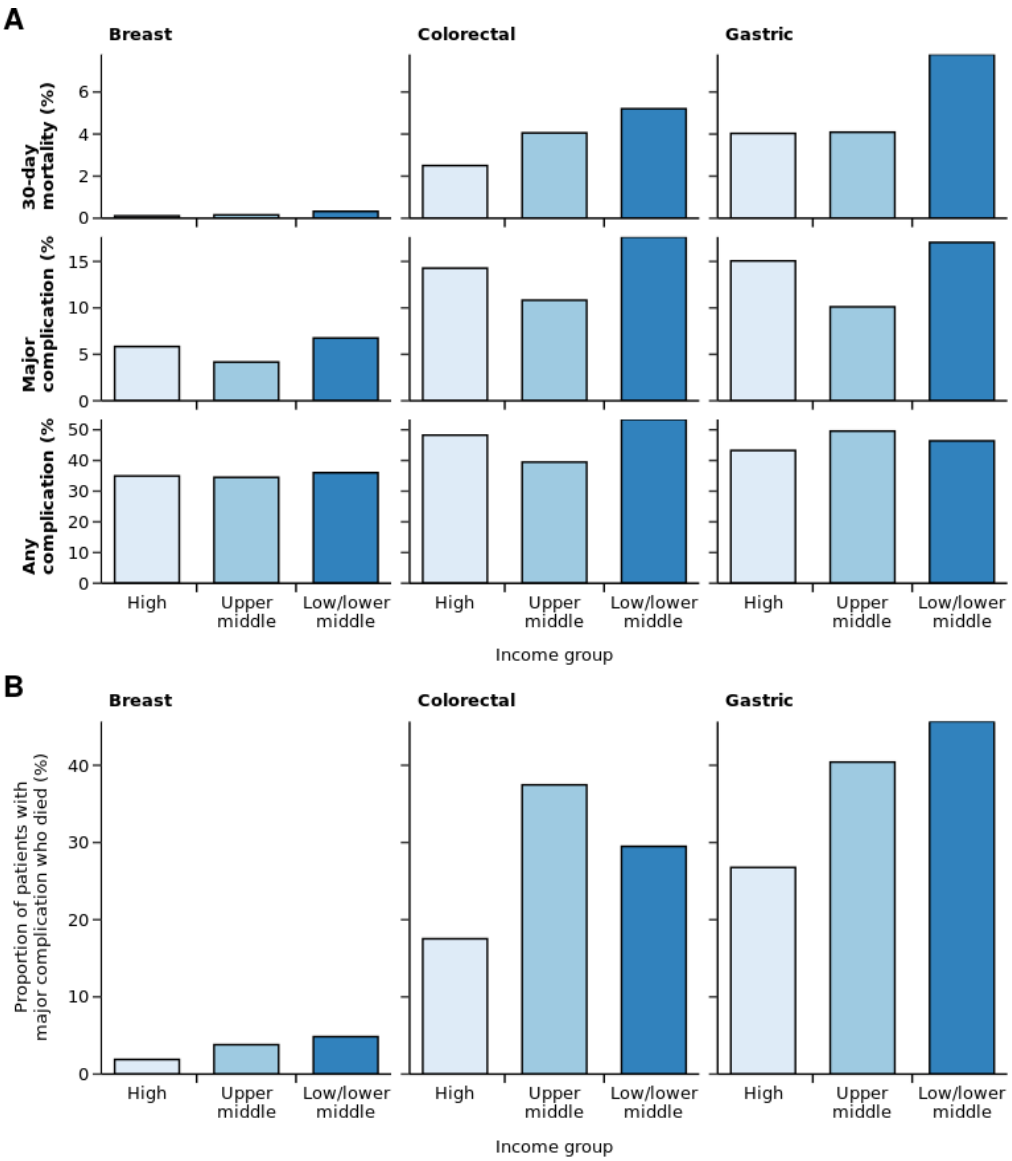


Table 10-2. Cancer stage by other predictors (breast).

		Tis N=514	L1/L2 N=4534	A N=137	R1/R2 N=2890	M+ N=281	P
Age (years)	Mean (SD)	56.9 (12.9)	58.4 (13.8)	57.3 (16.9)	53.0 (13.1)	53.9 (13.3)	<0.001
Sex	Male	3 (0.6)	40 (0.9)	5 (3.6)	37 (1.3)	3 (1.1)	0.013
	Female	510 (99.4)	4491 (99.1)	132 (96.4)	2850 (98.7)	278 (98.9)	
ASA	I	122 (26.2)	1108 (25.9)	31 (23.7)	816 (29.6)	69 (25.7)	<0.001
	II	273 (58.7)	2553 (59.6)	69 (52.7)	1625 (59.0)	142 (52.8)	
	III	66 (14.2)	599 (14.0)	30 (22.9)	303 (11.0)	48 (17.8)	
	IV	2 (0.4)	23 (0.5)	1 (0.8)	12 (0.4)	10 (3.7)	
	V	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
BMI	Normal weight (BMI 18.5 to 24.9)	172 (37.2)	1537 (36.9)	45 (34.4)	933 (34.2)	92 (34.3)	0.122
	Underweight (BMI < 18.5)	5 (1.1)	90 (2.2)	2 (1.5)	54 (2.0)	7 (2.6)	
	Overweight (BMI 25 to 30)	153 (33.1)	1529 (36.7)	45 (34.4)	1040 (38.1)	90 (33.6)	
	Obese (BMI >30)	132 (28.6)	1010 (24.2)	39 (29.8)	705 (25.8)	79 (29.5)	
>10% weight loss	No	397 (98.5)	3730 (96.5)	109 (90.8)	2388 (93.0)	216 (87.1)	<0.001
	Yes	6 (1.5)	136 (3.5)	11 (9.2)	179 (7.0)	32 (12.9)	
ECOG performance status	0	359 (76.9)	2903 (67.8)	72 (55.4)	1823 (65.8)	142 (52.0)	<0.001
	1	78 (16.7)	928 (21.7)	35 (26.9)	573 (20.7)	76 (27.8)	
	2	25 (5.4)	361 (8.4)	19 (14.6)	319 (11.5)	34 (12.5)	
	3	3 (0.6)	78 (1.8)	4 (3.1)	52 (1.9)	19 (7.0)	
	4	2 (0.4)	12 (0.3)	0 (0.0)	5 (0.2)	2 (0.7)	
Smoking	No, never	354 (76.5)	3373 (78.9)	115 (90.6)	2459 (88.8)	239 (90.9)	<0.001
	Stopped >6 weeks ago	53 (11.4)	420 (9.8)	9 (7.1)	143 (5.2)	9 (3.4)	
	Yes, current smoker	56 (12.1)	481 (11.3)	3 (2.4)	167 (6.0)	15 (5.7)	
Diabetes	No	444 (88.3)	3783 (86.5)	98 (81.0)	2286 (84.1)	228 (84.1)	0.004
	Diet	10 (2.0)	64 (1.5)	4 (3.3)	30 (1.1)	6 (2.2)	
	Medication (non-insulin)	39 (7.8)	392 (9.0)	12 (9.9)	285 (10.5)	24 (8.9)	
	Insulin	10 (2.0)	134 (3.1)	7 (5.8)	117 (4.3)	13 (4.8)	
HIV tested	No	456 (89.4)	3572 (79.3)	92 (67.2)	1809 (62.7)	170 (60.7)	<0.001
	Yes - Negative	52 (10.2)	927 (20.6)	45 (32.8)	1054 (36.6)	110 (39.3)	
	Yes - Positive	2 (0.4)	7 (0.2)	0 (0.0)	20 (0.7)	0 (0.0)	

Distance to home (km)	< 10 km	172 (36.8)	1415 (34.1)	33 (25.8)	617 (22.9)	76 (29.5)	<0.001
	10-20 km	120 (25.6)	909 (21.9)	16 (12.5)	489 (18.1)	52 (20.2)	
	20-50 km	96 (20.5)	840 (20.2)	31 (24.2)	532 (19.7)	59 (22.9)	
	50-100 km	41 (8.8)	415 (10.0)	20 (15.6)	306 (11.4)	22 (8.5)	
	>100 km	39 (8.3)	574 (13.8)	28 (21.9)	751 (27.9)	49 (19.0)	
Mode of diagnosis	Symptomatic	174 (34.7)	2547 (56.9)	120 (89.6)	2302 (80.3)	220 (78.9)	<0.001
	Screening	299 (59.7)	1519 (33.9)	6 (4.5)	267 (9.3)	25 (9.0)	
	Detected incidentally	28 (5.6)	410 (9.2)	8 (6.0)	296 (10.3)	34 (12.2)	
Urgency	Elective	511 (99.4)	4515 (99.6)	133 (97.1)	2872 (99.4)	273 (97.5)	<0.001
	Emergency	3 (0.6)	19 (0.4)	4 (2.9)	18 (0.6)	7 (2.5)	
Treatment intent	Palliative	5 (1.0)	50 (1.1)	10 (7.3)	81 (2.8)	98 (35.0)	<0.001
	Curative	509 (99.0)	4483 (98.9)	127 (92.7)	2809 (97.2)	182 (65.0)	
Primary procedure	B27 Mastectomy	161 (31.3)	1559 (34.4)	100 (73.0)	1747 (60.5)	193 (69.7)	<0.001
	B28 Partial mastectomy / wide local excision / lumpectomy	305 (59.3)	2790 (61.5)	34 (24.8)	1037 (35.9)	61 (22.0)	
	B32 Open biopsy of breast	21 (4.1)	54 (1.2)	1 (0.7)	15 (0.5)	5 (1.8)	
	B37 Other operations on breast	27 (5.3)	131 (2.9)	2 (1.5)	89 (3.1)	18 (6.5)	
SNLB	No, not available in this hospital	9 (1.8)	236 (5.3)	12 (9.0)	309 (11.2)	42 (15.9)	<0.001
	No, but available in this hospital	259 (52.1)	894 (20.1)	89 (66.4)	1784 (64.8)	165 (62.5)	
	Yes, single technique	131 (26.4)	1825 (41.1)	15 (11.2)	431 (15.7)	45 (17.0)	
	Yes, dual technique	98 (19.7)	1487 (33.5)	18 (13.4)	227 (8.3)	12 (4.5)	
Axilliary lymph node dissection	No	467 (91.7)	3263 (73.2)	50 (37.0)	560 (19.9)	57 (21.1)	<0.001
	Yes	42 (8.3)	1197 (26.8)	85 (63.0)	2254 (80.1)	213 (78.9)	
Margin check	No, not available in this hospital	23 (4.9)	344 (7.9)	14 (10.4)	307 (11.1)	40 (15.3)	<0.001
	No, but available in this hospital	193 (41.2)	1927 (44.5)	95 (70.4)	1681 (60.8)	139 (53.3)	
	Yes, by x-ray	198 (42.2)	1028 (23.7)	6 (4.4)	236 (8.5)	17 (6.5)	
	Yes, by frozen section	55 (11.7)	1034 (23.9)	20 (14.8)	540 (19.5)	65 (24.9)	
Primary reconstruction	No, not available in this hospital	28 (5.4)	306 (6.8)	13 (9.5)	307 (10.6)	34 (12.1)	<0.001
	No, but available in this hospital	358 (69.6)	3434 (75.8)	96 (70.1)	2116 (73.3)	199 (71.1)	
	Yes, immediate - prosthesis	52 (10.1)	227 (5.0)	2 (1.5)	117 (4.1)	4 (1.4)	
	Yes, immediate - flap	59 (11.5)	449 (9.9)	14 (10.2)	237 (8.2)	32 (11.4)	

	Yes, planned at later stage	17 (3.3)	117 (2.6)	12 (8.8)	109 (3.8)	11 (3.9)

Table 10-3. Cancer stage by other predictors (colon).

		L N=1802	A N=1386	R+ N=2128	M+ N=853	P
Age (years)	Mean (SD)	66.9 (13.0)	67.1 (13.6)	63.8 (13.8)	63.3 (14.0)	<0.001
Sex	Male	1026 (57.1)	771 (55.6)	1172 (55.1)	480 (56.4)	0.636
	Female	771 (42.9)	615 (44.4)	955 (44.9)	371 (43.6)	
ASA	I	207 (11.7)	193 (14.3)	264 (12.7)	104 (12.5)	<0.001
	II	892 (50.4)	679 (50.2)	1175 (56.5)	391 (46.9)	
	III	608 (34.4)	426 (31.5)	578 (27.8)	292 (35.0)	
	IV	59 (3.3)	45 (3.3)	60 (2.9)	43 (5.2)	
	V	4 (0.2)	9 (0.7)	4 (0.2)	4 (0.5)	
BMI	Normal weight (BMI 18.5 to 24.9)	621 (36.5)	570 (43.9)	900 (44.3)	377 (47.7)	<0.001
	Underweight (BMI < 18.5)	57 (3.4)	69 (5.3)	107 (5.3)	60 (7.6)	
	Overweight (BMI 25 to 30)	666 (39.2)	449 (34.6)	693 (34.1)	253 (32.0)	
	Obese (BMI >30)	356 (20.9)	210 (16.2)	331 (16.3)	100 (12.7)	
>10% weight loss	No	1249 (81.0)	846 (70.4)	1248 (65.4)	399 (53.8)	<0.001
	Yes	293 (19.0)	355 (29.6)	660 (34.6)	342 (46.2)	
ECOG performance status	0	963 (56.3)	640 (48.5)	1024 (50.0)	379 (46.3)	<0.001
	1	454 (26.5)	397 (30.1)	658 (32.1)	231 (28.2)	
	2	208 (12.2)	178 (13.5)	259 (12.6)	146 (17.8)	
	3	76 (4.4)	90 (6.8)	102 (5.0)	56 (6.8)	
	4	10 (0.6)	15 (1.1)	7 (0.3)	7 (0.9)	
Smoking	No, never	994 (61.8)	818 (66.2)	1283 (65.3)	485 (63.3)	0.154
	Stopped >6 weeks ago	390 (24.3)	253 (20.5)	410 (20.9)	176 (23.0)	
	Yes, current smoker	224 (13.9)	164 (13.3)	271 (13.8)	105 (13.7)	
Diabetes	No	1405 (80.1)	1096 (81.3)	1681 (80.7)	677 (81.2)	0.331
	Diet	41 (2.3)	42 (3.1)	61 (2.9)	15 (1.8)	
	Medication (non-insulin)	220 (12.5)	159 (11.8)	264 (12.7)	107 (12.8)	
	Insulin	89 (5.1)	51 (3.8)	78 (3.7)	35 (4.2)	
HIV tested	No	1630 (90.5)	1151 (83.0)	1760 (82.7)	718 (84.3)	<0.001
	Yes - Negative	166 (9.2)	232 (16.7)	365 (17.2)	129 (15.1)	
	Yes - Positive	5 (0.3)	3 (0.2)	2 (0.1)	5 (0.6)	
Distance to home (km)	< 10 km	663 (40.2)	458 (36.1)	688 (34.7)	259 (33.0)	<0.001
	10-20 km	342 (20.7)	296 (23.3)	408 (20.6)	196 (24.9)	

	20-50 km	355 (21.5)	246 (19.4)	414 (20.9)	166 (21.1)	
	50-100 km	142 (8.6)	117 (9.2)	180 (9.1)	70 (8.9)	
	>100 km	147 (8.9)	152 (12.0)	290 (14.6)	95 (12.1)	
Mode of diagnosis	Symptomatic	1101 (62.2)	1140 (82.8)	1815 (85.9)	746 (88.7)	<0.001
	Screening	478 (27.0)	154 (11.2)	205 (9.7)	54 (6.4)	
	Detected incidentally	192 (10.8)	82 (6.0)	92 (4.4)	41 (4.9)	
Urgency	Elective	1661 (92.2)	1191 (85.9)	1888 (88.7)	593 (69.5)	<0.001
	Emergency	141 (7.8)	195 (14.1)	240 (11.3)	260 (30.5)	
Treatment intent	Palliative	46 (2.6)	85 (6.1)	129 (6.1)	442 (51.8)	<0.001
	Curative	1756 (97.4)	1301 (93.9)	1999 (93.9)	411 (48.2)	
WHO checklist	No, not available in this hospital	145 (8.3)	202 (15.0)	235 (11.4)	99 (11.9)	<0.001
	No, but available in this hospital	63 (3.6)	67 (5.0)	106 (5.1)	46 (5.5)	
	Yes	1541 (88.1)	1079 (80.0)	1725 (83.5)	689 (82.6)	
Primary procedure	T309 Abdomen: Laparotomy with no other procedure	7 (0.4)	5 (0.4)	5 (0.2)	12 (1.4)	<0.001
	T43 Abdomen: Diagnostic laparoscopy with no other procedure	2 (0.1)	0 (0.0)	1 (0.0)	2 (0.2)	
	G74 Small bowel: Formation of ileostomy only	5 (0.3)	6 (0.4)	11 (0.5)	24 (2.8)	
	H04 Colon: Total excision of colon and rectum	13 (0.7)	10 (0.7)	16 (0.8)	10 (1.2)	
	H05 Colon: Total excision of colon	34 (1.9)	33 (2.4)	37 (1.7)	11 (1.3)	
	H06 Colon: Extended excision of right hemicolon	80 (4.4)	89 (6.4)	117 (5.5)	36 (4.2)	
	H07 Colon: Excision of right hemicolon	588 (32.7)	324 (23.4)	503 (23.6)	166 (19.5)	
	H08 Colon: Excision of transverse colon	24 (1.3)	14 (1.0)	22 (1.0)	9 (1.1)	
	H09 Colon: Excision of left hemicolon	142 (7.9)	110 (7.9)	139 (6.5)	54 (6.3)	
	H10 Colon: Excision of sigmoid colon	248 (13.8)	177 (12.8)	192 (9.0)	96 (11.3)	
	H11 Colon: Other excision of colon	35 (1.9)	38 (2.7)	26 (1.2)	22 (2.6)	
	H15 Colon: Formation of any colonic stoma	22 (1.2)	26 (1.9)	53 (2.5)	116 (13.6)	
	H19 Colon: Other open operations on colon	15 (0.8)	20 (1.4)	20 (0.9)	33 (3.9)	
	H331 Rectum: Abdominoperineal resection	83 (4.6)	116 (8.4)	217 (10.2)	51 (6.0)	
	H332 Rectum: Resection with anastomosis of colon to anus	57 (3.2)	28 (2.0)	93 (4.4)	17 (2.0)	

	H333 Rectum: Anterior resection with anastomosis	334 (18.6)	292 (21.1)	516 (24.3)	119 (14.0)	
	H335 Rectum: Resection with closure of rectal stump (Hartmanns)	48 (2.7)	74 (5.3)	120 (5.6)	53 (6.2)	
	H46 Rectum: Other open operations on rectum	63 (3.5)	24 (1.7)	39 (1.8)	22 (2.6)	
Approach	Open	763 (42.6)	774 (56.1)	1195 (56.3)	597 (70.4)	<0.001
	Minimally invasive	1027 (57.4)	606 (43.9)	928 (43.7)	251 (29.6)	
Site	Caecum	233 (13.1)	116 (8.4)	196 (9.3)	96 (11.4)	<0.001
	Ascending colon	385 (21.7)	240 (17.5)	372 (17.6)	129 (15.3)	
	Transverse colon	136 (7.7)	105 (7.6)	127 (6.0)	72 (8.6)	
	Descending colon	125 (7.0)	125 (9.1)	116 (5.5)	61 (7.2)	
	Sigmoid colon	402 (22.6)	310 (22.6)	387 (18.3)	212 (25.2)	
	High rectum (>10 to 15 cm)	178 (10.0)	173 (12.6)	256 (12.1)	111 (13.2)	
	Middle rectum (>5 to 10 cm)	131 (7.4)	131 (9.5)	283 (13.4)	68 (8.1)	
	Low rectum (< =5 cm from anal verge)	186 (10.5)	173 (12.6)	379 (17.9)	93 (11.0)	
Anastomosis	Not performed	269 (15.3)	330 (24.3)	495 (23.9)	327 (39.4)	<0.001
	Handsewn	330 (18.8)	300 (22.1)	391 (18.9)	153 (18.5)	
	Stapled	1161 (66.0)	727 (53.6)	1188 (57.3)	349 (42.1)	
Pre-op obstruction	No	1575 (91.0)	1075 (79.5)	1678 (81.4)	496 (60.0)	<0.001
	Yes	155 (9.0)	277 (20.5)	383 (18.6)	330 (40.0)	
Pre-op perforation	No	1750 (98.3)	1258 (93.0)	1983 (94.3)	745 (89.1)	<0.001
	Yes	30 (1.7)	94 (7.0)	120 (5.7)	91 (10.9)	
Stoma formed	No	1338 (75.4)	839 (61.2)	1143 (54.2)	423 (49.9)	<0.001
	Yes, loop ileostomy	173 (9.8)	173 (12.6)	378 (17.9)	102 (12.0)	
	Yes, end ileostomy	47 (2.6)	55 (4.0)	80 (3.8)	31 (3.7)	
	Yes, loop colostomy	51 (2.9)	54 (3.9)	122 (5.8)	105 (12.4)	
	Yes, end colostomy	165 (9.3)	251 (18.3)	385 (18.3)	187 (22.1)	

Table 10-4. Cancer stage by other predictors (gastric).

		L N=450	A N=235	R+ N=505	M+ N=133	P
Age (years)	Mean (SD)	64.6 (14.4)	62.7 (14.2)	63.1 (13.0)	61.2 (13.8)	0.068
Sex	Male	251 (55.8)	152 (64.7)	317 (62.8)	86 (64.7)	0.048
	Female	199 (44.2)	83 (35.3)	188 (37.2)	47 (35.3)	
ASA	I	66 (15.0)	38 (16.3)	101 (20.4)	23 (17.7)	<0.001
	II	222 (50.5)	110 (47.2)	242 (48.8)	60 (46.2)	
	III	142 (32.3)	78 (33.5)	140 (28.2)	34 (26.2)	
	IV	10 (2.3)	7 (3.0)	12 (2.4)	10 (7.7)	
	V	0 (0.0)	0 (0.0)	1 (0.2)	3 (2.3)	
BMI	Normal weight (BMI 18.5 to 24.9)	203 (47.9)	107 (48.6)	263 (54.0)	69 (54.8)	<0.001
	Underweight (BMI < 18.5)	25 (5.9)	21 (9.5)	55 (11.3)	22 (17.5)	
	Overweight (BMI 25 to 30)	134 (31.6)	79 (35.9)	122 (25.1)	29 (23.0)	
	Obese (BMI >30)	62 (14.6)	13 (5.9)	47 (9.7)	6 (4.8)	
>10% weight loss	No	285 (70.2)	104 (48.4)	202 (43.0)	33 (26.6)	<0.001
	Yes	121 (29.8)	111 (51.6)	268 (57.0)	91 (73.4)	
ECOG performance status	0	241 (55.5)	103 (45.2)	216 (43.7)	42 (32.3)	<0.001
	1	117 (27.0)	85 (37.3)	176 (35.6)	44 (33.8)	
	2	53 (12.2)	27 (11.8)	70 (14.2)	23 (17.7)	
	3	20 (4.6)	12 (5.3)	27 (5.5)	19 (14.6)	
	4	3 (0.7)	1 (0.4)	5 (1.0)	2 (1.5)	
Smoking	No, never	241 (62.0)	124 (57.4)	269 (59.1)	65 (58.6)	0.948
	Stopped >6 weeks ago	86 (22.1)	55 (25.5)	106 (23.3)	26 (23.4)	
	Yes, current smoker	62 (15.9)	37 (17.1)	80 (17.6)	20 (18.0)	
Diabetes	No	376 (85.3)	196 (85.2)	417 (84.2)	108 (81.8)	0.962
	Diet	8 (1.8)	5 (2.2)	9 (1.8)	1 (0.8)	
	Medication (non-insulin)	41 (9.3)	20 (8.7)	50 (10.1)	16 (12.1)	
	Insulin	16 (3.6)	9 (3.9)	19 (3.8)	7 (5.3)	
HIV tested	No	363 (80.7)	162 (68.9)	364 (72.1)	85 (63.9)	0.001
	Yes - Negative	86 (19.1)	73 (31.1)	140 (27.7)	47 (35.3)	

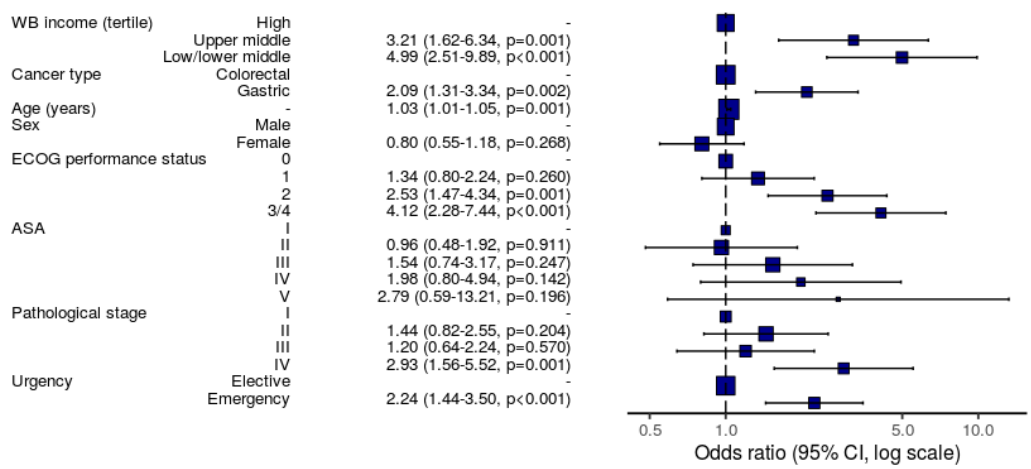
	Yes - Positive	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.8)	
Distance to home (km)	< 10 km	136 (32.9)	53 (24.5)	122 (25.7)	25 (20.7)	0.002
	10-20 km	89 (21.5)	41 (19.0)	87 (18.4)	26 (21.5)	
	20-50 km	75 (18.1)	40 (18.5)	106 (22.4)	24 (19.8)	
	50-100 km	51 (12.3)	26 (12.0)	40 (8.4)	10 (8.3)	
	>100 km	63 (15.2)	56 (25.9)	119 (25.1)	36 (29.8)	
Mode of diagnosis	Symptomatic	340 (76.7)	221 (95.7)	475 (95.4)	130 (97.7)	<0.001
	Screening	31 (7.0)	1 (0.4)	7 (1.4)	1 (0.8)	
	Detected incidentally	72 (16.3)	9 (3.9)	16 (3.2)	2 (1.5)	
Urgency	Elective	436 (96.9)	220 (93.6)	474 (93.9)	113 (85.0)	<0.001
	Emergency	14 (3.1)	15 (6.4)	31 (6.1)	20 (15.0)	
Treatment intent	Palliative	17 (3.8)	23 (9.8)	65 (12.9)	89 (66.9)	<0.001
	Curative	433 (96.2)	212 (90.2)	440 (87.1)	44 (33.1)	
WHO checklist	No, not available in this hospital	49 (11.3)	31 (13.4)	48 (9.8)	10 (7.9)	0.114
	No, but available in this hospital	18 (4.1)	20 (8.7)	24 (4.9)	8 (6.3)	
	Yes	367 (84.6)	180 (77.9)	417 (85.3)	108 (85.7)	
Primary procedure	T309 Abdomen: Laparotomy with no other procedure	7 (1.6)	4 (1.7)	13 (2.6)	13 (9.8)	<0.001
	T43 Abdomen: Diagnostic laparoscopy with no other procedure	7 (1.6)	6 (2.6)	9 (1.8)	5 (3.8)	
	G27 Stomach: Total excision of stomach	131 (29.1)	93 (39.6)	214 (42.4)	30 (22.6)	
	G28 Stomach: Partial excision of stomach	265 (58.9)	102 (43.4)	207 (41.0)	36 (27.1)	
	G32 Stomach: Connection of stomach to jejunum	17 (3.8)	20 (8.5)	42 (8.3)	35 (26.3)	
	G38 Stomach: Other open operations on stomach	23 (5.1)	10 (4.3)	20 (4.0)	14 (10.5)	
Approach	Open	280 (62.5)	182 (77.8)	413 (81.8)	117 (88.0)	<0.001
	Minimally invasive	168 (37.5)	52 (22.2)	92 (18.2)	16 (12.0)	
Site	Upper third (cardia/fundus)	87 (19.7)	39 (17.1)	109 (22.0)	25 (19.8)	0.125
	Middle third (body)	104 (23.5)	39 (17.1)	90 (18.2)	20 (15.9)	
	Distal third (antrium/pylorus)	195 (44.1)	109 (47.8)	210 (42.4)	56 (44.4)	
	Entire stomach	56 (12.7)	41 (18.0)	86 (17.4)	25 (19.8)	
Anastomosis	Not performed	83 (18.9)	29 (12.8)	38 (7.7)	28 (21.7)	<0.001
	Handsewn	116 (26.4)	81 (35.7)	152 (30.9)	54 (41.9)	

	Stapled	241 (54.8)	117 (51.5)	302 (61.4)	47 (36.4)	
D2 resection	No	205 (49.0)	97 (43.3)	166 (34.2)	87 (69.6)	<0.001
	Yes	213 (51.0)	127 (56.7)	320 (65.8)	38 (30.4)	
Pre-op obstruction	No	409 (93.4)	200 (87.0)	421 (84.7)	71 (55.9)	<0.001
	Yes	29 (6.6)	30 (13.0)	76 (15.3)	56 (44.1)	
Pre-op perforation	No	436 (98.9)	223 (96.5)	477 (95.8)	120 (91.6)	0.001
	Yes	5 (1.1)	8 (3.5)	21 (4.2)	11 (8.4)	

Figure 10-3. Capacity to rescue from major complication: sensitivity analysis using postoperative final pathological staging.

Multilevel logistic regression model for predictors of death after major complication in colorectal and gastric cancer (A). Proportion of 30-day mortality variation explained at the level of patient/disease, hospital, country, and country income group, in patients with colorectal or gastric cancer who died after major complication (B). The "variance explained" at each of the 4 levels of the model (marginal pseudo-R^2) is expressed as a proportion of the total "variance explained" (conditional pseudo-R^2).

A



B

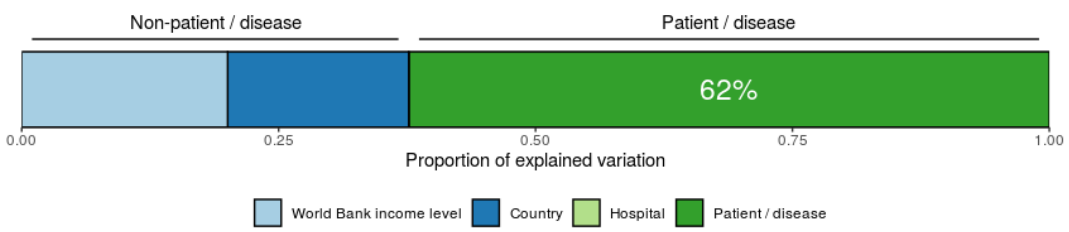


Table 10-5. Surgical procedure (breast).

		High N=4220	Upper middle N=1319	Low/lower middle N=2867
Mode of diagnosis	Symptomatic	2073 (49.1)	935 (70.9)	2397 (83.6)
	Screening	1831 (43.4)	177 (13.4)	115 (4.0)
	Detected incidentally	243 (5.8)	196 (14.9)	338 (11.8)
	(Missing)	73 (1.7)	11 (0.8)	17 (0.6)
Urgency	Elective	4200 (99.5)	1309 (99.2)	2842 (99.1)
	Emergency	19 (0.5)	10 (0.8)	22 (0.8)
	(Missing)	1 (0.0)	0 (0.0)	3 (0.1)
Treatment intent	Palliative	50 (1.2)	70 (5.3)	126 (4.4)
	Curative	4168 (98.8)	1249 (94.7)	2738 (95.5)
	(Missing)	2 (0.0)	0 (0.0)	3 (0.1)
WHO checklist	No, not available in this hospital	191 (4.5)	91 (6.9)	314 (11.0)
	No, but available in this hospital	206 (4.9)	76 (5.8)	164 (5.7)
	Yes	3616 (85.7)	1138 (86.3)	2358 (82.2)
	(Missing)	207 (4.9)	14 (1.1)	31 (1.1)
Primary procedure	B27 Mastectomy	1257 (29.8)	869 (65.9)	1658 (57.8)
	B28 Partial mastectomy / wide local excision / lumpectomy	2766 (65.5)	370 (28.1)	1109 (38.7)
	B32 Open biopsy of breast	58 (1.4)	22 (1.7)	16 (0.6)
	B37 Other operations on breast	137 (3.2)	57 (4.3)	78 (2.7)
	(Missing)	2 (0.0)	1 (0.1)	6 (0.2)
SNLB	No, not available in this hospital	33 (0.8)	279 (21.2)	303 (10.6)
	No, but available in this hospital	1021 (24.2)	503 (38.1)	1690 (58.9)
	Yes, single technique	1656 (39.2)	301 (22.8)	504 (17.6)
	Yes, dual technique	1446 (34.3)	206 (15.6)	192 (6.7)
	(Missing)	64 (1.5)	30 (2.3)	178 (6.2)
Axillary lymph node dissection	No	3177 (75.3)	479 (36.3)	770 (26.9)
	Yes	998 (23.6)	820 (62.2)	1989 (69.4)
	(Missing)	45 (1.1)	20 (1.5)	108 (3.8)
Margin check	No, not available in this hospital	199 (4.7)	289 (21.9)	246 (8.6)
	No, but available in this hospital	1664 (39.4)	562 (42.6)	1840 (64.2)
	Yes, by x-ray	1412 (33.5)	17 (1.3)	58 (2.0)

	Yes, by frozen section	678 (16.1)	416 (31.5)	624 (21.8)
	(Missing)	267 (6.3)	35 (2.7)	99 (3.5)
Primary reconstruction	No, not available in this hospital	190 (4.5)	243 (18.4)	260 (9.1)
	No, but available in this hospital	3170 (75.1)	816 (61.9)	2256 (78.7)
	Yes, immediate - prosthesis	243 (5.8)	118 (8.9)	41 (1.4)
	Yes, immediate - flap	466 (11.0)	125 (9.5)	202 (7.0)
	Yes, planned at later stage	146 (3.5)	16 (1.2)	105 (3.7)
	(Missing)	5 (0.1)	1 (0.1)	3 (0.1)

Data are n (%).

Table 10-6. Surgical procedure (colorectal).

		High N=4174	Upper middle N=1113	Low/lower middle N=928
Mode of diagnosis	Symptomatic	2939 (70.4)	1012 (90.9)	887 (95.6)
	Screening	841 (20.1)	43 (3.9)	10 (1.1)
	Detected incidentally	334 (8.0)	52 (4.7)	26 (2.8)
	(Missing)	60 (1.4)	6 (0.5)	5 (0.5)
Urgency	Elective	3644 (87.3)	952 (85.5)	773 (83.3)
	Emergency	530 (12.7)	161 (14.5)	155 (16.7)
Treatment intent	Palliative	367 (8.8)	177 (15.9)	165 (17.8)
	Curative	3807 (91.2)	936 (84.1)	763 (82.2)
WHO checklist	No, not available in this hospital	241 (5.8)	293 (26.3)	148 (15.9)
	No, but available in this hospital	152 (3.6)	43 (3.9)	89 (9.6)
	Yes	3649 (87.4)	755 (67.8)	673 (72.5)
	(Missing)	132 (3.2)	22 (2.0)	18 (1.9)
Primary procedure	T309 Abdomen: Laparotomy with no other procedure	12 (0.3)	4 (0.4)	13 (1.4)
	T43 Abdomen: Diagnostic laparoscopy with no other procedure	4 (0.1)	0 (0.0)	1 (0.1)
	G74 Small bowel: Formation of ileostomy only	26 (0.6)	15 (1.3)	5 (0.5)
	H04 Colon: Total excision of colon and rectum	25 (0.6)	10 (0.9)	14 (1.5)
	H05 Colon: Total excision of colon	77 (1.8)	23 (2.1)	20 (2.2)
	H06 Colon: Extended excision of right hemicolon	207 (5.0)	37 (3.3)	81 (8.7)
	H07 Colon: Excision of right hemicolon	1240 (29.7)	197 (17.7)	157 (16.9)
	H08 Colon: Excision of transverse colon	45 (1.1)	13 (1.2)	12 (1.3)
	H09 Colon: Excision of left hemicolon	300 (7.2)	81 (7.3)	69 (7.4)
	H10 Colon: Excision of sigmoid colon	436 (10.4)	150 (13.5)	132 (14.2)
	H11 Colon: Other excision of colon	97 (2.3)	13 (1.2)	13 (1.4)
	H15 Colon: Formation of any colonic stoma	105 (2.5)	47 (4.2)	67 (7.2)
	H19 Colon: Other open operations on colon	49 (1.2)	32 (2.9)	7 (0.8)
	H331 Rectum: Abdominoperineal resection	260 (6.2)	97 (8.7)	114 (12.3)
	H332 Rectum: Resection with anastomosis of colon to anus	114 (2.7)	43 (3.9)	38 (4.1)
	H333 Rectum: Anterior resection with anastomosis	865 (20.7)	274 (24.6)	125 (13.5)
	H335 Rectum: Resection with closure of rectal stump (Hartmann's)	196 (4.7)	59 (5.3)	42 (4.5)
	H46 Rectum: Other open operations on rectum	115 (2.8)	17 (1.5)	16 (1.7)

	(Missing)	1 (0.0)	1 (0.1)	2 (0.2)
Approach	Open	1729 (41.4)	681 (61.2)	654 (70.5)
	Laparoscopic (+/- open specimen extraction)	2092 (50.1)	363 (32.6)	233 (25.1)
	Laparoscopic converted to open	213 (5.1)	46 (4.1)	39 (4.2)
	Robotic	113 (2.7)	22 (2.0)	0 (0.0)
	Robotic converted to open	2 (0.0)	0 (0.0)	0 (0.0)
	(Missing)	25 (0.6)	1 (0.1)	2 (0.2)
Site	Caecum	494 (11.8)	82 (7.4)	72 (7.8)
	Ascending colon	832 (19.9)	152 (13.7)	153 (16.5)
	Transverse colon	319 (7.6)	65 (5.8)	63 (6.8)
	Descending colon	273 (6.5)	77 (6.9)	80 (8.6)
	Sigmoid colon	830 (19.9)	274 (24.6)	212 (22.8)
	High rectum (>10 to 15 cm)	473 (11.3)	156 (14.0)	93 (10.0)
	Middle rectum (>5 to 10 cm)	411 (9.8)	134 (12.0)	70 (7.5)
	Low rectum (< =5 cm from anal verge)	505 (12.1)	158 (14.2)	173 (18.6)
	(Missing)	37 (0.9)	15 (1.3)	12 (1.3)
Anastomosis	Not performed	872 (20.9)	293 (26.3)	265 (28.6)
	Handsewn	664 (15.9)	222 (19.9)	296 (31.9)
	Stapled	2555 (61.2)	575 (51.7)	319 (34.4)
	(Missing)	83 (2.0)	23 (2.1)	48 (5.2)
Pre-op obstruction	No	3366 (80.6)	836 (75.1)	656 (70.7)
	Yes	653 (15.6)	260 (23.4)	242 (26.1)
	(Missing)	155 (3.7)	17 (1.5)	30 (3.2)
Pre-op perforation	No	3891 (93.2)	1028 (92.4)	852 (91.8)
	Yes	228 (5.5)	69 (6.2)	46 (5.0)
	(Missing)	55 (1.3)	16 (1.4)	30 (3.2)
Stoma formed	No	2750 (65.9)	561 (50.4)	460 (49.6)
	Yes, loop ileostomy	512 (12.3)	196 (17.6)	123 (13.3)
	Yes, end ileostomy	130 (3.1)	53 (4.8)	31 (3.3)
	Yes, loop colostomy	161 (3.9)	82 (7.4)	92 (9.9)
	Yes, end colostomy	597 (14.3)	204 (18.3)	193 (20.8)
	(Missing)	24 (0.6)	17 (1.5)	29 (3.1)

Data are n (%).

Table 10-7. Surgical procedure (gastric).

		High N=712	Upper middle N=289	Low/lower middle N=336
Mode of diagnosis	Symptomatic	577 (81.0)	272 (94.1)	326 (97.0)
	Screening	35 (4.9)	5 (1.7)	1 (0.3)
	Detected incidentally	85 (11.9)	9 (3.1)	7 (2.1)
	(Missing)	15 (2.1)	3 (1.0)	2 (0.6)
Urgency	Elective	681 (95.6)	273 (94.5)	300 (89.3)
	Emergency	30 (4.2)	16 (5.5)	36 (10.7)
	(Missing)	1 (0.1)	0 (0.0)	0 (0.0)
Treatment intent	Palliative	79 (11.1)	45 (15.6)	71 (21.1)
	Curative	632 (88.8)	244 (84.4)	265 (78.9)
	(Missing)	1 (0.1)	0 (0.0)	0 (0.0)
WHO checklist	No, not available in this hospital	65 (9.1)	38 (13.1)	35 (10.4)
	No, but available in this hospital	32 (4.5)	3 (1.0)	37 (11.0)
	Yes	579 (81.3)	243 (84.1)	261 (77.7)
	(Missing)	36 (5.1)	5 (1.7)	3 (0.9)
Primary procedure	T309 Abdomen: Laparotomy with no other procedure	12 (1.7)	11 (3.8)	14 (4.2)
	T43 Abdomen: Diagnostic laparoscopy with no other procedure	14 (2.0)	8 (2.8)	6 (1.8)
	G27 Stomach: Total excision of stomach	269 (37.8)	117 (40.5)	84 (25.0)
	G28 Stomach: Partial excision of stomach	338 (47.5)	126 (43.6)	154 (45.8)
	G32 Stomach: Connection of stomach to jejunum	52 (7.3)	18 (6.2)	46 (13.7)
	G38 Stomach: Other open operations on stomach	26 (3.7)	9 (3.1)	32 (9.5)
	(Missing)	1 (0.1)	0 (0.0)	0 (0.0)
Approach	Open	435 (61.1)	225 (77.9)	284 (84.5)
	Laparoscopic (+/- open specimen extraction)	242 (34.0)	49 (17.0)	28 (8.3)
	Laparoscopic converted to open	23 (3.2)	12 (4.2)	24 (7.1)
	Robotic	8 (1.1)	3 (1.0)	0 (0.0)
	Robotic converted to open	0 (0.0)	0 (0.0)	0 (0.0)
	(Missing)	4 (0.6)	0 (0.0)	0 (0.0)
Site	Upper third (cardia/fundus)	142 (19.9)	45 (15.6)	73 (21.7)
	Middle third (body)	172 (24.2)	49 (17.0)	34 (10.1)
	Distal third (antrum/pylorus)	291 (40.9)	120 (41.5)	167 (49.7)

	Entire stomach	95 (13.3)	67 (23.2)	49 (14.6)
	(Missing)	12 (1.7)	8 (2.8)	13 (3.9)
Anastomosis	Not performed	106 (14.9)	31 (10.7)	44 (13.1)
	Handsewn	146 (20.5)	86 (29.8)	172 (51.2)
	Stapled	448 (62.9)	162 (56.1)	106 (31.5)
	(Missing)	12 (1.7)	10 (3.5)	14 (4.2)
D2 resection	No	309 (43.4)	92 (31.8)	156 (46.4)
	Yes	369 (51.8)	185 (64.0)	154 (45.8)
	(Missing)	34 (4.8)	12 (4.2)	26 (7.7)
Pre-op obstruction	No	619 (86.9)	254 (87.9)	239 (71.1)
	Yes	81 (11.4)	29 (10.0)	83 (24.7)
	(Missing)	12 (1.7)	6 (2.1)	14 (4.2)
Pre-op perforation	No	683 (95.9)	278 (96.2)	307 (91.4)
	Yes	24 (3.4)	8 (2.8)	14 (4.2)
	(Missing)	5 (0.7)	3 (1.0)	15 (4.5)

Data are n (%).

Table 10-8. Detailed outcomes stratified by cancer and country income level.

		Breast High	Breast Upper middle	Breast Low/lower middle	Colorectal| High	Colorectal Upper middle	Colorectal Low/lower middle	Gastric High	Gastric Upper middle	Gastric Low/lower middle
		N=4220	N=1319	N=2867	N=4174	N=1113	N=928	N=712	N=289	N=336
30-day mortality	Alive	4203 (99.6)	1293 (98.0)	2822 (98.4)	4048 (97.0)	1055 (94.8)	842 (90.7)	675 (94.8)	272 (94.1)	293 (87.2)
	Dead	4 (0.1)	2 (0.2)	10 (0.3)	94 (2.3)	47 (4.2)	63 (6.8)	27 (3.8)	11 (3.8)	33 (9.8)
	(Missing)	13 (0.3)	24 (1.8)	35 (1.2)	32 (0.8)	11 (1.0)	23 (2.5)	10 (1.4)	6 (2.1)	10 (3.0)
Minor complication (CD1)	No	3122 (74.0)	901 (68.3)	1897 (66.2)	2875 (68.9)	772 (69.4)	556 (59.9)	518 (72.8)	171 (59.2)	215 (64.0)
	Yes	1069 (25.3)	392 (29.7)	923 (32.2)	1252 (30.0)	321 (28.8)	339 (36.5)	188 (26.4)	112 (38.8)	103 (30.7)
	(Missing)	29 (0.7)	26 (2.0)	47 (1.6)	47 (1.1)	20 (1.8)	33 (3.6)	6 (0.8)	6 (2.1)	18 (5.4)
Minor complication (CD2)	No	3908 (92.6)	1137 (86.2)	2388 (83.3)	3106 (74.4)	884 (79.4)	601 (64.8)	538 (75.6)	202 (69.9)	237 (70.5)
	Yes	283 (6.7)	156 (11.8)	426 (14.9)	1026 (24.6)	210 (18.9)	292 (31.5)	169 (23.7)	81 (28.0)	82 (24.4)
	(Missing)	29 (0.7)	26 (2.0)	53 (1.8)	42 (1.0)	19 (1.7)	35 (3.8)	5 (0.7)	6 (2.1)	17 (5.1)
Re-intervention (CD3)	No	3990 (94.5)	1248 (94.6)	2571 (89.7)	3672 (88.0)	1016 (91.3)	777 (83.7)	632 (88.8)	267 (92.4)	292 (86.9)
	Yes, NOT under general anaesthetic	71 (1.7)	19 (1.4)	140 (4.9)	135 (3.2)	25 (2.2)	46 (5.0)	31 (4.4)	6 (2.1)	12 (3.6)
	Yes under general anaesthetic	142 (3.4)	31 (2.4)	63 (2.2)	333 (8.0)	53 (4.8)	70 (7.5)	45 (6.3)	10 (3.5)	17 (5.1)
	(Missing)	17 (0.4)	21 (1.6)	93 (3.2)	34 (0.8)	19 (1.7)	35 (3.8)	4 (0.6)	6 (2.1)	15 (4.5)
Life-threatening complication (CD4)	No	4195 (99.4)	1280 (97.0)	2803 (97.8)	3902 (93.5)	1042 (93.6)	818 (88.1)	662 (93.0)	264 (91.3)	289 (86.0)
	Yes, single organ failure	3 (0.1)	14 (1.1)	5 (0.2)	138 (3.3)	24 (2.2)	40 (4.3)	23 (3.2)	9 (3.1)	16 (4.8)
	Yes, multi organ failure	3 (0.1)	3 (0.2)	3 (0.1)	95 (2.3)	30 (2.7)	40 (4.3)	24 (3.4)	10 (3.5)	15 (4.5)
	(Missing)	19 (0.5)	22 (1.7)	56 (2.0)	39 (0.9)	17 (1.5)	30 (3.2)	3 (0.4)	6 (2.1)	16 (4.8)
Readmission	No	4034 (95.6)	1247 (94.5)	2778 (96.9)	3828 (91.7)	1012 (90.9)	799 (86.1)	661 (92.8)	252 (87.2)	295 (87.8)
	Yes	171 (4.1)	52 (3.9)	42 (1.5)	310 (7.4)	86 (7.7)	99 (10.7)	47 (6.6)	31 (10.7)	25 (7.4)
	(Missing)	15 (0.4)	20 (1.5)	47 (1.6)	36 (0.9)	15 (1.3)	30 (3.2)	4 (0.6)	6 (2.1)	16 (4.8)
Surgical site infection	No	3878 (91.9)	1144 (86.7)	2346 (81.8)	3562 (85.3)	893 (80.2)	615 (66.3)	637 (89.5)	221 (76.5)	271 (80.7)
	Yes, no treatment/wound opened only (CD 1)	54 (1.3)	61 (4.6)	141 (4.9)	177 (4.2)	81 (7.3)	75 (8.1)	22 (3.1)	22 (7.6)	16 (4.8)
	Yes, antibiotics only (CD 2)	168 (4.0)	77 (5.8)	205 (7.2)	261 (6.3)	85 (7.6)	156 (16.8)	34 (4.8)	36 (12.5)	22 (6.5)

	Yes, return to operating theatre (CD 3)	27 (0.6)	9 (0.7)	91 (3.2)	76 (1.8)	26 (2.3)	30 (3.2)	5 (0.7)	2 (0.7)	6 (1.8)
	Yes, requiring critical care admission (CD 4)	0 (0.0)	0 (0.0)	2 (0.1)	15 (0.4)	8 (0.7)	4 (0.4)	3 (0.4)	0 (0.0)	3 (0.9)
	Yes, resulting in death (CD 5)	0 (0.0)	0 (0.0)	1 (0.0)	3 (0.1)	4 (0.4)	6 (0.6)	2 (0.3)	1 (0.3)	0 (0.0)
	(Missing)	93 (2.2)	28 (2.1)	81 (2.8)	80 (1.9)	16 (1.4)	42 (4.5)	9 (1.3)	7 (2.4)	18 (5.4)
Abscess (OSI)	No				3857 (92.4)	1039 (93.4)	805 (86.7)	654 (91.9)	262 (90.7)	300 (89.3)
	Yes, no intervention (CD 1)				20 (0.5)	2 (0.2)	6 (0.6)	2 (0.3)	3 (1.0)	1 (0.3)
	Yes, antibiotics only (CD 2)				78 (1.9)	19 (1.7)	14 (1.5)	14 (2.0)	10 (3.5)	4 (1.2)
	Yes, surgical/radiological drainage (CD 3)				114 (2.7)	22 (2.0)	21 (2.3)	28 (3.9)	5 (1.7)	6 (1.8)
	Yes, critical care admission (CD 4)				22 (0.5)	5 (0.4)	4 (0.4)	2 (0.3)	1 (0.3)	1 (0.3)
	Yes, resulting in death (CD 5)				12 (0.3)	4 (0.4)	4 (0.4)	3 (0.4)	0 (0.0)	0 (0.0)
	(Missing)				71 (1.7)	22 (2.0)	74 (8.0)	9 (1.3)	8 (2.8)	24 (7.1)
Anastomotic leak	No				3916 (93.8)	1052 (94.5)	836 (90.1)	670 (94.1)	271 (93.8)	292 (86.9)
	Yes, no intervention required (CD 1)				18 (0.4)	8 (0.7)	24 (2.6)	4 (0.6)	1 (0.3)	5 (1.5)
	Yes, drug treatment only (CD 2)				41 (1.0)	7 (0.6)	2 (0.2)	7 (1.0)	2 (0.7)	2 (0.6)
	Yes, intervention required (CD 3)				104 (2.5)	19 (1.7)	24 (2.6)	18 (2.5)	3 (1.0)	9 (2.7)
	Yes, critical care admission &/or intervention (CD 4)				61 (1.5)	8 (0.7)	7 (0.8)	7 (1.0)	3 (1.0)	7 (2.1)
	Yes, resulting in death (CD 5)				11 (0.3)	5 (0.4)	3 (0.3)	3 (0.4)	2 (0.7)	0 (0.0)
	(Missing)				23 (0.6)	14 (1.3)	32 (3.4)	3 (0.4)	7 (2.4)	21 (6.2)
Post-operative bleed	No	4015 (95.1)	1208 (91.6)	2752 (96.0)	3941 (94.4)	1041 (93.5)	856 (92.2)	671 (94.2)	237 (82.0)	302 (89.9)
	Yes, no intervention required (CD 1)	102 (2.4)	74 (5.6)	45 (1.6)	56 (1.3)	35 (3.1)	17 (1.8)	8 (1.1)	27 (9.3)	5 (1.5)
	Yes, transfusion only (CD 2)	8 (0.2)	1 (0.1)	13 (0.5)	87 (2.1)	18 (1.6)	10 (1.1)	15 (2.1)	13 (4.5)	2 (0.6)
	Yes, surgical/radiological	61 (1.4)	12 (0.9)	17 (0.6)	38 (0.9)	5 (0.4)	7 (0.8)	5 (0.7)	0 (0.0)	2 (0.6)

	intervention required (CD 3)									
	Yes, critical care admission &/or intervention (CD 4)	0 (0.0)	1 (0.1)	0 (0.0)	10 (0.2)	3 (0.3)	6 (0.6)	6 (0.8)	3 (1.0)	5 (1.5)
	Yes, resulting in death (CD 5)	0 (0.0)	0 (0.0)	1 (0.0)	4 (0.1)	2 (0.2)	3 (0.3)	3 (0.4)	1 (0.3)	2 (0.6)
	(Missing)	34 (0.8)	23 (1.7)	39 (1.4)	38 (0.9)	9 (0.8)	29 (3.1)	4 (0.6)	8 (2.8)	18 (5.4)
Seroma	No	3340 (79.1)	1039 (78.8)	2040 (71.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Yes, no intervention/aspiration only (CD 1)	653 (15.5)	206 (15.6)	552 (19.3)						
	Yes, antibiotic treatment only (CD 2)	45 (1.1)	33 (2.5)	35 (1.2)						
	Yes, intervention required (CD 3)	62 (1.5)	9 (0.7)	62 (2.2)						
	Yes, critical care admission &/or intervention (CD 4)	0 (0.0)	0 (0.0)	0 (0.0)						
	Yes, resulting in death (CD 5)	0 (0.0)	0 (0.0)	0 (0.0)						
	(Missing)	120 (2.8)	32 (2.4)	178 (6.2)						
Length of Stay (days)	Mean (SD)	1.8 (2.3)	3.1 (3.1)	2.7 (3.7)	10.1 (8.8)	8.9 (6.8)	9.0 (7.1)	12.0 (31.3)	9.9 (6.2)	10.3 (7.0)

Table 10-9. Breast cancer logistic regression analyses: 30-day mortality.

Dependent: 30-day mortality		Alive	Dead	OR (univariable)	OR (multivariable)	OR (multivariable reduced)	OR (multilevel)
WB income (tertile)	High	4203 (99.9)	4 (0.1)	-	-	-	-
	Upper middle	1293 (99.8)	2 (0.2)	1.63 (0.23-8.34, P=0.575)	1.41 (0.17-8.66, P=0.721)	1.79 (0.24-9.76, P=0.518)	1.90 (0.07-50.90, P=0.702)
	Low/lower middle	2822 (99.6)	10 (0.4)	3.72 (1.24-13.58, P=0.026)	3.19 (0.75-15.53, P=0.127)	4.32 (1.18-18.27, P=0.033)	8.46 (0.66-108.04, P=0.100)
Age (years)	Mean (SD)	0.0 (1.0)	0.5 (1.0)	1.67 (1.02-2.77, P=0.042)	1.61 (0.88-3.09, P=0.138)	1.63 (0.92-2.99, P=0.105)	2.10 (1.03-4.28, P=0.041)
>10% weight loss	No	6815 (99.9)	10 (0.1)	-	-	-	-
	Yes	362 (99.5)	2 (0.5)	3.77 (0.58-14.35, P=0.088)	1.32 (0.17-6.34, P=0.758)	-	-
	(Missing)	1141 (99.7)	4 (0.3)	2.39 (0.65-7.16, P=0.142)	2.46 (0.53-8.65, P=0.192)	-	-
ECOG performance status	0	5276 (99.9)	4 (0.1)	-	-	-	-
	1	1688 (99.6)	6 (0.4)	4.69 (1.34-18.36, P=0.017)	2.79 (0.70-11.75, P=0.140)	3.55 (0.98-14.35, P=0.056)	4.34 (1.04-18.11, P=0.044)
	2	748 (99.9)	1 (0.1)	1.76 (0.09-11.94, P=0.612)	1.08 (0.05-7.79, P=0.946)	1.18 (0.06-8.37, P=0.883)	0.69 (0.05-9.63, P=0.782)
	3/4	172 (97.7)	4 (2.3)	30.67 (7.20-130.70, P<0.001)	11.02 (2.03-58.54, P=0.004)	11.16 (2.16-57.05, P=0.003)	15.38 (2.06-114.76, P=0.008)
Diabetes	No	6811 (99.8)	11 (0.2)	-	-	-	-
	Yes	1139 (99.7)	4 (0.3)	2.17 (0.60-6.37, P=0.184)	1.37 (0.35-4.44, P=0.617)	1.19 (0.32-3.71, P=0.775)	1.02 (0.24-4.39, P=0.975)
Urgency	Elective	8270 (99.8)	15 (0.2)	-	-	-	-
	Emergency	48 (98.0)	1 (2.0)	11.49 (0.63-58.43, P=0.019)	4.92 (0.23-33.88, P=0.179)	-	-
Treatment intent	Palliative	239 (98.4)	4 (1.6)	-	-	-	-
	Curative	8078 (99.9)	12 (0.1)	0.09 (0.03-0.32, P<0.001)	0.36 (0.08-1.90, P=0.196)	0.20 (0.06-0.83, P=0.016)	0.14 (0.03-0.63, P=0.011)
Stage	0	509 (99.8)	1 (0.2)	-	-	-	-
	I	4504 (99.9)	3 (0.1)	0.34 (0.04-6.86, P=0.349)	0.24 (0.03-4.97, P=0.226)	-	-
	II	134 (99.3)	1 (0.7)	3.80 (0.15-96.48, P=0.346)	1.39 (0.05-39.74, P=0.828)	-	-
	III	2859 (99.8)	6 (0.2)	1.07 (0.18-20.20, P=0.951)	0.66 (0.09-13.66, P=0.720)	-	-

IV	271 (98.9)	3 (1.1)	5.63 (0.72-114.21, P=0.135)	1.03 (0.08-26.27, P=0.983)	-	-

Table 10-10. Breast cancer logistic regression analyses: major complication.

Dependent: Major complication		No	Yes	OR (univariable)	OR (multivariable)	OR (multivariable reduced)	OR (multilevel)
WB income (tertile)	High	3997 (94.8)	218 (5.2)	-	-	-	-
	Upper middle	1245 (95.3)	61 (4.7)	0.90 (0.67-1.19, P=0.470)	0.70 (0.50-0.97, P=0.038)	0.71 (0.51-0.97, P=0.038)	0.53 (0.31-0.90, P=0.018)
	Low/lower middle	2628 (92.4)	217 (7.6)	1.51 (1.25-1.84, P<0.001)	1.22 (0.93-1.60, P=0.147)	1.21 (0.94-1.56, P=0.134)	0.84 (0.53-1.35, P=0.479)
Age (years)	Mean (SD)	0.0 (1.0)	-0.1 (1.0)	0.94 (0.86-1.03, P=0.199)	0.90 (0.81-1.01, P=0.083)	0.91 (0.82-1.02, P=0.121)	0.92 (0.82-1.04, P=0.175)
BMI	Normal weight (BMI 18.5 to 24.9)	2633 (94.8)	145 (5.2)	-	-	-	-
	Underweight (BMI < 18.5)	154 (96.9)	5 (3.1)	0.59 (0.21-1.32, P=0.253)	0.49 (0.15-1.19, P=0.168)	0.51 (0.16-1.24, P=0.195)	0.53 (0.19-1.49, P=0.230)
	Overweight (BMI 25 to 30)	2689 (94.0)	171 (6.0)	1.15 (0.92-1.45, P=0.216)	1.18 (0.93-1.51, P=0.171)	1.18 (0.93-1.51, P=0.170)	1.23 (0.96-1.58, P=0.106)
	Obese (BMI >30)	1825 (92.7)	143 (7.3)	1.42 (1.12-1.81, P=0.004)	1.42 (1.09-1.85, P=0.008)	1.43 (1.10-1.85, P=0.007)	1.54 (1.16-2.04, P=0.003)
	(Missing)	569 (94.7)	32 (5.3)	1.02 (0.68-1.49, P=0.917)	1.43 (0.89-2.22, P=0.120)	1.38 (0.87-2.11, P=0.151)	1.48 (0.90-2.46, P=0.126)
>10% weight loss	No	6443 (94.0)	409 (6.0)	-	-	-	-
	Yes	340 (93.2)	25 (6.8)	1.16 (0.74-1.72, P=0.491)	1.26 (0.79-1.92, P=0.311)	-	-
	(Missing)	1087 (94.6)	62 (5.4)	0.90 (0.68-1.17, P=0.445)	0.94 (0.66-1.30, P=0.721)	-	-
ECOG performance status	0	4987 (94.1)	315 (5.9)	-	-	-	-
	1	1606 (94.6)	92 (5.4)	0.91 (0.71-1.15, P=0.423)	0.86 (0.66-1.11, P=0.255)	0.87 (0.67-1.12, P=0.293)	0.85 (0.65-1.12, P=0.253)
	2	706 (93.6)	48 (6.4)	1.08 (0.78-1.46, P=0.646)	0.91 (0.63-1.29, P=0.599)	0.91 (0.63-1.29, P=0.620)	1.02 (0.68-1.54, P=0.918)
	3/4	159 (90.3)	17 (9.7)	1.69 (0.98-2.75, P=0.044)	1.39 (0.74-2.44, P=0.274)	1.39 (0.74-2.40, P=0.270)	1.40 (0.74-2.65, P=0.296)
Smoking	No	6752 (93.9)	437 (6.1)	-	-	-	-
	Yes	684 (95.0)	36 (5.0)	0.81 (0.56-1.14, P=0.245)	0.99 (0.67-1.41, P=0.940)	-	-
	(Missing)	434 (95.0)	23 (5.0)	0.82 (0.52-1.23, P=0.363)	0.98 (0.56-1.61, P=0.946)	-	-

Diabetes	No	6463 (94.4)	381 (5.6)	-	-	-	-
	Yes	1062 (92.3)	89 (7.7)	1.42 (1.11-1.80, P=0.004)	1.40 (1.07-1.81, P=0.014)	1.38 (1.05-1.79, P=0.017)	1.29 (0.98-1.70, P=0.070)
Mode of diagnosis	Symptomatic	5014 (93.3)	359 (6.7)	-	-	-	-
	Screening	2011 (94.9)	109 (5.1)	0.76 (0.60-0.94, P=0.013)	0.99 (0.76-1.30, P=0.961)	0.99 (0.76-1.29, P=0.945)	0.95 (0.71-1.25, P=0.693)
	Detected incidentally	750 (97.0)	23 (3.0)	0.43 (0.27-0.64, P<0.001)	0.42 (0.25-0.67, P=0.001)	0.42 (0.25-0.67, P=0.001)	0.46 (0.28-0.77, P=0.003)
Urgency	Elective	7827 (94.1)	488 (5.9)	-	-	-	-
	Emergency	43 (84.3)	8 (15.7)	2.98 (1.29-6.04, P=0.005)	2.69 (1.08-5.80, P=0.020)	2.77 (1.12-5.94, P=0.015)	2.58 (1.07-6.19, P=0.034)
Treatment intent	Palliative	227 (93.4)	16 (6.6)	-	-	-	-
	Curative	7642 (94.1)	480 (5.9)	0.89 (0.55-1.55, P=0.661)	1.15 (0.65-2.19, P=0.640)	-	-
Primary procedure	B27 Mastectomy	3465 (92.2)	293 (7.8)	-	-	-	-
	B28 Partial mastectomy / wide local excision / lumpectomy	4051 (95.6)	187 (4.4)	0.55 (0.45-0.66, P<0.001)	0.56 (0.45-0.70, P<0.001)	0.56 (0.45-0.70, P<0.001)	0.54 (0.43-0.68, P<0.001)
	B32 Open biopsy of breast	93 (97.9)	2 (2.1)	0.25 (0.04-0.81, P=0.056)	0.31 (0.05-1.01, P=0.108)	0.31 (0.05-0.99, P=0.103)	0.33 (0.08-1.40, P=0.133)
	B37 Other operations on breast	257 (95.2)	13 (4.8)	0.60 (0.32-1.02, P=0.077)	0.71 (0.38-1.21, P=0.243)	0.69 (0.37-1.19, P=0.212)	0.77 (0.42-1.41, P=0.395)
Stage	0	491 (95.7)	22 (4.3)	-	-	-	-
	I	4270 (94.4)	252 (5.6)	1.32 (0.86-2.11, P=0.226)	1.15 (0.75-1.87, P=0.540)	-	-
	II	119 (88.1)	16 (11.9)	3.00 (1.51-5.86, P=0.001)	1.66 (0.75-3.50, P=0.193)	-	-
	III	2695 (93.7)	181 (6.3)	1.50 (0.97-2.42, P=0.080)	1.02 (0.64-1.69, P=0.936)	-	-
	IV	253 (92.0)	22 (8.0)	1.94 (1.05-3.59, P=0.033)	1.25 (0.63-2.47, P=0.521)	-	-

Multilevel model includes hospital and country as random intercepts.

Table 10-11. Breast cancer logistic regression analyses: all complications.

Dependent: Any complication		No	Yes	OR (univariable)	OR (multivariable)	OR (multivariable reduced)	OR (multilevel)
WB income (tertile)	High	2869 (68.1)	1346 (31.9)	-	-	-	-
	Upper middle	829 (63.5)	477 (36.5)	1.23 (1.08-1.40, P=0.002)	0.98 (0.84-1.14, P=0.820)	0.99 (0.85-1.15, P=0.921)	1.13 (0.66-1.92, P=0.658)
	Low/lower middle	1644 (57.8)	1201 (42.2)	1.56 (1.41-1.72, P<0.001)	1.06 (0.93-1.22, P=0.377)	1.08 (0.94-1.24, P=0.288)	0.90 (0.54-1.51, P=0.688)
Age (years)	Mean (SD)	-0.0 (1.0)	0.0 (1.0)	1.06 (1.02-1.11, P=0.006)	1.09 (1.03-1.16, P=0.002)	1.09 (1.03-1.16, P=0.002)	1.07 (1.01-1.14, P=0.022)
ASA (>3)	No	5081 (64.6)	2784 (35.4)	-	-	-	-
	Yes	261 (52.1)	240 (47.9)	1.68 (1.40-2.01, P<0.001)	1.77 (1.33-2.35, P<0.001)	1.76 (1.32-2.32, P<0.001)	1.86 (1.30-2.66, P=0.001)
BMI	Normal weight (BMI 18.5 to 24.9)	1860 (67.0)	918 (33.0)	-	-	-	-
	Underweight (BMI < 18.5)	105 (66.0)	54 (34.0)	1.04 (0.74-1.45, P=0.811)	0.93 (0.64-1.34, P=0.709)	0.96 (0.66-1.37, P=0.824)	0.82 (0.55-1.21, P=0.322)
	Overweight (BMI 25 to 30)	1801 (63.0)	1059 (37.0)	1.19 (1.07-1.33, P=0.002)	1.09 (0.96-1.22, P=0.173)	1.08 (0.96-1.22, P=0.187)	1.16 (1.03-1.32, P=0.019)
	Obese (BMI >30)	1154 (58.6)	814 (41.4)	1.43 (1.27-1.61, P<0.001)	1.27 (1.11-1.44, P<0.001)	1.26 (1.10-1.43, P=0.001)	1.42 (1.22-1.65, P<0.001)
	(Missing)	422 (70.2)	179 (29.8)	0.86 (0.71-1.04, P=0.122)	0.82 (0.64-1.04, P=0.110)	0.80 (0.63-1.01, P=0.068)	1.07 (0.80-1.42, P=0.654)
>10% weight loss	No	4384 (64.0)	2468 (36.0)	-	-	-	-
	Yes	203 (55.6)	162 (44.4)	1.42 (1.15-1.75, P=0.001)	1.18 (0.93-1.49, P=0.163)	-	-
	(Missing)	755 (65.7)	394 (34.3)	0.93 (0.81-1.06, P=0.258)	0.88 (0.74-1.03, P=0.118)	-	-
ECOG performance status	0	3564 (67.2)	1738 (32.8)	-	-	-	-
	1	1007 (59.3)	691 (40.7)	1.41 (1.26-1.57, P<0.001)	1.21 (1.07-1.37, P=0.002)	1.22 (1.07-1.38, P=0.002)	1.26 (1.10-1.45, P=0.001)
	2	440 (58.4)	314 (41.6)	1.46 (1.25-1.71, P<0.001)	1.30 (1.10-1.55, P=0.003)	1.31 (1.10-1.56, P=0.002)	1.64 (1.32-2.04, P<0.001)
	3/4	83 (47.2)	93 (52.8)	2.30 (1.70-3.11, P<0.001)	1.74 (1.24-2.44, P=0.001)	1.75 (1.25-2.44, P=0.001)	1.82 (1.24-2.67, P=0.002)
Smoking	No	4588 (63.8)	2601 (36.2)	-	-	-	-

	Yes	461 (64.0)	259 (36.0)	0.99 (0.84-1.16, P=0.912)	1.23 (1.03-1.46, P=0.021)	1.23 (1.03-1.46, P=0.021)	1.32 (1.10-1.59, P=0.003)
	(Missing)	293 (64.1)	164 (35.9)	0.99 (0.81-1.20, P=0.899)	0.97 (0.74-1.24, P=0.785)	0.94 (0.73-1.21, P=0.631)	1.02 (0.77-1.36, P=0.869)
Diabetes	No	4506 (65.8)	2338 (34.2)	-	-	-	-
	Yes	672 (58.4)	479 (41.6)	1.37 (1.21-1.56, P<0.001)	1.14 (0.99-1.32, P=0.063)	1.15 (0.99-1.32, P=0.059)	1.05 (0.90-1.23, P=0.508)
Mode of diagnosis	Symptomatic	3292 (61.3)	2081 (38.7)	-	-	-	-
	Screening	1512 (71.3)	608 (28.7)	0.64 (0.57-0.71, P<0.001)	0.88 (0.77-1.00, P=0.047)	0.87 (0.76-0.99, P=0.040)	0.80 (0.69-0.92, P=0.002)
	Detected incidentally	468 (60.5)	305 (39.5)	1.03 (0.88-1.20, P=0.699)	1.00 (0.84-1.19, P=0.986)	1.00 (0.84-1.19, P=0.982)	0.87 (0.71-1.07, P=0.189)
Urgency	Elective	5316 (63.9)	2999 (36.1)	-	-	-	-
	Emergency	26 (51.0)	25 (49.0)	1.70 (0.98-2.96, P=0.058)	1.22 (0.67-2.20, P=0.503)	-	-
Treatment intent	Palliative	142 (58.4)	101 (41.6)	-	-	-	-
	Curative	5200 (64.0)	2922 (36.0)	0.79 (0.61-1.03, P=0.075)	1.04 (0.77-1.42, P=0.787)	-	-
Primary procedure	B27 Mastectomy	2077 (55.3)	1681 (44.7)	-	-	-	-
	B28 Partial mastectomy / wide local excision / lumpectomy	3004 (70.9)	1234 (29.1)	0.51 (0.46-0.56, P<0.001)	0.57 (0.52-0.64, P<0.001)	0.57 (0.52-0.64, P<0.001)	0.57 (0.51-0.64, P<0.001)
	B32 Open biopsy of breast	82 (86.3)	13 (13.7)	0.20 (0.10-0.34, P<0.001)	0.27 (0.14-0.48, P<0.001)	0.27 (0.14-0.47, P<0.001)	0.22 (0.11-0.42, P<0.001)
	B37 Other operations on breast	175 (64.8)	95 (35.2)	0.67 (0.52-0.87, P=0.002)	0.81 (0.62-1.07, P=0.143)	0.81 (0.62-1.07, P=0.145)	0.85 (0.62-1.17, P=0.317)
Stage	0	365 (71.2)	148 (28.8)	-	-	-	-
	I	3068 (67.8)	1454 (32.2)	1.17 (0.96-1.43, P=0.128)	1.01 (0.81-1.26, P=0.941)	1.01 (0.82-1.27, P=0.906)	0.98 (0.78-1.24, P=0.889)
	II	68 (50.4)	67 (49.6)	2.43 (1.65-3.58, P<0.001)	1.37 (0.88-2.13, P=0.157)	1.39 (0.89-2.15, P=0.143)	1.29 (0.81-2.07, P=0.285)
	III	1655 (57.5)	1221 (42.5)	1.82 (1.49-2.24, P<0.001)	1.27 (1.01-1.60, P=0.046)	1.28 (1.01-1.62, P=0.039)	1.31 (1.02-1.68, P=0.036)
	IV	153 (55.6)	122 (44.4)	1.97 (1.45-2.67, P<0.001)	1.23 (0.87-1.75, P=0.238)	1.24 (0.89-1.73, P=0.208)	1.22 (0.85-1.75, P=0.278)

Multilevel model includes hospital and country as random intercepts.

Table 10-12. Colorectal cancer logistic regression analyses: mortality.

Dependent: 30-day mortality		Alive	Dead	OR (univariable)	OR (multivariable)	OR (multivariable reduced)	OR (multilevel)
WB income (tertile)	High	4048 (97.7)	94 (2.3)	-	-	-	-
	Upper middle	1055 (95.7)	47 (4.3)	1.92 (1.33-2.73, P<0.001)	2.11 (1.35-3.28, P=0.001)	2.20 (1.42-3.37, P<0.001)	2.06 (1.11-3.83, P=0.021)
	Low/lower middle	842 (93.0)	63 (7.0)	3.22 (2.31-4.46, P<0.001)	3.46 (2.13-5.62, P<0.001)	3.75 (2.37-5.93, P<0.001)	4.59 (2.39-8.80, P<0.001)
Age (years)	Mean (SD)	-0.0 (1.0)	0.4 (1.1)	1.53 (1.31-1.79, P<0.001)	1.61 (1.33-1.96, P<0.001)	1.65 (1.37-1.99, P<0.001)	1.69 (1.39-2.07, P<0.001)
Sex	Male	3316 (96.5)	119 (3.5)	-	-	-	-
	Female	2622 (96.9)	84 (3.1)	0.89 (0.67-1.18, P=0.433)	0.65 (0.46-0.92, P=0.015)	0.67 (0.48-0.94, P=0.020)	0.68 (0.48-0.96, P=0.028)
ASA (>3)	No	5626 (97.2)	164 (2.8)	-	-	-	-
	Yes	319 (88.9)	40 (11.1)	4.30 (2.96-6.13, P<0.001)	1.82 (1.11-2.94, P=0.015)	1.82 (1.12-2.91, P=0.013)	2.03 (1.22-3.40, P=0.007)
BMI	Normal weight (BMI 18.5 to 24.9)	2386 (97.0)	75 (3.0)	-	-	-	-
	Underweight (BMI < 18.5)	250 (87.7)	35 (12.3)	4.45 (2.89-6.74, P<0.001)	2.33 (1.38-3.87, P=0.001)	2.51 (1.52-4.07, P<0.001)	2.51 (1.49-4.23, P=0.001)
	Overweight (BMI 25 to 30)	2015 (98.0)	42 (2.0)	0.66 (0.45-0.97, P=0.035)	0.78 (0.50-1.20, P=0.261)	0.79 (0.51-1.20, P=0.268)	0.81 (0.52-1.27, P=0.360)
	Obese (BMI >30)	977 (97.5)	25 (2.5)	0.81 (0.50-1.27, P=0.379)	0.96 (0.54-1.64, P=0.873)	0.92 (0.52-1.54, P=0.750)	0.98 (0.56-1.72, P=0.956)
	(Missing)	317 (92.2)	27 (7.8)	2.71 (1.69-4.22, P<0.001)	1.88 (0.94-3.62, P=0.065)	1.49 (0.78-2.70, P=0.208)	1.51 (0.79-2.90, P=0.215)
>10% weight loss	No	3660 (98.0)	76 (2.0)	-	-	-	-
	Yes	1555 (94.2)	96 (5.8)	2.97 (2.19-4.05, P<0.001)	1.23 (0.84-1.82, P=0.289)	-	-
	(Missing)	730 (95.8)	32 (4.2)	2.11 (1.37-3.18, P<0.001)	0.85 (0.45-1.52, P=0.591)	-	-
ECOG performance status	0	2959 (98.9)	33 (1.1)	-	-	-	-

	1	1690 (97.3)	47 (2.7)	2.49 (1.60-3.94, P<0.001)	1.67 (1.02-2.76, P=0.044)	1.70 (1.05-2.80, P=0.032)	1.64 (0.99-2.71, P=0.053)
	2	740 (93.8)	49 (6.2)	5.94 (3.81-9.37, P<0.001)	2.92 (1.75-4.94, P<0.001)	2.98 (1.81-4.98, P<0.001)	2.95 (1.75-4.98, P<0.001)
	3/4	299 (81.5)	68 (18.5)	20.39 (13.34-31.77, P<0.001)	6.71 (3.99-11.46, P<0.001)	7.07 (4.27-11.88, P<0.001)	6.98 (4.08-11.95, P<0.001)
Smoking	No	4638 (96.7)	157 (3.3)	-	-	-	-
	Yes	746 (97.4)	20 (2.6)	0.79 (0.48-1.24, P=0.333)	0.86 (0.48-1.47, P=0.601)	-	-
	(Missing)	561 (95.4)	27 (4.6)	1.42 (0.92-2.12, P=0.099)	0.90 (0.48-1.58, P=0.717)	-	-
Diabetes	No	4696 (97.0)	144 (3.0)	-	-	-	-
	Yes	1108 (95.6)	51 (4.4)	1.50 (1.07-2.06, P=0.015)	1.18 (0.79-1.74, P=0.405)	-	-
Mode of diagnosis	Symptomatic	4607 (96.2)	181 (3.8)	-	-	-	-
	Screening	877 (99.0)	9 (1.0)	0.26 (0.12-0.48, P<0.001)	1.00 (0.43-2.04, P=0.992)	-	-
	Detected incidentally	396 (96.8)	13 (3.2)	0.84 (0.45-1.42, P=0.538)	1.04 (0.47-2.07, P=0.914)	-	-
Urgency	Elective	5199 (97.7)	121 (2.3)	-	-	-	-
	Emergency	746 (90.0)	83 (10.0)	4.78 (3.57-6.38, P<0.001)	1.60 (1.00-2.57, P=0.049)	1.63 (1.03-2.58, P=0.038)	1.70 (1.05-2.75, P=0.032)
Treatment intent	Palliative	606 (87.8)	84 (12.2)	-	-	-	-
	Curative	5339 (97.8)	120 (2.2)	0.16 (0.12-0.22, P<0.001)	0.33 (0.22-0.52, P<0.001)	0.35 (0.23-0.54, P<0.001)	0.34 (0.21-0.53, P<0.001)
Approach	Open	3144 (94.9)	169 (5.1)	-	-	-	-
	Minimally invasive	2774 (98.8)	34 (1.2)	0.23 (0.15-0.33, P<0.001)	0.62 (0.40-0.95, P=0.032)	0.60 (0.38-0.91, P=0.019)	0.65 (0.41-1.02, P=0.063)
Operative site	Right-side	2121 (96.2)	84 (3.8)	-	-	-	-
	Left-side	1651 (95.7)	75 (4.3)	1.15 (0.83-1.58, P=0.398)	0.91 (0.62-1.32, P=0.610)	0.88 (0.60-1.27, P=0.483)	0.84 (0.57-1.24, P=0.378)
	High/mid rectum	1297 (97.7)	31 (2.3)	0.60 (0.39-0.91, P=0.018)	0.59 (0.35-0.97, P=0.042)	0.67 (0.41-1.08, P=0.107)	0.66 (0.40-1.09, P=0.105)

	Low rectum	818 (98.8)	10 (1.2)	0.31 (0.15-0.57, P<0.001)	0.43 (0.20-0.85, P=0.025)	0.42 (0.19-0.83, P=0.020)	0.42 (0.20-0.89, P=0.024)
Pre-op obstruction	No	4718 (97.9)	102 (2.1)	-	-	-	-
	Yes	1038 (91.5)	96 (8.5)	4.28 (3.21-5.70, P<0.001)	1.16 (0.73-1.82, P=0.533)	1.17 (0.75-1.82, P=0.488)	1.14 (0.72-1.82, P=0.576)
Pre-op perforation	No	5551 (97.1)	165 (2.9)	-	-	-	-
	Yes	303 (90.2)	33 (9.8)	3.66 (2.44-5.35, P<0.001)	1.63 (0.98-2.65, P=0.051)	1.66 (1.02-2.66, P=0.038)	1.75 (1.05-2.92, P=0.031)
Stage	0	0 (NaN)	0 (NaN)	-	-	-	-
	I	1744 (97.6)	43 (2.4)	-	-	-	-
	II	1330 (96.9)	43 (3.1)	1.31 (0.85-2.02, P=0.215)	0.87 (0.51-1.47, P=0.593)	0.91 (0.55-1.51, P=0.704)	0.97 (0.57-1.63, P=0.896)
	III	2051 (97.1)	62 (2.9)	1.23 (0.83-1.83, P=0.311)	0.98 (0.60-1.61, P=0.935)	0.99 (0.62-1.61, P=0.978)	0.97 (0.59-1.59, P=0.900)
	IV	780 (93.4)	55 (6.6)	2.86 (1.91-4.32, P<0.001)	0.83 (0.46-1.50, P=0.540)	0.85 (0.48-1.52, P=0.587)	0.85 (0.47-1.55, P=0.599)

Data are n (%). Multilevel model includes hospital and country as random intercepts.

Table 10-13. Colorectal cancer logistic regression analyses: major complication.

Dependent: Major complication		No	Yes	OR (univariable)	OR (multivariable)	OR (multivariable reduced)	OR (multilevel)
WB income (tertile)	High	3572 (85.8)	590 (14.2)	-	-	-	-
	Upper middle	982 (88.7)	125 (11.3)	0.77 (0.63-0.94, P=0.013)	0.71 (0.56-0.89, P=0.004)	0.73 (0.58-0.91, P=0.006)	0.70 (0.48-1.02, P=0.061)
	Low/lower middle	738 (80.9)	174 (19.1)	1.43 (1.18-1.72, P<0.001)	1.38 (1.07-1.77, P=0.012)	1.38 (1.08-1.74, P=0.008)	1.25 (0.84-1.86, P=0.276)
Age (years)	Mean (SD)	-0.0 (1.0)	0.1 (1.0)	1.14 (1.06-1.23, P<0.001)	1.15 (1.05-1.27, P=0.003)	1.13 (1.03-1.23, P=0.010)	1.14 (1.04-1.25, P=0.007)
Sex	Male	2920 (84.6)	531 (15.4)	-	-	-	-
	Female	2365 (86.9)	357 (13.1)	0.83 (0.72-0.96, P=0.012)	0.80 (0.68-0.94, P=0.008)	0.78 (0.67-0.92, P=0.003)	0.78 (0.67-0.92, P=0.003)
ASA (>3)	No	5034 (86.5)	785 (13.5)	-	-	-	-
	Yes	258 (71.3)	104 (28.7)	2.58 (2.03-3.28, P<0.001)	2.07 (1.52-2.81, P<0.001)	2.05 (1.52-2.74, P<0.001)	2.22 (1.64-3.01, P<0.001)
BMI	Normal weight (BMI 18.5 to 24.9)	2139 (86.5)	335 (13.5)	-	-	-	-
	Underweight (BMI < 18.5)	220 (75.6)	71 (24.4)	2.06 (1.53-2.74, P<0.001)	1.78 (1.27-2.46, P=0.001)	1.72 (1.24-2.36, P=0.001)	1.67 (1.20-2.32, P=0.002)
	Overweight (BMI 25 to 30)	1796 (87.0)	268 (13.0)	0.95 (0.80-1.13, P=0.582)	0.98 (0.81-1.18, P=0.813)	0.98 (0.81-1.18, P=0.838)	0.98 (0.81-1.19, P=0.870)
	Obese (BMI >30)	850 (84.7)	154 (15.3)	1.16 (0.94-1.42, P=0.167)	1.16 (0.91-1.47, P=0.222)	1.18 (0.94-1.48, P=0.152)	1.19 (0.95-1.51, P=0.136)
	(Missing)	287 (82.5)	61 (17.5)	1.36 (1.00-1.82, P=0.046)	1.04 (0.69-1.54, P=0.847)	0.93 (0.63-1.34, P=0.696)	0.92 (0.62-1.36, P=0.664)
>10% weight loss	No	3251 (86.7)	497 (13.3)	-	-	-	-
	Yes	1379 (83.1)	281 (16.9)	1.33 (1.14-1.56, P<0.001)	1.02 (0.84-1.24, P=0.835)	-	-
	(Missing)	662 (85.6)	111 (14.4)	1.10 (0.87-1.36, P=0.415)	0.83 (0.62-1.11, P=0.214)	-	-
ECOG performance status	0	2672 (89.0)	331 (11.0)	-	-	-	-
	1	1504 (86.0)	244 (14.0)	1.31 (1.10-1.56, P=0.003)	1.19 (0.98-1.44, P=0.079)	1.19 (0.99-1.44, P=0.069)	1.19 (0.98-1.45, P=0.078)
	2	640 (80.5)	155 (19.5)	1.96 (1.58-2.41, P<0.001)	1.55 (1.22-1.97, P<0.001)	1.57 (1.24-1.98, P<0.001)	1.54 (1.21-1.96, P<0.001)

	3/4	248 (67.2)	121 (32.8)	3.94 (3.08-5.03, P<0.001)	2.27 (1.68-3.05, P<0.001)	2.24 (1.67-2.99, P<0.001)	2.16 (1.59-2.91, P<0.001)
Smoking	No	4151 (86.1)	668 (13.9)	-	-	-	-
	Yes	643 (83.6)	126 (16.4)	1.22 (0.99-1.49, P=0.063)	1.26 (0.99-1.59, P=0.053)	-	-
	(Missing)	498 (84.0)	95 (16.0)	1.19 (0.93-1.49, P=0.155)	0.99 (0.73-1.33, P=0.967)	-	-
Diabetes	No	4207 (86.4)	661 (13.6)	-	-	-	-
	Yes	961 (82.6)	202 (17.4)	1.34 (1.12-1.59, P=0.001)	1.21 (0.99-1.46, P=0.060)	1.22 (1.01-1.47, P=0.041)	1.18 (0.98-1.44, P=0.085)
Mode of diagnosis	Symptomatic	4082 (84.9)	728 (15.1)	-	-	-	-
	Screening	806 (90.4)	86 (9.6)	0.60 (0.47-0.75, P<0.001)	0.85 (0.65-1.11, P=0.246)	-	-
	Detected incidentally	345 (83.7)	67 (16.3)	1.09 (0.82-1.42, P=0.541)	1.16 (0.84-1.58, P=0.363)	-	-
Urgency	Elective	4654 (87.1)	688 (12.9)	-	-	-	-
	Emergency	638 (76.0)	201 (24.0)	2.13 (1.78-2.54, P<0.001)	1.59 (1.20-2.10, P=0.001)	1.56 (1.24-1.95, P<0.001)	1.55 (1.23-1.96, P<0.001)
Treatment intent	Palliative	554 (79.0)	147 (21.0)	-	-	-	-
	Curative	4738 (86.5)	742 (13.5)	0.59 (0.49-0.72, P<0.001)	0.91 (0.69-1.20, P=0.482)	0.94 (0.74-1.19, P=0.592)	0.91 (0.71-1.16, P=0.439)
Approach	Open	2768 (83.0)	568 (17.0)	-	-	-	-
	Minimally invasive	2500 (88.7)	317 (11.3)	0.62 (0.53-0.72, P<0.001)	0.84 (0.71-1.00, P=0.053)	0.83 (0.70-0.98, P=0.027)	0.80 (0.67-0.96, P=0.017)
Operative site	Right-side	1932 (86.9)	290 (13.1)	-	-	-	-
	Left-side	1476 (85.0)	260 (15.0)	1.17 (0.98-1.41, P=0.082)	1.13 (0.92-1.38, P=0.238)	1.12 (0.92-1.36, P=0.260)	1.13 (0.92-1.38, P=0.243)
	High/mid rectum	1132 (84.9)	201 (15.1)	1.18 (0.97-1.44, P=0.090)	1.36 (1.09-1.70, P=0.006)	1.38 (1.11-1.71, P=0.003)	1.41 (1.13-1.75, P=0.002)
	Low rectum	703 (84.9)	125 (15.1)	1.18 (0.94-1.48, P=0.143)	1.51 (1.17-1.94, P=0.001)	1.48 (1.15-1.88, P=0.002)	1.53 (1.19-1.96, P=0.001)
Pre-op obstruction	No	4215 (87.1)	625 (12.9)	-	-	-	-
	Yes	915 (79.9)	230 (20.1)	1.70 (1.43-2.00, P<0.001)	0.94 (0.72-1.21, P=0.618)	-	-
Pre-op perforation	No	4974 (86.6)	768 (13.4)	-	-	-	-
	Yes	238 (69.6)	104 (30.4)	2.83 (2.21-3.60, P<0.001)	1.94 (1.45-2.57, P<0.001)	1.98 (1.49-2.61, P<0.001)	1.93 (1.45-2.57, P<0.001)
Stage	0	0 (NaN)	0 (NaN)	-	-	-	-

I	1579 (88.0)	216 (12.0)	-	-	-	-
II	1162 (84.3)	216 (15.7)	1.36 (1.11-1.67, P=0.003)	1.14 (0.91-1.44, P=0.252)	-	-
III	1814 (85.6)	305 (14.4)	1.23 (1.02-1.48, P=0.031)	1.09 (0.87-1.35, P=0.460)	-	-
IV	700 (82.6)	147 (17.4)	1.54 (1.22-1.93, P<0.001)	1.08 (0.80-1.45, P=0.618)	-	-

Data are n (%). Multilevel model includes hospital and country as random intercepts.

Table 10-14. Colorectal cancer logistic regression analyses: all complications.

Dependent: Any complication		No	Yes	OR (univariable)	OR (multivariable)	OR (multivariable reduced)	OR (multilevel)
WB income (tertile)	High	2188 (52.5)	1977 (47.5)	-	-	-	-
	Upper middle	660 (59.5)	449 (40.5)	0.75 (0.66-0.86, P<0.001)	0.67 (0.58-0.78, P<0.001)	0.68 (0.58-0.79, P<0.001)	0.84 (0.55-1.28, P=0.419)
	Low/lower middle	405 (44.4)	508 (55.6)	1.39 (1.20-1.60, P<0.001)	1.26 (1.04-1.52, P=0.019)	1.28 (1.07-1.54, P=0.007)	1.28 (0.83-1.98, P=0.265)
Age (years)	Mean (SD)	-0.0 (1.0)	0.0 (1.0)	1.10 (1.04-1.15, P<0.001)	1.12 (1.05-1.19, P=0.001)	1.11 (1.04-1.18, P=0.002)	1.15 (1.07-1.23, P<0.001)
Sex	Male	1773 (51.3)	1681 (48.7)	-	-	-	-
	Female	1474 (54.1)	1251 (45.9)	0.90 (0.81-0.99, P=0.031)	0.87 (0.77-0.97, P=0.014)	0.86 (0.77-0.96, P=0.009)	0.85 (0.75-0.96, P=0.010)
ASA (>3)	No	3094 (53.1)	2731 (46.9)	-	-	-	-
	Yes	159 (43.9)	203 (56.1)	1.45 (1.17-1.79, P=0.001)	1.13 (0.85-1.52, P=0.393)	1.16 (0.88-1.55, P=0.295)	1.33 (0.98-1.81, P=0.066)
BMI	Normal weight (BMI 18.5 to 24.9)	1333 (53.8)	1145 (46.2)	-	-	-	-
	Underweight (BMI < 18.5)	126 (43.3)	165 (56.7)	1.52 (1.19-1.95, P=0.001)	1.24 (0.94-1.64, P=0.126)	1.33 (1.02-1.75, P=0.039)	1.31 (0.97-1.76, P=0.076)
	Overweight (BMI 25 to 30)	1128 (54.6)	937 (45.4)	0.97 (0.86-1.09, P=0.576)	1.04 (0.92-1.19, P=0.519)	1.02 (0.89-1.16, P=0.800)	0.99 (0.86-1.14, P=0.864)
	Obese (BMI >30)	474 (47.2)	531 (52.8)	1.30 (1.13-1.51, P<0.001)	1.38 (1.17-1.64, P<0.001)	1.35 (1.15-1.59, P<0.001)	1.24 (1.03-1.48, P=0.021)
	(Missing)	192 (55.2)	156 (44.8)	0.95 (0.75-1.18, P=0.629)	0.77 (0.57-1.05, P=0.100)	0.74 (0.55-0.99, P=0.047)	0.80 (0.57-1.13, P=0.205)
>10% weight loss	No	2041 (54.4)	1708 (45.6)	-	-	-	-
	Yes	792 (47.7)	870 (52.3)	1.31 (1.17-1.47, P<0.001)	1.14 (0.99-1.31, P=0.078)	-	-
	(Missing)	420 (54.1)	356 (45.9)	1.01 (0.87-1.18, P=0.872)	0.98 (0.80-1.19, P=0.832)	-	-
ECOG performance status	0	1747 (58.2)	1257 (41.8)	-	-	-	-
	1	908 (51.9)	841 (48.1)	1.29 (1.14-1.45, P<0.001)	1.17 (1.03-1.34, P=0.017)	1.21 (1.06-1.37, P=0.004)	1.22 (1.06-1.42, P=0.007)
	2	351 (44.1)	445 (55.9)	1.76 (1.51-2.06, P<0.001)	1.48 (1.24-1.78, P<0.001)	1.54 (1.29-1.83, P<0.001)	1.53 (1.25-1.87, P<0.001)

	3/4	111 (30.0)	259 (70.0)	3.24 (2.57-4.11, P<0.001)	2.22 (1.70-2.93, P<0.001)	2.31 (1.78-3.02, P<0.001)	2.28 (1.70-3.06, P<0.001)
Smoking	No	2546 (52.8)	2278 (47.2)	-	-	-	-
	Yes	381 (49.5)	388 (50.5)	1.14 (0.98-1.33, P=0.096)	1.29 (1.08-1.53, P=0.004)	1.28 (1.08-1.52, P=0.004)	1.36 (1.13-1.64, P=0.001)
	(Missing)	326 (54.9)	268 (45.1)	0.92 (0.77-1.09, P=0.332)	0.83 (0.67-1.03, P=0.092)	0.84 (0.68-1.03, P=0.095)	0.91 (0.72-1.15, P=0.436)
Diabetes	No	2629 (54.0)	2242 (46.0)	-	-	-	-
	Yes	547 (46.9)	619 (53.1)	1.33 (1.17-1.51, P<0.001)	1.19 (1.03-1.38, P=0.019)	1.21 (1.05-1.39, P=0.010)	1.16 (1.00-1.36, P=0.056)
Mode of diagnosis	Symptomatic	2474 (51.4)	2340 (48.6)	-	-	-	-
	Screening	525 (58.8)	368 (41.2)	0.74 (0.64-0.86, P<0.001)	0.95 (0.80-1.13, P=0.585)	-	-
	Detected incidentally	218 (52.9)	194 (47.1)	0.94 (0.77-1.15, P=0.553)	1.00 (0.80-1.26, P=0.974)	-	-
Urgency	Elective	2924 (54.7)	2423 (45.3)	-	-	-	-
	Emergency	329 (39.2)	511 (60.8)	1.87 (1.62-2.18, P<0.001)	1.75 (1.40-2.19, P<0.001)	1.78 (1.44-2.22, P<0.001)	1.71 (1.35-2.18, P<0.001)
Treatment intent	Palliative	323 (46.1)	378 (53.9)	-	-	-	-
	Curative	2930 (53.4)	2556 (46.6)	0.75 (0.64-0.87, P<0.001)	1.10 (0.88-1.38, P=0.398)	-	-
Approach	Open	1554 (46.5)	1785 (53.5)	-	-	-	-
	Minimally invasive	1682 (59.6)	1138 (40.4)	0.59 (0.53-0.65, P<0.001)	0.67 (0.59-0.76, P<0.001)	0.65 (0.58-0.73, P<0.001)	0.56 (0.48-0.64, P<0.001)
Operative site	Right-side	1173 (52.7)	1051 (47.3)	-	-	-	-
	Left-side	967 (55.6)	772 (44.4)	0.89 (0.79-1.01, P=0.073)	0.88 (0.76-1.02, P=0.095)	0.88 (0.76-1.01, P=0.065)	0.89 (0.76-1.04, P=0.140)
	High/mid rectum	696 (52.2)	637 (47.8)	1.02 (0.89-1.17, P=0.759)	1.22 (1.04-1.44, P=0.013)	1.19 (1.02-1.38, P=0.028)	1.31 (1.11-1.54, P=0.002)
	Low rectum	393 (47.4)	436 (52.6)	1.24 (1.06-1.45, P=0.009)	1.47 (1.20-1.80, P<0.001)	1.48 (1.24-1.77, P<0.001)	1.66 (1.36-2.01, P<0.001)
Anastomosis	Not performed	661 (46.6)	757 (53.4)	-	-	-	-
	Handsewn	569 (48.4)	607 (51.6)	0.93 (0.80-1.09, P=0.369)	1.12 (0.93-1.36, P=0.237)	-	-
	Stapled	1946 (56.5)	1497 (43.5)	0.67 (0.59-0.76, P<0.001)	0.93 (0.79-1.10, P=0.414)	-	-
Pre-op obstruction	No	2609 (53.9)	2235 (46.1)	-	-	-	-

	Yes	542 (47.3)	604 (52.7)	1.30 (1.14-1.48, P<0.001)	0.85 (0.70-1.02, P=0.088)	0.82 (0.68-0.99, P=0.041)	0.93 (0.75-1.14, P=0.480)
Pre-op perforation	No	3082 (53.6)	2666 (46.4)	-	-	-	-
	Yes	121 (35.4)	221 (64.6)	2.11 (1.69-2.66, P<0.001)	1.73 (1.33-2.26, P<0.001)	1.67 (1.29-2.17, P<0.001)	1.65 (1.24-2.19, P=0.001)
Stage	0	0 (NaN)	0 (NaN)	-	-	-	-
	I	979 (54.5)	818 (45.5)	-	-	-	-
	II	726 (52.6)	653 (47.4)	1.08 (0.94-1.24, P=0.305)	0.93 (0.79-1.10, P=0.409)	0.96 (0.82-1.12, P=0.587)	1.06 (0.89-1.27, P=0.504)
	III	1118 (52.7)	1003 (47.3)	1.07 (0.95-1.22, P=0.269)	0.95 (0.82-1.11, P=0.536)	0.97 (0.84-1.12, P=0.684)	1.00 (0.85-1.17, P=0.968)
	IV	407 (48.0)	441 (52.0)	1.30 (1.10-1.53, P=0.002)	1.03 (0.83-1.28, P=0.769)	1.03 (0.85-1.25, P=0.735)	1.04 (0.84-1.28, P=0.709)

Data are n (%). Multilevel model includes hospital and country as random intercepts.

Table 10-15. Gastric cancer logistic regression analyses: mortality.

Dependent: 30-day mortality		Alive	Dead	OR (univariable)	OR (multivariable)	OR (multivariable reduced)	OR (multilevel)
WB income (tertile)	High	675 (96.2)	27 (3.8)	-	-	-	-
	Upper middle	272 (96.1)	11 (3.9)	1.01 (0.47-2.01, P=0.976)	1.06 (0.40-2.60, P=0.897)	1.12 (0.44-2.66, P=0.807)	1.12 (0.46-2.74, P=0.807)
	Low/lower middle	293 (89.9)	33 (10.1)	2.82 (1.67-4.80, P<0.001)	2.84 (1.21-6.84, P=0.018)	3.72 (1.72-8.28, P=0.001)	3.72 (1.70-8.16, P=0.001)
Age (years)	Mean (SD)	-0.0 (1.0)	0.5 (1.0)	1.74 (1.33-2.30, P<0.001)	2.08 (1.39-3.21, P=0.001)	2.02 (1.39-3.02, P<0.001)	2.02 (1.38-2.98, P<0.001)
Sex	Male	752 (93.8)	50 (6.2)	-	-	-	-
	Female	488 (95.9)	21 (4.1)	0.65 (0.38-1.08, P=0.102)	0.80 (0.38-1.62, P=0.545)	-	-
ASA (>3)	No	1192 (95.7)	54 (4.3)	-	-	-	-
	Yes	48 (73.8)	17 (26.2)	7.82 (4.13-14.28, P<0.001)	2.55 (0.99-6.24, P=0.045)	2.38 (0.94-5.70, P=0.057)	2.38 (0.97-5.83, P=0.057)
BMI	Normal weight (BMI 18.5 to 24.9)	604 (94.5)	35 (5.5)	-	-	-	-
	Underweight (BMI < 18.5)	112 (92.6)	9 (7.4)	1.39 (0.61-2.85, P=0.399)	0.56 (0.19-1.47, P=0.259)	0.49 (0.18-1.23, P=0.148)	0.49 (0.19-1.29, P=0.148)
	Overweight (BMI 25 to 30)	348 (95.6)	16 (4.4)	0.79 (0.42-1.43, P=0.454)	1.17 (0.51-2.54, P=0.705)	1.05 (0.49-2.17, P=0.895)	1.05 (0.50-2.20, P=0.895)
	Obese (BMI >30)	121 (96.0)	5 (4.0)	0.71 (0.24-1.70, P=0.489)	0.83 (0.18-2.79, P=0.782)	0.76 (0.17-2.43, P=0.674)	0.76 (0.21-2.76, P=0.674)
	(Missing)	55 (90.2)	6 (9.8)	1.88 (0.69-4.38, P=0.173)	0.96 (0.18-3.94, P=0.957)	0.77 (0.15-3.07, P=0.728)	0.77 (0.17-3.42, P=0.728)
ECOG performance status	0	595 (98.7)	8 (1.3)	-	-	-	-
	1	395 (95.0)	21 (5.0)	3.95 (1.80-9.58, P=0.001)	4.08 (1.50-13.15, P=0.010)	3.10 (1.22-8.96, P=0.024)	3.10 (1.16-8.25, P=0.024)
	2	150 (87.7)	21 (12.3)	10.41 (4.69-25.45, P<0.001)	8.73 (3.10-28.92, P<0.001)	6.94 (2.71-20.32, P<0.001)	6.94 (2.57-18.74, P<0.001)
	3/4	64 (77.1)	19 (22.9)	22.08 (9.60-55.43, P<0.001)	8.41 (2.45-32.09, P=0.001)	7.08 (2.33-23.37, P=0.001)	7.08 (2.27-22.09, P=0.001)
Smoking	No	927 (95.5)	44 (4.5)	-	-	-	-
	Yes	182 (92.9)	14 (7.1)	1.62 (0.84-2.95, P=0.128)	3.00 (1.35-6.53, P=0.006)	2.70 (1.27-5.55, P=0.008)	2.70 (1.30-5.62, P=0.008)

	(Missing)	131 (91.0)	13 (9.0)	2.09 (1.06-3.88, P=0.025)	2.93 (1.05-7.59, P=0.032)	3.00 (1.16-7.24, P=0.018)	3.00 (1.21-7.43, P=0.018)
Diabetes	No	1032 (95.1)	53 (4.9)	-	-	-	-
	Yes	189 (93.6)	13 (6.4)	1.34 (0.69-2.43, P=0.360)	0.82 (0.35-1.79, P=0.636)	-	-
Mode of diagnosis	Symptomatic	1088 (94.4)	65 (5.6)	-	-	-	-
	Screening	40 (97.6)	1 (2.4)	0.42 (0.02-1.97, P=0.393)	1.64 (0.08-9.90, P=0.654)	1.76 (0.09-9.99, P=0.601)	1.76 (0.21-14.61, P=0.601)
	Detected incidentally	96 (97.0)	3 (3.0)	0.52 (0.13-1.44, P=0.280)	0.69 (0.09-3.02, P=0.663)	0.62 (0.09-2.62, P=0.566)	0.62 (0.12-3.18, P=0.566)
Urgency	Elective	1180 (95.8)	52 (4.2)	-	-	-	-
	Emergency	60 (75.9)	19 (24.1)	7.19 (3.93-12.75, P<0.001)	3.26 (1.33-7.61, P=0.008)	2.63 (1.14-5.81, P=0.019)	2.63 (1.17-5.92, P=0.019)
Treatment intent	Palliative	158 (84.5)	29 (15.5)	-	-	-	-
	Curative	1082 (96.3)	42 (3.7)	0.21 (0.13-0.35, P<0.001)	1.23 (0.48-3.29, P=0.666)	-	-
Approach	Open	926 (94.1)	58 (5.9)	-	-	-	-
	Minimally invasive	311 (96.0)	13 (4.0)	0.67 (0.35-1.20, P=0.197)	1.06 (0.43-2.39, P=0.895)	-	-
Site	Upper third (cardia/fundus)	243 (94.2)	15 (5.8)	-	-	-	-
	Middle third (body)	244 (96.8)	8 (3.2)	0.53 (0.21-1.25, P=0.157)	0.47 (0.15-1.35, P=0.173)	-	-
	Distal third (antrium/pylorus)	533 (93.8)	35 (6.2)	1.06 (0.58-2.04, P=0.846)	0.62 (0.28-1.44, P=0.256)	-	-
	Entire stomach	197 (94.7)	11 (5.3)	0.90 (0.40-2.00, P=0.806)	1.13 (0.40-3.07, P=0.811)	-	-
D2 resection	No	500 (91.7)	45 (8.3)	-	-	-	-
	Yes	683 (96.7)	23 (3.3)	0.37 (0.22-0.62, P<0.001)	0.82 (0.40-1.67, P=0.584)	0.82 (0.43-1.58, P=0.561)	0.82 (0.43-1.58, P=0.561)
Pre-op obstruction	No	1062 (96.4)	40 (3.6)	-	-	-	-
	Yes	159 (85.0)	28 (15.0)	4.68 (2.78-7.76, P<0.001)	2.06 (0.93-4.46, P=0.071)	1.81 (0.89-3.61, P=0.093)	1.81 (0.91-3.63, P=0.093)
Pre-op perforation	No	1190 (95.0)	63 (5.0)	-	-	-	-
	Yes	37 (84.1)	7 (15.9)	3.57 (1.41-7.88, P=0.003)	2.49 (0.75-7.36, P=0.114)	2.41 (0.77-6.75, P=0.110)	2.41 (0.82-7.06, P=0.110)
Stage	0	0 (NaN)	0 (NaN)	-	-	-	-
	I	427 (96.6)	15 (3.4)	-	-	-	-

II	221 (96.1)	9 (3.9)	1.16 (0.48-2.65, P=0.731)	0.93 (0.29-2.81, P=0.903)	0.83 (0.27-2.37, P=0.731)	0.83 (0.28-2.41, P=0.731)
III	473 (95.4)	23 (4.6)	1.38 (0.72-2.74, P=0.337)	1.05 (0.43-2.62, P=0.923)	1.11 (0.49-2.60, P=0.806)	1.11 (0.48-2.54, P=0.806)
IV	108 (83.1)	22 (16.9)	5.80 (2.93-11.77, P<0.001)	3.26 (1.06-10.25, P=0.041)	2.60 (1.03-6.77, P=0.046)	2.60 (1.02-6.63, P=0.046)

Data are n (%). Multilevel model includes hospital and country as random intercepts.

Table 10-16. Gastric cancer logistic regression analyses: major complication.

Dependent: Major complication		No	Yes	OR (univariable)	OR (multivariable)	OR (multivariable reduced)	OR (multilevel)
WB income (tertile)	High	604 (85.2)	105 (14.8)	-	-	-	-
	Upper middle	258 (90.8)	26 (9.2)	0.58 (0.36-0.90, P=0.018)	0.60 (0.35-1.00, P=0.058)	0.60 (0.36-0.98, P=0.046)	0.55 (0.30-1.02, P=0.057)
	Low/lower middle	267 (81.4)	61 (18.6)	1.31 (0.93-1.85, P=0.123)	1.16 (0.68-1.97, P=0.587)	1.29 (0.80-2.06, P=0.293)	1.25 (0.71-2.22, P=0.436)
Age (years)	Mean (SD)	-0.0 (1.0)	0.3 (0.9)	1.49 (1.27-1.77, P<0.001)	1.49 (1.19-1.88, P=0.001)	1.51 (1.22-1.88, P<0.001)	1.53 (1.21-1.92, P<0.001)
Sex	Male	677 (84.1)	128 (15.9)	-	-	-	-
	Female	452 (87.6)	64 (12.4)	0.75 (0.54-1.03, P=0.079)	0.88 (0.59-1.30, P=0.515)	-	-
ASA (>3)	No	1088 (86.7)	167 (13.3)	-	-	-	-
	Yes	41 (62.1)	25 (37.9)	3.97 (2.33-6.66, P<0.001)	1.85 (0.90-3.74, P=0.090)	2.63 (1.39-4.89, P=0.003)	3.15 (1.57-6.31, P=0.001)
BMI	Normal weight (BMI 18.5 to 24.9)	546 (85.0)	96 (15.0)	-	-	-	-
	Underweight (BMI < 18.5)	105 (84.7)	19 (15.3)	1.03 (0.59-1.72, P=0.916)	0.64 (0.32-1.21, P=0.182)	0.60 (0.31-1.09, P=0.106)	0.61 (0.32-1.18, P=0.141)
	Overweight (BMI 25 to 30)	312 (85.2)	54 (14.8)	0.98 (0.68-1.41, P=0.932)	1.04 (0.67-1.60, P=0.852)	1.10 (0.73-1.65, P=0.647)	1.07 (0.70-1.65, P=0.746)
	Obese (BMI >30)	113 (88.3)	15 (11.7)	0.75 (0.41-1.31, P=0.343)	0.77 (0.37-1.49, P=0.458)	0.80 (0.41-1.48, P=0.494)	0.74 (0.38-1.47, P=0.394)
	(Missing)	53 (86.9)	8 (13.1)	0.86 (0.37-1.77, P=0.699)	0.54 (0.16-1.51, P=0.277)	0.77 (0.26-1.94, P=0.600)	0.77 (0.27-2.18, P=0.616)
ECOG performance status	0	557 (92.4)	46 (7.6)	-	-	-	-
	1	346 (82.4)	74 (17.6)	2.59 (1.76-3.85, P<0.001)	2.34 (1.49-3.70, P<0.001)	2.31 (1.51-3.57, P<0.001)	2.40 (1.52-3.78, P<0.001)
	2	139 (79.9)	35 (20.1)	3.05 (1.88-4.91, P<0.001)	2.24 (1.26-3.93, P=0.005)	2.16 (1.26-3.67, P=0.005)	2.10 (1.18-3.72, P=0.011)
	3/4	55 (64.0)	31 (36.0)	6.82 (3.99-11.62, P<0.001)	3.73 (1.76-7.82, P<0.001)	4.02 (2.10-7.63, P<0.001)	3.97 (1.97-8.01, P<0.001)
Smoking	No	842 (86.1)	136 (13.9)	-	-	-	-
	Yes	163 (82.3)	35 (17.7)	1.33 (0.87-1.98, P=0.171)	1.85 (1.13-2.98, P=0.012)	1.78 (1.12-2.79, P=0.013)	1.68 (1.04-2.72, P=0.036)

	(Missing)	124 (85.5)	21 (14.5)	1.05 (0.62-1.69, P=0.852)	1.08 (0.53-2.05, P=0.830)	0.81 (0.42-1.49, P=0.522)	0.80 (0.41-1.56, P=0.507)
Diabetes	No	944 (86.3)	150 (13.7)	-	-	-	-
	Yes	168 (82.8)	35 (17.2)	1.31 (0.87-1.94, P=0.188)	0.97 (0.59-1.57, P=0.911)	-	-
Mode of diagnosis	Symptomatic	991 (85.3)	171 (14.7)	-	-	-	-
	Screening	34 (82.9)	7 (17.1)	1.19 (0.48-2.58, P=0.676)	1.45 (0.46-3.77, P=0.484)	1.53 (0.53-3.79, P=0.386)	1.63 (0.58-4.57, P=0.351)
	Detected incidentally	90 (90.0)	10 (10.0)	0.64 (0.31-1.20, P=0.200)	0.60 (0.24-1.33, P=0.236)	0.48 (0.19-1.04, P=0.081)	0.51 (0.21-1.22, P=0.130)
Urgency	Elective	1081 (87.2)	159 (12.8)	-	-	-	-
	Emergency	48 (59.3)	33 (40.7)	4.67 (2.89-7.48, P<0.001)	3.62 (1.93-6.74, P<0.001)	3.70 (2.07-6.56, P<0.001)	4.06 (2.17-7.60, P<0.001)
Treatment intent	Palliative	145 (76.3)	45 (23.7)	-	-	-	-
	Curative	984 (87.0)	147 (13.0)	0.48 (0.33-0.71, P<0.001)	1.16 (0.62-2.23, P=0.643)	0.95 (0.57-1.63, P=0.857)	0.99 (0.56-1.74, P=0.961)
Approach	Open	843 (85.1)	148 (14.9)	-	-	-	-
	Minimally invasive	284 (86.9)	43 (13.1)	0.86 (0.59-1.23, P=0.427)	1.03 (0.65-1.62, P=0.890)	-	-
Site	Upper third (cardia/fundus)	220 (84.6)	40 (15.4)	-	-	-	-
	Middle third (body)	214 (84.6)	39 (15.4)	1.00 (0.62-1.62, P=0.992)	1.09 (0.62-1.92, P=0.758)	0.99 (0.58-1.69, P=0.966)	0.96 (0.55-1.70, P=0.899)
	Distal third (antrium/pylorus)	497 (86.9)	75 (13.1)	0.83 (0.55-1.27, P=0.379)	0.59 (0.35-0.99, P=0.045)	0.64 (0.40-1.02, P=0.059)	0.62 (0.38-1.02, P=0.060)
	Entire stomach	174 (82.9)	36 (17.1)	1.14 (0.69-1.86, P=0.607)	1.45 (0.81-2.59, P=0.209)	1.39 (0.81-2.38, P=0.233)	1.42 (0.80-2.54, P=0.235)
Anastomosis	Not performed	158 (88.8)	20 (11.2)	-	-	-	-
	Handsewn	337 (85.1)	59 (14.9)	1.38 (0.82-2.43, P=0.240)	1.76 (0.88-3.66, P=0.119)	-	-
	Stapled	607 (85.0)	107 (15.0)	1.39 (0.85-2.37, P=0.202)	1.88 (0.99-3.74, P=0.061)	-	-
D2 resection	No	459 (83.3)	92 (16.7)	-	-	-	-
	Yes	614 (86.8)	93 (13.2)	0.76 (0.55-1.03, P=0.079)	1.06 (0.70-1.62, P=0.776)	-	-
Pre-op obstruction	No	973 (87.7)	136 (12.3)	-	-	-	-
	Yes	139 (73.2)	51 (26.8)	2.62 (1.81-3.77, P<0.001)	1.81 (1.07-3.04, P=0.025)	-	-

Pre-op perforation	No	1084 (86.0)	177 (14.0)	-	-	-	-
	Yes	34 (73.9)	12 (26.1)	2.16 (1.06-4.14, P=0.026)	1.50 (0.63-3.42, P=0.341)	-	-
Stage	0	0 (NaN)	0 (NaN)	-	-	-	-
	I	392 (87.9)	54 (12.1)	-	-	-	-
	II	203 (87.9)	28 (12.1)	1.00 (0.61-1.62, P=0.996)	0.79 (0.43-1.43, P=0.445)	0.83 (0.47-1.44, P=0.511)	0.90 (0.50-1.63, P=0.723)
	III	423 (84.6)	77 (15.4)	1.32 (0.91-1.93, P=0.144)	1.03 (0.64-1.65, P=0.916)	1.15 (0.75-1.78, P=0.529)	1.30 (0.81-2.08, P=0.279)
	IV	100 (76.3)	31 (23.7)	2.25 (1.36-3.67, P=0.001)	1.52 (0.73-3.12, P=0.262)	1.53 (0.78-2.95, P=0.208)	1.75 (0.86-3.57, P=0.126)

Data are n (%). Multilevel model includes hospital and country as random intercepts.

Table 10-17. Gastric cancer logistic regression analyses: all complications.

Dependent: Any complication		No	Yes	OR (univariable)	OR (multivariable)	OR (multivariable reduced)	OR (multilevel)
WB income (tertile)	High	398 (56.1)	311 (43.9)	-	-	-	-
	Upper middle	142 (50.0)	142 (50.0)	1.28 (0.97-1.69, P=0.080)	1.33 (0.96-1.84, P=0.089)	1.34 (0.99-1.81, P=0.059)	1.71 (0.85-3.43, P=0.130)
	Low/lower middle	169 (51.5)	159 (48.5)	1.20 (0.93-1.57, P=0.166)	1.18 (0.81-1.71, P=0.388)	1.21 (0.86-1.69, P=0.281)	1.05 (0.57-1.92, P=0.881)
Age (years)	Mean (SD)	-0.1 (1.0)	0.1 (1.0)	1.16 (1.04-1.30, P=0.008)	1.11 (0.97-1.28, P=0.138)	1.10 (0.96-1.25, P=0.178)	1.13 (0.96-1.33, P=0.129)
Sex	Male	421 (52.3)	384 (47.7)	-	-	-	-
	Female	288 (55.8)	228 (44.2)	0.87 (0.69-1.08, P=0.211)	0.92 (0.71-1.19, P=0.505)	-	-
ASA (>3)	No	681 (54.3)	574 (45.7)	-	-	-	-
	Yes	28 (42.4)	38 (57.6)	1.61 (0.98-2.68, P=0.062)	1.36 (0.72-2.61, P=0.350)	1.36 (0.76-2.46, P=0.308)	1.65 (0.83-3.27, P=0.154)
BMI	Normal weight (BMI 18.5 to 24.9)	338 (52.6)	304 (47.4)	-	-	-	-
	Underweight (BMI < 18.5)	67 (54.0)	57 (46.0)	0.95 (0.64-1.39, P=0.777)	0.86 (0.55-1.35, P=0.522)	0.79 (0.52-1.21, P=0.288)	0.93 (0.57-1.52, P=0.774)
	Overweight (BMI 25 to 30)	193 (52.7)	173 (47.3)	1.00 (0.77-1.29, P=0.979)	0.92 (0.68-1.23, P=0.563)	0.97 (0.74-1.29, P=0.854)	1.01 (0.73-1.40, P=0.943)
	Obese (BMI >30)	73 (57.0)	55 (43.0)	0.84 (0.57-1.23, P=0.364)	0.73 (0.46-1.14, P=0.172)	0.75 (0.49-1.13, P=0.173)	0.78 (0.48-1.27, P=0.312)
	(Missing)	38 (62.3)	23 (37.7)	0.67 (0.39-1.15, P=0.151)	0.45 (0.20-0.95, P=0.041)	0.44 (0.21-0.87, P=0.023)	0.39 (0.17-0.88, P=0.024)
>10% weight loss	No	342 (54.7)	283 (45.3)	-	-	-	-
	Yes	310 (52.7)	278 (47.3)	1.08 (0.86-1.36, P=0.485)	0.85 (0.63-1.13, P=0.262)	-	-
	(Missing)	57 (52.8)	51 (47.2)	1.08 (0.72-1.63, P=0.708)	0.99 (0.59-1.66, P=0.963)	-	-
ECOG performance status	0	362 (60.0)	241 (40.0)	-	-	-	-
	1	217 (51.7)	203 (48.3)	1.41 (1.09-1.81, P=0.008)	1.40 (1.05-1.88, P=0.022)	1.36 (1.03-1.79, P=0.029)	1.57 (1.13-2.20, P=0.008)
	2	86 (49.4)	88 (50.6)	1.54 (1.10-2.16, P=0.013)	1.47 (0.98-2.20, P=0.064)	1.37 (0.93-2.01, P=0.108)	1.51 (0.96-2.38, P=0.077)

	3/4	30 (34.9)	56 (65.1)	2.80 (1.76-4.54, P<0.001)	2.24 (1.21-4.21, P=0.011)	2.64 (1.50-4.75, P=0.001)	3.66 (1.87-7.17, P<0.001)
Smoking	No	517 (52.9)	461 (47.1)	-	-	-	-
	Yes	112 (56.6)	86 (43.4)	0.86 (0.63-1.17, P=0.341)	1.07 (0.75-1.51, P=0.705)	-	-
	(Missing)	80 (55.2)	65 (44.8)	0.91 (0.64-1.29, P=0.603)	0.87 (0.55-1.39, P=0.574)	-	-
Diabetes	No	612 (55.9)	482 (44.1)	-	-	-	-
	Yes	86 (42.4)	117 (57.6)	1.73 (1.28-2.34, P<0.001)	1.69 (1.19-2.41, P=0.003)	1.76 (1.26-2.47, P=0.001)	1.61 (1.09-2.37, P=0.017)
Mode of diagnosis	Symptomatic	623 (53.6)	539 (46.4)	-	-	-	-
	Screening	21 (51.2)	20 (48.8)	1.10 (0.59-2.06, P=0.763)	1.31 (0.64-2.67, P=0.454)	-	-
	Detected incidentally	56 (56.0)	44 (44.0)	0.91 (0.60-1.37, P=0.646)	1.07 (0.66-1.74, P=0.776)	-	-
Urgency	Elective	679 (54.8)	561 (45.2)	-	-	-	-
	Emergency	30 (37.0)	51 (63.0)	2.06 (1.30-3.31, P=0.002)	2.06 (1.17-3.67, P=0.013)	1.95 (1.17-3.31, P=0.012)	2.27 (1.23-4.19, P=0.009)
Treatment intent	Palliative	97 (51.1)	93 (48.9)	-	-	-	-
	Curative	612 (54.1)	519 (45.9)	0.88 (0.65-1.20, P=0.434)	0.87 (0.55-1.40, P=0.574)	-	-
Approach	Open	515 (52.0)	476 (48.0)	-	-	-	-
	Minimally invasive	192 (58.7)	135 (41.3)	0.76 (0.59-0.98, P=0.034)	0.84 (0.62-1.14, P=0.261)	-	-
Site	Upper third (cardia/fundus)	134 (51.5)	126 (48.5)	-	-	-	-
	Middle third (body)	144 (56.9)	109 (43.1)	0.81 (0.57-1.14, P=0.222)	0.90 (0.61-1.33, P=0.590)	0.89 (0.61-1.29, P=0.533)	0.81 (0.52-1.25, P=0.342)
	Distal third (antrium/pylorus)	318 (55.6)	254 (44.4)	0.85 (0.63-1.14, P=0.277)	0.83 (0.59-1.16, P=0.272)	0.77 (0.56-1.07, P=0.124)	0.63 (0.43-0.93, P=0.019)
	Entire stomach	99 (47.1)	111 (52.9)	1.19 (0.83-1.72, P=0.344)	1.26 (0.84-1.90, P=0.270)	1.21 (0.82-1.79, P=0.348)	0.99 (0.62-1.59, P=0.970)
Anastomosis	Not performed	113 (63.5)	65 (36.5)	-	-	-	-
	Handsewn	210 (53.0)	186 (47.0)	1.54 (1.07-2.22, P=0.020)	1.92 (1.21-3.07, P=0.006)	1.79 (1.19-2.72, P=0.006)	2.37 (1.45-3.89, P=0.001)
	Stapled	374 (52.4)	340 (47.6)	1.58 (1.13-2.23, P=0.008)	2.00 (1.31-3.10, P=0.002)	1.79 (1.23-2.62, P=0.002)	2.16 (1.38-3.38, P=0.001)
D2 resection	No	297 (53.9)	254 (46.1)	-	-	-	-

	Yes	380 (53.7)	327 (46.3)	1.01 (0.80-1.26, P=0.957)	0.96 (0.72-1.27, P=0.756)	-	-
Pre-op obstruction	No	595 (53.7)	514 (46.3)	-	-	-	-
	Yes	100 (52.6)	90 (47.4)	1.04 (0.76-1.42, P=0.794)	0.78 (0.52-1.18, P=0.240)	-	-
Pre-op perforation	No	678 (53.8)	583 (46.2)	-	-	-	-
	Yes	22 (47.8)	24 (52.2)	1.27 (0.70-2.30, P=0.428)	0.92 (0.44-1.91, P=0.824)	-	-
Stage	0	0 (NaN)	0 (NaN)	-	-	-	-
	I	248 (55.6)	198 (44.4)	-	-	-	-
	II	125 (54.1)	106 (45.9)	1.06 (0.77-1.46, P=0.711)	0.91 (0.62-1.32, P=0.610)	-	-
	III	265 (53.0)	235 (47.0)	1.11 (0.86-1.44, P=0.422)	0.88 (0.64-1.21, P=0.439)	-	-
	IV	65 (49.6)	66 (50.4)	1.27 (0.86-1.88, P=0.227)	1.03 (0.60-1.75, P=0.927)	-	-

Data are n (%). Multilevel model includes hospital and country as random intercepts.

Table 10-18. Complications in patients who died.

			High	Upper middle	Low/lower middle
Breast	Minor complication (CD1)	Yes	1 (25.0)	0 (0.0)	1 (16.7)
	Minor complication (CD2)	Yes	1 (25.0)	0 (0.0)	2 (33.3)
	Reintervention (CD3)	No	2 (50.0)	2 (100.0)	6 (100.0)
		Yes, NOT under general anaesthetic	1 (25.0)	0 (0.0)	0 (0.0)
		Yes under general anaesthetic	1 (25.0)	0 (0.0)	0 (0.0)
	Life-threatening complication (CD4)	No	2 (50.0)	0 (0.0)	2 (33.3)
		Yes, single organ failure	1 (25.0)	0 (0.0)	2 (33.3)
		Yes, multi organ failure	1 (25.0)	2 (100.0)	2 (33.3)
	Any complication	Yes	4 (100.0)	2 (100.0)	10 (100.0)
	Readmission	Yes	1 (25.0)	0 (0.0)	2 (40.0)
	Surgical site infection	No	4 (100.0)	2 (100.0)	3 (50.0)
		Yes, no treatment/wound opened only (CD 1)	0 (0.0)	0 (0.0)	1 (16.7)
		Yes, antibiotics only (CD 2)	0 (0.0)	0 (0.0)	1 (16.7)
		Yes, return to operating theatre (CD 3)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, requiring critical care admission (CD 4)	0 (0.0)	0 (0.0)	1 (16.7)
		Yes, resulting in death (CD 5)	0 (0.0)	0 (0.0)	0 (0.0)
	Post-op bleed	No	4 (100.0)	2 (100.0)	6 (85.7)
		Yes, no intervention required (CD 1)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, transfusion only (CD 2)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, surgical/radiological intervention required (CD 3)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, critical care admission &/or intervention (CD 4)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, resulting in death (CD 5)	0 (0.0)	0 (0.0)	1 (14.3)
	Seroma	No	4 (100.0)	2 (100.0)	4 (66.7)
		Yes, no intervention/aspiration only (CD 1)	0 (0.0)	0 (0.0)	2 (33.3)
		Yes, antibiotic treatment only (CD 2)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, intervention required (CD 3)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, critical care admission &/or intervention (CD 4)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, resulting in death (CD 5)	0 (0.0)	0 (0.0)	0 (0.0)

Gastric	Minor complication (CD1)	Yes	10 (37.0)	2 (18.2)	9 (32.1)
	Minor complication (CD2)	Yes	14 (51.9)	3 (27.3)	13 (44.8)
	Reintervention (CD3)	No	17 (63.0)	6 (54.5)	24 (77.4)
		Yes, NOT under general anaesthetic	0 (0.0)	2 (18.2)	0 (0.0)
		Yes, under general anaesthetic	10 (37.0)	3 (27.3)	7 (22.6)
	Life-threatening complication (CD4)	No	9 (33.3)	2 (18.2)	15 (48.4)
		Yes, single organ failure	3 (11.1)	3 (27.3)	3 (9.7)
		Yes, multi organ failure	15 (55.6)	6 (54.5)	13 (41.9)
	Any complication	Yes	27 (100.0)	11 (100.0)	33 (100.0)
	Readmission	Yes	2 (7.4)	2 (18.2)	6 (20.0)
	Surgical site infection	No	18 (72.0)	9 (81.8)	22 (78.6)
		Yes, no treatment/wound opened only (CD 1)	1 (4.0)	0 (0.0)	1 (3.6)
		Yes, antibiotics only (CD 2)	2 (8.0)	1 (9.1)	4 (14.3)
		Yes, return to operating theatre (CD 3)	1 (4.0)	0 (0.0)	0 (0.0)
		Yes, requiring critical care admission (CD 4)	1 (4.0)	0 (0.0)	1 (3.6)
		Yes, resulting in death (CD 5)	2 (8.0)	1 (9.1)	0 (0.0)
	Abscess (OSI)	No	18 (69.2)	10 (90.9)	24 (96.0)
		Yes, no intervention (CD 1)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, antibiotics only (CD 2)	1 (3.8)	0 (0.0)	0 (0.0)
		Yes, surgical/radiological drainage (CD 3)	2 (7.7)	1 (9.1)	1 (4.0)
		Yes, critical care admission (CD 4)	2 (7.7)	0 (0.0)	0 (0.0)
		Yes, resulting in death (CD 5)	3 (11.5)	0 (0.0)	0 (0.0)
	Anastomotic leak	No	20 (74.1)	7 (63.6)	23 (82.1)
		Yes, no intervention required (CD 1)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, drug treatment only (CD 2)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, intervention required (CD 3)	1 (3.7)	1 (9.1)	3 (10.7)
		Yes, critical care admission &/or intervention (CD 4)	3 (11.1)	1 (9.1)	2 (7.1)
		Yes, resulting in death (CD 5)	3 (11.1)	2 (18.2)	0 (0.0)
	Post-op bleed	No	23 (85.2)	8 (80.0)	23 (82.1)
		Yes, no intervention required (CD 1)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, transfusion only (CD 2)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, surgical/radiological intervention required (CD 3)	0 (0.0)	0 (0.0)	1 (3.6)
		Yes, critical care admission &/or intervention (CD 4)	1 (3.7)	1 (10.0)	2 (7.1)

		Yes, resulting in death (CD 5)	3 (11.1)	1 (10.0)	2 (7.1)
Colorectal	Minor complication (CD1)	Yes	30 (32.3)	10 (22.7)	26 (47.3)
	Minor complication (CD2)	Yes	36 (39.1)	13 (29.5)	32 (57.1)
	Reintervention (CD3)	No	63 (67.0)	33 (73.3)	35 (61.4)
		Yes, NOT under general anaesthetic	4 (4.3)	0 (0.0)	5 (8.8)
		Yes, under general anaesthetic	27 (28.7)	12 (26.7)	17 (29.8)
	Life-threatening complication (CD4)	No	32 (34.4)	16 (34.8)	12 (20.3)
		Yes, single organ failure	13 (14.0)	5 (10.9)	11 (18.6)
		Yes, multi organ failure	48 (51.6)	25 (54.3)	36 (61.0)
	Any complication	Yes	94 (100.0)	47 (100.0)	63 (100.0)
	Readmission	Yes	9 (9.7)	9 (20.0)	16 (27.6)
	Surgical site infection	No	70 (77.8)	26 (60.5)	27 (50.9)
		Yes, no treatment/wound opened only (CD 1)	2 (2.2)	4 (9.3)	4 (7.5)
		Yes, antibiotics only (CD 2)	7 (7.8)	3 (7.0)	8 (15.1)
		Yes, return to operating theatre (CD 3)	6 (6.7)	1 (2.3)	5 (9.4)
		Yes, requiring critical care admission (CD 4)	2 (2.2)	5 (11.6)	3 (5.7)
		Yes, resulting in death (CD 5)	3 (3.3)	4 (9.3)	6 (11.3)
	Abscess (OSI)	No	72 (80.0)	31 (70.5)	34 (70.8)
		Yes, no intervention (CD 1)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, antibiotics only (CD 2)	3 (3.3)	4 (9.1)	3 (6.2)
		Yes, surgical/radiological drainage (CD 3)	3 (3.3)	2 (4.5)	4 (8.3)
		Yes, critical care admission (CD 4)	0 (0.0)	3 (6.8)	3 (6.2)
		Yes, resulting in death (CD 5)	12 (13.3)	4 (9.1)	4 (8.3)
	Anastomotic leak	No	77 (85.6)	32 (74.4)	40 (76.9)
		Yes, no intervention required (CD 1)	0 (0.0)	1 (2.3)	2 (3.8)
		Yes, drug treatment only (CD 2)	0 (0.0)	0 (0.0)	0 (0.0)
		Yes, intervention required (CD 3)	2 (2.2)	1 (2.3)	4 (7.7)
		Yes, critical care admission &/or intervention (CD 4)	0 (0.0)	4 (9.3)	3 (5.8)
		Yes, resulting in death (CD 5)	11 (12.2)	5 (11.6)	3 (5.8)
	Post-op bleed	No	81 (88.0)	42 (93.3)	43 (76.8)
		Yes, no intervention required (CD 1)	1 (1.1)	0 (0.0)	0 (0.0)
		Yes, transfusion only (CD 2)	3 (3.3)	0 (0.0)	3 (5.4)
		Yes, surgical/radiological intervention required (CD 3)	3 (3.3)	0 (0.0)	2 (3.6)

Yes, critical care admission &/or intervention (CD 4)	0 (0.0)	1 (2.2)	5 (8.9)
Yes, resulting in death (CD 5)	4 (4.3)	2 (4.4)	3 (5.4)

Data are n (%).

Table 10-19. Summary of hospital care services for centres treating gastric and colon cancer stratified by country income group.

WB income (tertile)		High N=232	Upper middle N=72	Low/lower middle N=95	Total N=399
Hospital type	Non-referral hospital	25 (10.8)	5 (6.9)	7 (7.4)	37 (9.3)
	Referral hospital	54 (23.3)	47 (65.3)	70 (73.7)	171 (42.9)
	Specialist cancer hospital	9 (3.9)	7 (9.7)	11 (11.6)	27 (6.8)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
Hospital catchment	< 50 000	5 (2.2)	9 (12.5)	22 (23.2)	36 (9.0)
	50 000 - 199 999	31 (13.4)	12 (16.7)	7 (7.4)	50 (12.5)
	200 000 - 499 999	29 (12.5)	2 (2.8)	7 (7.4)	38 (9.5)
	500 000 - 999 999	13 (5.6)	11 (15.3)	12 (12.6)	36 (9.0)
	1 000 000 - 1 999 999	6 (2.6)	11 (15.3)	10 (10.5)	27 (6.8)
	Over 2 000 000	4 (1.7)	14 (19.4)	30 (31.6)	48 (12.0)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
MDT / Tumour board	None	2 (0.9)	12 (16.7)	23 (24.2)	37 (9.3)
	Yes, for some cancers	16 (6.9)	22 (30.6)	39 (41.1)	77 (19.3)
	Yes, for all cancers	70 (30.2)	25 (34.7)	26 (27.4)	121 (30.3)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
Oncologist	Not available	6 (2.6)	11 (15.3)	24 (25.3)	41 (10.3)
	Available in hospital	82 (35.3)	40 (55.6)	57 (60.0)	179 (44.9)
	(Not sampled)	144 (62.1)	21 (29.2)	14 (14.7)	179 (44.9)
Palliative care specialist	Not available	23 (9.9)	32 (44.4)	52 (54.7)	107 (26.8)
	Available in hospital	65 (28.0)	27 (37.5)	36 (37.9)	128 (32.1)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
CT scan	No CT scan	0 (0.0)	3 (4.2)	17 (17.9)	20 (5.0)
	On site, not always available	4 (1.7)	7 (9.7)	16 (16.8)	27 (6.8)
	On site, always available	84 (36.2)	49 (68.1)	55 (57.9)	188 (47.1)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
Access to opioid medication	No	0 (0.0)	1 (1.4)	2 (2.1)	3 (0.8)
	Yes, some of the time	7 (3.0)	11 (15.3)	39 (41.1)	57 (14.3)
	Yes, all of the time	81 (34.9)	47 (65.3)	47 (49.5)	175 (43.9)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
Designated perioperative recovery area	No	2 (0.9)	5 (6.9)	7 (7.4)	14 (3.5)
	Yes, some of the time	3 (1.3)	8 (11.1)	17 (17.9)	28 (7.0)
	Yes, all of the time	83 (35.8)	46 (63.9)	64 (67.4)	193 (48.4)

	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
Highest level of postoperative care	Ward level only	7 (3.0)	16 (22.2)	30 (31.6)	53 (13.3)
	ICU/HDU	81 (34.9)	43 (59.7)	58 (61.1)	182 (45.6)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
Pathology services	Not available	0 (0.0)	1 (1.4)	3 (3.2)	4 (1.0)
	Available at another hospital	8 (3.4)	7 (9.7)	16 (16.8)	31 (7.8)
	On site, not always available	16 (6.9)	4 (5.6)	9 (9.5)	29 (7.3)
	On site, always available	64 (27.6)	47 (65.3)	60 (63.2)	171 (42.9)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
Radiotherapy	No radiotherapy available	1 (0.4)	2 (2.8)	16 (16.8)	19 (4.8)
	> 50 km from hospital	15 (6.5)	6 (8.3)	19 (20.0)	40 (10.0)
	10 - 50 km from hospital	12 (5.2)	8 (11.1)	12 (12.6)	32 (8.0)
	Within 10 km from hospital	19 (8.2)	16 (22.2)	10 (10.5)	45 (11.3)
	Radiotherapy on site	41 (17.7)	27 (37.5)	31 (32.6)	99 (24.8)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
Chemotherapy	No chemotherapy available	0 (0.0)	2 (2.8)	2 (2.1)	4 (1.0)
	> 50 km from hospital	0 (0.0)	1 (1.4)	11 (11.6)	12 (3.0)
	10 - 50 km from hospital	2 (0.9)	4 (5.6)	8 (8.4)	14 (3.5)
	Within 10 km from hospital	11 (4.7)	9 (12.5)	7 (7.4)	27 (6.8)
	Chemotherapy on site	75 (32.3)	43 (59.7)	60 (63.2)	178 (44.6)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
Postoperative care infrastructure	Absent	12 (5.2)	26 (36.1)	55 (57.9)	93 (23.3)
	Present	76 (32.8)	33 (45.8)	33 (34.7)	142 (35.6)
	(Not sampled)	144 (62.1)	13 (18.1)	7 (7.4)	164 (41.1)
Cancer care pathway	Absent	47 (20.3)	32 (44.4)	57 (60.0)	136 (34.1)
	Present	41 (17.7)	25 (34.7)	30 (31.6)	96 (24.1)
	(Not sampled)	144 (62.1)	15 (20.8)	8 (8.4)	167 (41.9)

Table 10-20. 30-day mortality in patients who sustained a major complication - capacity to rescue models.

Figure 5-6 (A) uses the multilevel model. Figure 5-7 and 5-8 use the multivariable and multivariable including postoperative care infrastructure models.

Dependent: 30-day mortality		Alive	Dead	OR (univariable)	OR (multivariable)	OR (multivariable including postoperative care infrastructure)	OR (multilevel)
WB income (tertile)	High	572 (82.5)	121 (17.5)	-	-	-	-
	Upper middle	93 (61.6)	58 (38.4)	2.95 (2.01-4.31, P<0.001)	3.64 (2.29-5.78, P<0.001)	3.04 (1.84-4.99, P<0.001)	3.89 (2.08-7.29, P<0.001)
	Low/lower middle	137 (58.8)	96 (41.2)	3.31 (2.39-4.59, P<0.001)	5.28 (3.34-8.41, P<0.001)	4.46 (2.74-7.31, P<0.001)	6.15 (3.26-11.59, P<0.001)
Age (years)	Mean (SD)	66.0 (12.7)	70.2 (14.8)	1.03 (1.01-1.04, P<0.001)	1.03 (1.02-1.05, P<0.001)	1.03 (1.02-1.05, P<0.001)	1.03 (1.01-1.05, P<0.001)-
Sex	Male	488 (74.3)	169 (25.7)	-	-	-	-
	Female	314 (74.9)	105 (25.1)	0.97 (0.73-1.28, P=0.808)	0.80 (0.57-1.13, P=0.218)	0.82 (0.58-1.16, P=0.267)	0.80 (0.56-1.15, P=0.237)
Cancer type	Colorectal	682 (77.0)	204 (23.0)	-	-	-	-
	Gastric	120 (62.8)	71 (37.2)	1.98 (1.41-2.75, P<0.001)	1.75 (1.16-2.63, P=0.008)	1.79 (1.18-2.69, P=0.006)	1.81 (1.17-2.78, P=0.007)
ECOG performance status	0	335 (89.1)	41 (10.9)	-	-	-	-
	1	249 (78.5)	68 (21.5)	2.23 (1.47-3.42, P<0.001)	1.65 (1.04-2.63, P=0.033)	1.64 (1.04-2.61, P=0.036)	1.67 (1.03-2.71, P=0.037)
	2	118 (62.8)	70 (37.2)	4.85 (3.14-7.57, P<0.001)	2.87 (1.74-4.77, P<0.001)	2.86 (1.73-4.75, P<0.001)	3.01 (1.77-5.13, P<0.001)
	3/4	65 (42.8)	87 (57.2)	10.94 (6.98-17.42, P<0.001)	4.89 (2.88-8.38, P<0.001)	4.63 (2.72-7.98, P<0.001)	5.02 (2.83-8.91, P<0.001)
ASA	I	85 (81.7)	19 (18.3)	-	-	-	-
	II	349 (80.2)	86 (19.8)	1.10 (0.65-1.96, P=0.729)	1.05 (0.57-2.00, P=0.877)	1.04 (0.56-1.98, P=0.906)	1.02 (0.53-1.97, P=0.958)

	III	297 (72.4)	113 (27.6)	1.70 (1.01-3.00, P=0.055)	1.48 (0.77-2.91, P=0.244)	1.51 (0.79-2.98, P=0.220)	1.48 (0.73-2.98, P=0.274)
	IV	47 (51.6)	44 (48.4)	4.19 (2.23-8.13, P<0.001)	2.35 (1.06-5.29, P=0.037)	2.35 (1.06-5.33, P=0.037)	2.45 (1.03-5.82, P=0.042)
	V	5 (41.7)	7 (58.3)	6.26 (1.81-23.26, P=0.004)	2.19 (0.52-10.30, P=0.294)	2.09 (0.49-9.97, P=0.331)	2.67 (0.55-12.88, P=0.221)
Stage	I	212 (78.5)	58 (21.5)	-	-	-	-
	II	190 (78.5)	52 (21.5)	1.00 (0.65-1.53, P=0.999)	0.88 (0.53-1.44, P=0.608)	0.85 (0.51-1.40, P=0.519)	0.88 (0.52-1.47, P=0.614)
	III	297 (77.7)	85 (22.3)	1.05 (0.72-1.53, P=0.815)	0.87 (0.56-1.36, P=0.544)	0.85 (0.54-1.33, P=0.463)	0.84 (0.52-1.34, P=0.458)
	IV	100 (56.5)	77 (43.5)	2.81 (1.86-4.28, P<0.001)	1.84 (1.09-3.09, P=0.022)	1.80 (1.07-3.03, P=0.027)	1.80 (1.04-3.12, P=0.036)
Urgency	Elective	673 (79.6)	173 (20.4)	-	-	-	-
	Emergency	129 (55.8)	102 (44.2)	3.08 (2.26-4.19, P<0.001)	2.18 (1.49-3.20, P<0.001)	2.21 (1.50-3.25, P<0.001)	2.40 (1.59-3.62, P<0.001)
Postoperative care infrastructure	Absent	126 (57.5)	93 (42.5)	-	-	-	
	Present	676 (78.8)	182 (21.2)	0.36 (0.27-0.50, P<0.001)	-	0.64 (0.41-0.98, P=0.040)	

Data are n (%). Multilevel model includes hospital and country as random intercepts.

Table 10-21. Three-way mediation decomposition of proportion of effect of country income group on 30-day mortality mediated by the absence of postoperative care infrastructure.

No significant exposure-mediator interaction was seen so a two-way decomposition is presented. Variables in the Table 10-20 multivariable model were included as covariates. Given that the potential mediator in this case is a hospital-level factor, it was assumed that there was no causal relationship between this and covariates at the patient level. Similarly, no mediator-outcome confounders were specified. These models therefore represent the change in country income group coefficients on the introduction of the postoperative care infrastructure variable. Uncertainty was determined using bootstrap resampling (5000 draws) and confidence intervals constructed using percentiles.

Low/lower middle	Median	Lower 95% CI	Upper 95% CI	P
Total natural effect	5.50	3.36	8.97	
Total natural direct effect	4.62	2.78	7.83	
Total natural indirect effect	1.19	1.01	1.42	0.040
Proportion of total effect which is indirect	0.10	0.002	0.22	0.040

Upper middle	Median	Lower 95% CI	Upper 95% CI	P
Total natural effect	3.75	2.27	5.81	
Total natural direct effect	3.15	1.89	5.15	
Total natural indirect effect	1.19	1.01	1.42	0.040
Proportion of total effect which is indirect	0.14	0.003	0.32	0.040

Table 10-22. Absolute risk difference for 30-day mortality after major complication in the presence of consistently available postoperative care infrastructure.

Probabilities are predicted from multivariable model in table 10-20 at fixed covariate levels (age 55 years, ECOG performance status 1, ASA grade II, cancer stage II, and elective surgery). Confidence intervals and two-sided p-values are generated from bootstrap resampling (5000 replications).

WB income (tertile)	Sex	Cancer type	Postoperative care infrastructure	Predicted probability of death	Absolute difference (95% confidence interval, P-value)	Number needed to treat (benefit) (95% confidence interval)
Low/lower middle	Male	Gastric	Present	0.287 (0.155 to 0.440)	-	-
Low/lower middle	Male	Gastric	Absent	0.383 (0.234 to 0.556)	0.096 (0.002 to 0.199, P=0.048)	10 (581 to 5, P=0.048)
Upper middle	Male	Gastric	Present	0.213 (0.097 to 0.375)	-	-
Upper middle	Male	Gastric	Absent	0.298 (0.146 to 0.486)	0.081 (0.002 to 0.177, P=0.045)	12 (540 to 6, P=0.045)
High	Male	Gastric	Present	0.082 (0.037 to 0.147)	-	-
High	Male	Gastric	Absent	0.123 (0.052 to 0.228)	0.038 (-0.000 to 0.104, P=0.052)	26 (-2623 to ∞ to 10, P=0.052)
Low/lower middle	Male	Colorectal	Present	0.182 (0.099 to 0.291)	-	-
Low/lower middle	Male	Colorectal	Absent	0.259 (0.153 to 0.377)	0.075 (-0.001 to 0.153, P=0.051)	13 (-1608 to ∞ to 7, P=0.051)
Upper middle	Male	Colorectal	Present	0.132 (0.059 to 0.233)	-	-
Upper middle	Male	Colorectal	Absent	0.192 (0.098 to 0.321)	0.057 (0.000 to 0.133, P=0.050)	17 (27205 to 7, P=0.050)
High	Male	Colorectal	Present	0.048 (0.023 to 0.080)	-	-
High	Male	Colorectal	Absent	0.073 (0.034 to 0.126)	0.024 (0.001 to 0.063, P=0.044)	42 (1661 to 16, P=0.044)
Low/lower middle	Female	Gastric	Present	0.246 (0.128 to 0.398)	-	-
Low/lower middle	Female	Gastric	Absent	0.339 (0.196 to 0.506)	0.090 (0.001 to 0.188, P=0.049)	11 (1384 to 5, P=0.049)
Upper middle	Female	Gastric	Present	0.182 (0.083 to 0.333)	-	-
Upper middle	Female	Gastric	Absent	0.259 (0.125 to 0.438)	0.073 (-0.001 to 0.166, P=0.051)	14 (-1278 to ∞ to 6, P=0.051)
High	Female	Gastric	Present	0.068 (0.029 to 0.127)	-	-
High	Female	Gastric	Absent	0.103 (0.043 to 0.197)	0.032 (-0.000 to 0.090, P=0.052)	31 (-4042 to ∞ to 11, P=0.052)
Low/lower middle	Female	Colorectal	Present	0.155 (0.080 to 0.250)	-	-
Low/lower middle	Female	Colorectal	Absent	0.223 (0.123 to 0.335)	0.066 (-0.001 to 0.141, P=0.051)	15 (-1725 to ∞ to 7, P=0.051)
Upper middle	Female	Colorectal	Present	0.111 (0.050 to 0.200)	-	-
Upper middle	Female	Colorectal	Absent	0.163 (0.083 to 0.278)	0.049 (0.001 to 0.118, P=0.046)	20 (1368 to 8, P=0.046)

High	Female	Colorectal	Present	0.039 (0.018 to 0.068)	-	-
High	Female	Colorectal	Absent	0.060 (0.027 to 0.109)	0.019 (0.000 to 0.053, P=0.048)	52 (4332 to 19, P=0.048)

10.4 Supplementary material for Chapter 6

Hospital-level survey and definitions.

Hospital characteristics

1. Please select your hospital (dropdown list)

2. What is the approximate size of population for which your hospital provides cancer care for?

   <50,000 | 50,000-199,999 | 200,000-499,999 | 500,000-999,999 | 1,000,000-1,999,999 | 2,000,000+

   How certain are you of this figure: Total guess | Uncertain | Reasonably sure | Certain

3. What type of hospital is your centre? *Please select the most appropriate description*
   - Non-referral hospital
     Receive referrals only from community clinics and general practitioners
   - Referral hospital
     Receive referrals from other trained surgeons, as well as from community clinics and general practitioners
   - Specialist cancer hospital
     A hospital which solely treats patients with cancer

Diagnosis

For the following questions please answer for the last six months for patients undergoing surgery for cancer

4. If I want to request an ultrasound for my patient, either free or by payment, it is usually:
   - Not available at all
   - On site and always available
   - On site but not working / available all the time
   - Available at another hospital (patients are transferred)

5. If I want to request a computed tomography scan during standard working hours (0800 to 1700), either free or by payment, it is usually:
    - Not available at all
    - On site and always available
    - On site but not working / available all the time
    - Available at another hospital (patients are transferred)

6. If I want to request pathology services, either free or by payment, for cancer biopsies or resected specimens it is usually: (please s*elect the most commonly encountered situation)*
    - Not available
    - On site and always available
    - On site but only available intermittently
    - Available at another hospital
    - Available in another country

7. Branching logic: If pathology for a cancer specimen is requested on a routine (non-urgent) basis, on average, how long on average does it take for this result to be available (in weeks)?

8. Branching logic: In the last six months, what proportion of patients received a pathology result following their cancer resection (for all cancers treated at your hospital)?
   Slider: 0 – 100
   How certain are you of this figure: Total guess | Uncertain | Reasonably sure | Certain

Patient journey

9. Do you have a Multidisciplinary Team (MDT) meeting to discuss treatment options for patients with breast, gastric and/or colorectal cancer at your site or another hospital?

   Definition of MDT: Meeting of a group of professionals from two or more clinical disciplines who together make decisions regarding cancer treatment or care of individual patients[1]
    - No
    - Yes – only for some cancers at my hospital
    - Yes – for all cancers (breast, colorectal & gastric)

10. Branching logic: For the last 10 patients with breast, gastric and/or colorectal cancer who received elective (non-emergency) surgery, how many were discussed in the multi-disciplinary team (MDT) meeting?
    None | 1-2 | 3-4 | 5-7 | 8-9 | All 10 patients
    These were: Breast cancer only | GI cancer only | Breast and GI cancer (if only some cancers)

11. Branching logic: Please select the appropriate response for each professional
    Not available | Available in hospital but attends <75% MDTs | Available in hospital and attends >75% MDTs
    - Oncologist (including radiotherapy / chemotherapy specialists or both)
    - Radiologist
    - Pathologist
    - Specialist cancer nurse / clinical nurse specialist
    - Palliative care specialist
    - Surgeon

    Oncologist definition: Healthcare professional trained in and provides medical treatment for cancer (radiotherapy, chemotherapy, hormone therapy)[2]

    Specialist cancer nurse definition: A registered nurse with additional education/training, skill and specialisation in cancer care[3,4]

    Palliative care specialist definition: a person who organises care and aims to improve quality of life of patients and their families facing the problem of a life-threatening illness[5]

12. Branching logic (if no MDT is present): Is there an oncologist at your hospital? *(select the most appropriate response for your hospital)*

    Oncologist definition: Healthcare professional (or surgeon) trained in and provides medical treatment for cancer (radiotherapy, chemotherapy, hormone therapy)[1]

- No
- Yes – a clinician who provides cancer care as well as care of non-cancer conditions
- Yes – a clinician who only provides cancer care

13. Branching logic (if no MDT is present): Do you have a trained doctor or healthcare professional in palliative medicine?

    Defined as a Person who organises care and aims to improve quality of life of patients and their families facing the problem of a life-threatening illness.[3] *This includes*

    - No
    - Yes

Oncology treatment

For the following questions please answer for the last six months for cancers surgically treated at your hospital (unless otherwise specified)

14. Is radiotherapy usually available for your patients (either free or by payment)?
    - No
    - Yes - at the same hospital
    - Yes - at another hospital (within 10 km)
    - Yes - at another hospital (10 - 50 km)
    - Yes - at another hospital (> 50 km away)
    - Yes - in another country

Distance measured using road network and shortest distance (not straight line distance)

15. Branching logic: What type of radiotherapy machine is available?
    - Cobalt accelerator
    - Linear accelerator

16. Are chemotherapy drugs usually available for your patients (either free or by payment)?
    - No
    - Yes - at the same hospital
    - Yes - at another hospital (within 10 km)
    - Yes – at another hospital (10 - 50 km)
    - Yes – at another hospital (>50 km away)
    - Yes - in another country

17. Do patients at your hospital make out of pocket (cash) payments for their surgical care (i.e. their surgery, postoperative care, medications, consumables)? (*Please select the most appropriate)*
    - No patients make out of pocket payments
    - Yes - patients who do not have insurance make out of pocket payments for at least some part of their care
    - Yes - those patients that are able to afford to do so are asked to make out of pocket payments for at least some part of their care
    - Yes - all patients make out of pocket payments for at least some part of their care

18. Do you have a designated area for post-operative care at your hospital?

    Post-operative care area: Defined as continuous patient monitoring of vital signs, including the use of a pulse oximeter, immediately after surgery by a designated carer for immediate intervention if required)[6]
    - No
    - Yes - sometimes
    - Yes - all of the time

19. What is the highest level of bed available for patients receiving cancer surgery at your hospital (if required)?
    - Post-operative ward bed only
    - Specialist ward(s) providing intensive treatment and monitoring (HDU / ITU)

20. Do your patients have access to opiate pain medication within the first 24 hours of admission and following surgery?

    Opiate analgesia defined as Pethidine, Fentanyl or Morphine[4]

    - No
    - Yes – but not always available
    - Yes – available all of the time

Surgical management

21. For the following operations for cancer, have you performed any of these in the past three months?

    For each cancer: No | This cancer is referred to another hospital routinely | Yes, as an emergency only | Yes, as a planned elective procedure (with or without emergency procedures)

    - Breast: wide local excision / mastectomy
    - Oesophageal cancer (including oesophogastric junctional tumours): oesophagectomy
    - Lung: lobectomy / pneumonectomy / laryngectomy
    - Stomach (including GISTs): total/partial gastrectomy / gastrojejunostomy
    - Colon (excluding rectum): colonic resection
    - Rectum: anterior resection / abdomino-peroneal excision
    - Liver: hepatectomy
    - Pancreas: pancreatectomy (all types)
    - Kidney: nephrectomy
    - Bladder cancer: cystectomy
    - Prostate: prostatectomy
    - Cervical and uterine cancer: hysterectomy / trachelectomy
    - Ovarian: oophrectomy
    - Thyroid: hemi-thyroidectomy / total thyroidectomy
    - Lip and oral cavity: wide local excision / Mohs micrographic surgery / glossectomy
    - Malignant melanoma: surgical excision

Table 10-23. Proportion of hospitals performing elective operations for each cancer by income group.

Operation	High (n = 91)	Upper middle (n = 57)	Low/lower middle (n = 90)	P
Breast	75 (82.4)	50 (87.7)	84 (93.3)	0.080
Oesophagus	44 (48.4)	34 (59.6)	46 (51.1)	0.397
Lung	42 (46.2)	30 (52.6)	38 (42.2)	0.467
Gastric	76 (83.5)	53 (93.0)	73 (81.1)	0.132
Liver	50 (54.9)	42 (73.7)	35 (38.9)	<0.001
Pancreas	52 (57.1)	44 (77.2)	42 (46.7)	0.001
Renal	72 (79.1)	44 (77.2)	66 (73.3)	0.649
Colorectal	87 (95.6)	56 (98.2)	85 (94.4)	0.531
Rectum	83 (91.2)	53 (93.0)	73 (81.1)	0.045
Cervical	72 (79.1)	44 (77.2)	64 (71.1)	0.433
Ovarian	71 (78.0)	49 (86.0)	65 (72.2)	0.148

Table 10-24. Proportion of hospitals performing elective operations for each cancer stratified by included cancers in GlobalSurg 3.

	All hospitals				LMIC hospitals			
Operation	Breast only (n = 29)	Colorectal and gastric (n = 21)	All cancers (n = 180)	P	Breast only (n = 17)	Colorectal and gastric (n = 8)	All cancers (n = 117)	P
Oesophagus	0 (0.0)	8 (38.1)	115 (63.9)	<0.001	0 (0.0)	2 (25.0)	77 (65.8)	<0.001
Lung	1 (3.4)	6 (28.6)	102 (56.7)	<0.001	0 (0.0)	3 (37.5)	65 (55.6)	<0.001
Liver	1 (3.4)	11 (52.4)	114 (63.3)	<0.001	1 (5.9)	5 (62.5)	70 (59.8)	<0.001
Pancreas	1 (3.4)	12 (57.1)	125 (69.4)	<0.001	1 (5.9)	6 (75.0)	79 (67.5)	<0.001
Renal	14 (48.3)	17 (81.0)	151 (83.9)	<0.001	10 (58.8)	7 (87.5)	93 (79.5)	0.127
Rectum	18 (62.1)	19 (90.5)	170 (94.4)	<0.001	9 (52.9)	7 (87.5)	108 (92.3)	<0.001
Cervical	18 (62.1)	12 (57.1)	149 (82.8)	0.003	13 (76.5)	5 (62.5)	89 (76.1)	0.685
Ovarian	19 (65.5)	12 (57.1)	153 (85.0)	0.001	13 (76.5)	5 (62.5)	95 (81.2)	0.422

Figure 10-4. Relationship between hospital facilities and country income group.

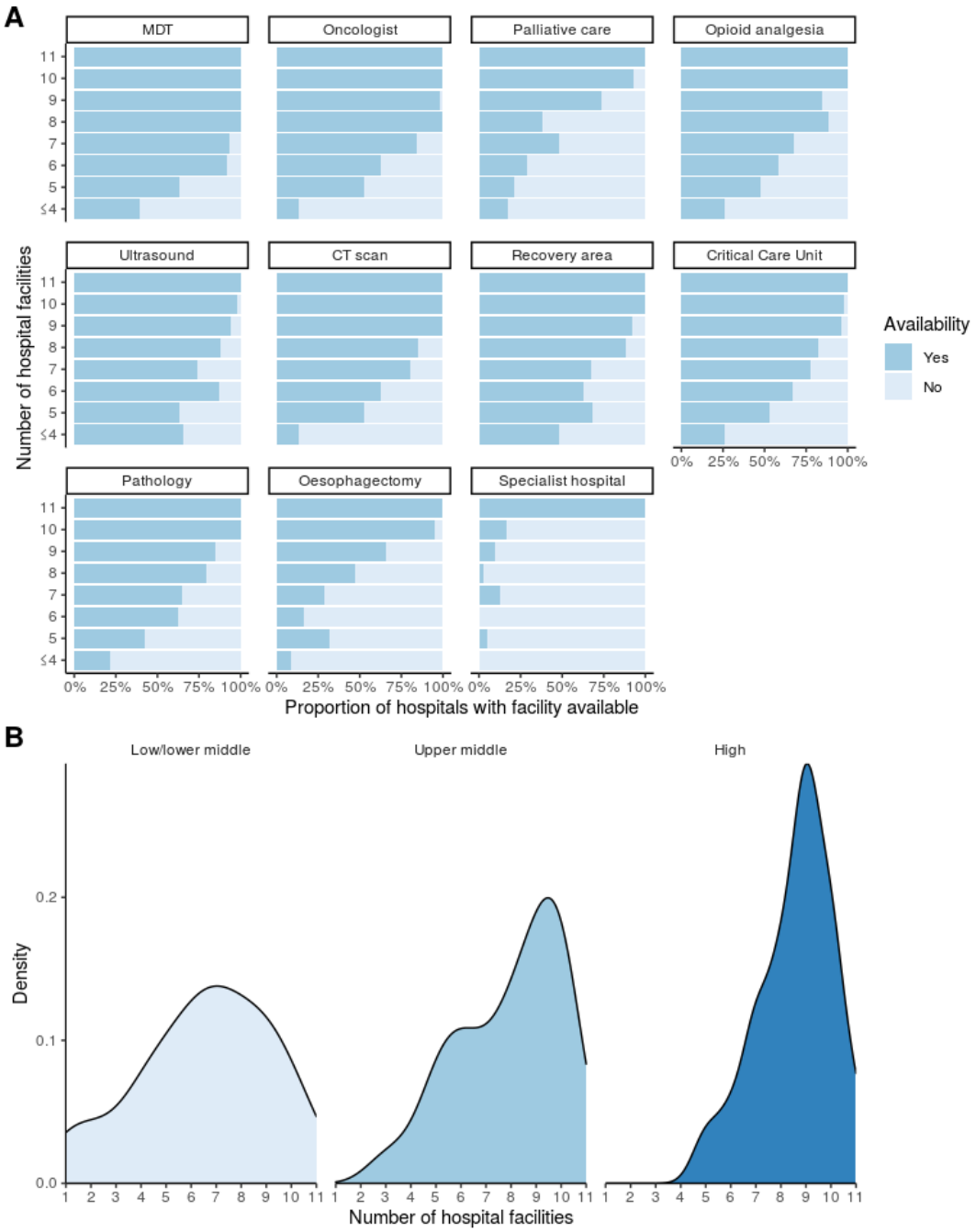


Figure 10-5. Distribution of outcomes across number of available hospital facilities.

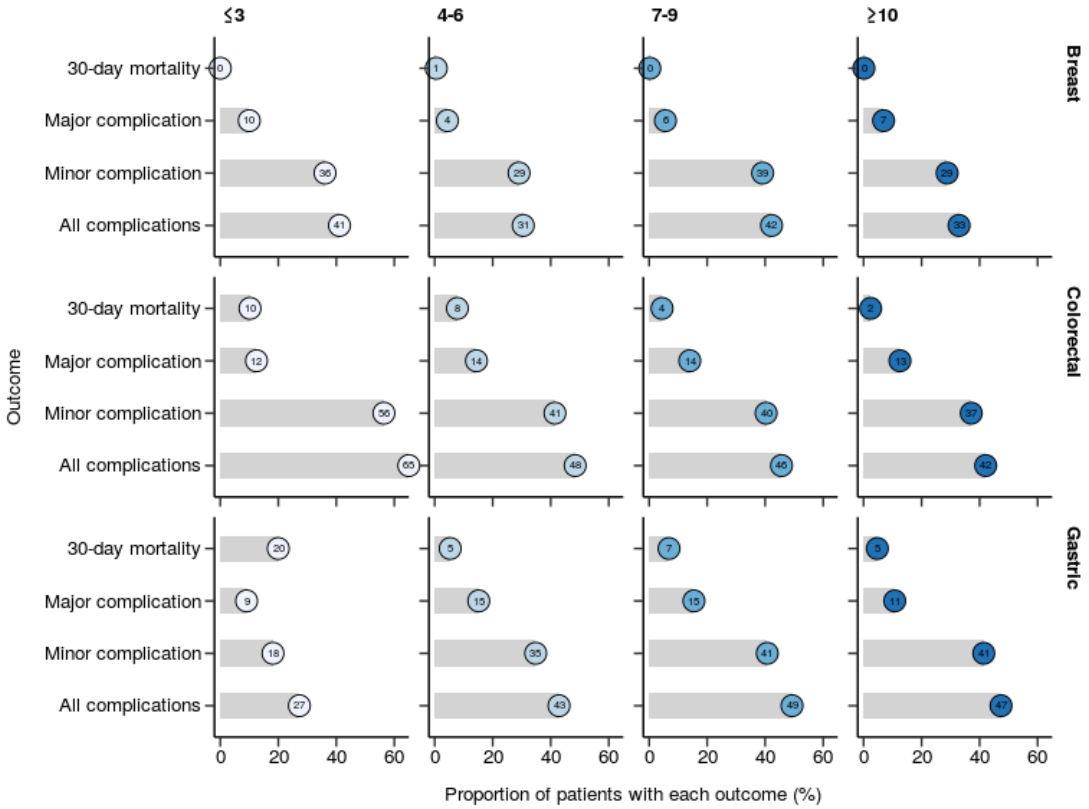


Table 10-25. Case volume stratified by hospital inclusion.

Case volumes were calculated as the median number of patients recruited across each hospital during a 28-day data collection period.

		Hospital-level data available		
Cancer type	WB tertile	Yes	No	P
Breast	High	9.0 (4.0 to 19.8)	10.0 (5.0 to 18.0)	0.655
	Upper middle	5.0 (2.0 to 8.5)	2.0 (1.5 to 5.5)	0.182
	Low/lower middle	3.0 (1.0 to 6.0)	2.0 (2.0 to 3.0)	0.358
Colorectal	High	6.0 (4.0 to 11.0)	8.0 (5.0 to 12.0)	0.095
	Upper middle	4.0 (2.0 to 7.0)	2.0 (1.0 to 3.5)	0.052
	Low/lower middle	2.0 (1.0 to 4.8)	2.0 (1.0 to 4.0)	0.524
Gastric	High	2.0 (1.0 to 3.0)	2.0 (1.0 to 3.0)	0.884
	Upper middle	2.0 (1.0 to 3.0)	1.5 (1.0 to 3.5)	0.755
	Low/lower middle	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)	0.980

Table 10-26. Adjusted mortality rates stratified by hospital inclusion.

Adjusted mortality rates were calculated using generalised estimating equations (GEE) to account for potential confounders (WB tertile, age, gender, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with all confounders as covariates.

WB tertile	Hospital-level data available	Hospital number	Patient number	Adjusted mortality (95% CI)	Odds ratio	P
High	Yes	90	3202	1.4 (1.3 to 1.5)	Ref	
	No	150	5038	1.4 (1.3 to 1.5)	0.98 (0.67 to 1.42)	0.92
Upper middle	Yes	57	2011	2.2 (2 to 2.4)	Ref	
	No	24	563	2.2 (1.8 to 2.6)	0.97 (0.51 to 1.86)	1.00
Low/lower middle	Yes	91	3655	2.5 (2.3 to 2.7)	Ref	
	No	16	186	4.3 (3.3 to 5.4)	1.76 (0.84 to 3.68)	0.15

Table 10-27. Relationship between hospital facility level and postoperative complication rates.

	Hospital facility level		5 (n = 3834)	4 (n = 1192)	≤3 (n = 625)	P
Breast	Surgical site infection	No	387 (10.1)	125 (10.5)	100 (16.0)	<0.001
	Postoperative haemorrhage	Yes	118 (3.1)	40 (3.4)	20 (3.2)	0.864
	Seroma	No	738 (19.2)	231 (19.4)	147 (23.5)	0.030

	Hospital facility count	5 (n = 2544)	4 (n = 821)	≤3 (n = 669)	P
Colorectal and gastric	Surgical site infection	384 (15.1)	115 (14.0)	189 (28.3)	<0.001
	Intra-abdominal abscess	125 (4.9)	44 (5.4)	34 (5.1)	0.835
	Anastomotic leak	125 (4.9)	49 (6.0)	40 (6.0)	0.303
	Postoperative haemorrhage	105 (4.1)	39 (4.8)	28 (4.2)	0.730

Table 10-28. Relationship between hospital facility level and patient safety and quality of cancer care metrics.

Hospital facility level		>3 (n = 8391)	≤3 (n = 1294)	P
Surgical safety checklist used		6872 (83.7)	910 (73.6)	<0.001
Anastomosis performed		2553 (77.5)	467 (72.9)	0.013
Negative margin		7015 (90.8)	948 (87.5)	0.001
Length of stay (days)		3.0 (1.0 to 7.0)	5.0 (3.0 to 9.0)	<0.001
Readmission		397 (4.8)	68 (5.4)	0.404
Method of follow-up at 30 days	Still inpatient or readmitted	250 (3.0)	79 (6.2)	<0.001
	Clinic review	6273 (75.9)	584 (45.6)	
	Telephone review	1414 (17.1)	578 (45.2)	
	Community/home review	27 (0.3)	1 (0.1)	
	Discharged before 30 days and not contacted again	298 (3.6)	38 (3.0)	
Radiotherapy available		6620 (78.9)	588 (45.4)	<0.001
Chemotherapy available		7808 (93.1)	958 (74.0)	<0.001
Multidisciplinary tumour board available for all cancers treated in hospital		6568 (78.3)	405 (31.3)	<0.001

Table 10-29. Adjusted mortality rate for colorectal and gastric cancer across hospital facility level.

Adjusted mortality rates were calculated using generalised estimating equations (GEE) to account for clustering of patients in hospital and for potential confounders (WB tertile, age, gender, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) fitted using the multilevel logistic regression model with the number of hospital facilities and all confounders as covariates.

	Hospital facility level	Patient n (%)	Adjusted mortality (95% CI)
Colorectal	5	1877 (63.3)	3.5 (3.3 to 3.8)
	4	610 (20.6)	3.9 (3.4 to 4.5)
	≤3	478 (16.1)	8.8 (7.6 to 9.9)
Gastric	5	511 (65.7)	4.9 (4.3 to 5.5)
	4	143 (18.4)	4.2 (3.1 to 5.3)
	≤3	124 (15.9)	11.3 (8.8 to 13.8)

Table 10-30. Sensitivity analysis using imputed dataset.

Adjusted mortality rate

Adjusted mortality rates were calculated using generalised estimating equations (GEE) to account for clustering of patients in hospital and for potential confounders (WB tertile, age, gender, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with the number of hospital facilities and all confounders as covariates.

	Hospital facility level	Hospital number	Patient number	Adjusted mortality rate (95% CI)	Odds ratio	P
All cancers	5	215	9617	1.5 (1.4 to 1.6)	Ref	
	4	140	3736	1.9 (1.8 to 2.1)	1.29 (0.97 to 1.72)	0.079
	≤3	72	1302	4.8 (4.2 to 5.3)	3.29 (2.43 to 4.46)	<0.001
Colorectal and gastric cancer	5	205	4407	3.0 (2.9 to 3.2)	Ref	
	4	127	1932	3.5 (3.2 to 3.8)	1.15 (0.86 to 1.56)	0.350
	≤3	66	670	9.1 (8 to 10.1)	3.22 (2.35 to 4.41)	<0.001

Major complication rates

Adjusted major complication rates were calculated using generalised estimating equations (GEE) to account for clustering of patients in hospital and for potential confounders (WB tertile, age, gender, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with the number of hospital facilities and all confounders as covariates.

	Hospital facility level	Hospital number	Patient number	Adjusted major complication rate (95% CI)	Odds ratio	P
All cancers	5	215	9669	9.7 (9.6 to 9.8)	Ref	
	4	140	3742	10.0 (9.8 to 10.3)	1.04 (0.91 to 1.18)	0.560
	≤3	73	1311	11.5 (11.1 to 12.0)	1.21 (1.01 to 1.46)	0.043
Colorectal and gastric cancer	5	205	4434	13.7 (13.5 to 13.9)	Ref	
	4	127	1938	14.9 (14.5 to 15.3)	1.11 (0.95 to 1.29)	0.196
	≤3	67	676	17.8 (17 to 18.6)	1.38 (1.11 to 1.71)	0.005

Table 10-31. Sensitivity analysis for adjusted outcome rates across all eleven hospital facilities.

All eleven hospital facilities were included within a sensitivity analysis, with hospitals categorised into different facility levels by patient distribution. Adjusted mortality rates were calculated using generalised estimating equations (GEE) to account for clustering of patients in hospital and for potential confounders (WB tertile, age, gender, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with the number of hospital facilities and all confounders as covariates.

	Hospital facility level	Hospital number	Patient number	Adjusted mortality (95% CI)	Odds ratio	P
All cancers	10-11	54	4009	0.9 (0.6 to 1.2)	Ref	
	8-9	87	2665	1.2 (0.8 to 1.6)	1.3 (0.8 to 2.1)	0.320
	≤7	96	2194	2.7 (2.1 to 3.4)	3.1 (2.05 to 4.71)	<0.001
Colorectal and gastric cancer	10-11	50	1443	4 (3.7 to 4.3)	Ref	
	8-9	81	1325	4.3 (3.9 to 4.7)	1.07 (0.74 to 1.56)	0.775
	≤7	88	975	6.5 (5.8 to 7.1)	1.65 (1.14 to 2.38)	0.008

Table 10-32. Adjusted major complication rates across hospital facility level.

Adjusted major complication rates were calculated using generalised estimating equations (GEE) to account for clustering of patients in hospital and for potential confounders (WB tertile, age, gender, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with the number of hospital facilities and all confounders as covariates.

	Hospital facility level	Hospital number	Patient number	Adjusted major complication rate (95% CI)	Odds ratio	P
All cancers	10-11	54	4038	8.6 (8.4 to 8.8)	Ref	
	8-9	87	2676	10.3 (10.1 to 10.6)	1.23 (1.04 to 1.45)	0.014
	≤7	97	2201	10.8 (10.4 to 11.1)	1.29 (1.08 to 1.53)	0.005
Colorectal and gastric cancer	10-11	50	1452	13.8 (13.4 to 14.2)	Ref	
	8-9	81	1334	14.6 (14.2 to 15.1)	1.07 (0.87 to 1.33)	0.550
	≤7	89	982	16.4 (15.7 to 17.0)	1.23 (0.98 to 1.54)	0.081

Table 10-33. Capacity to rescue patients following major complication following case-mix adjustment.

Adjusted mortality rates after major complication were calculated using generalised estimating equations (GEE) to account for clustering of patients in hospital and for potential confounders (WB tertile, age, gender, cancer type, ECOG performance status, ASA grade, disease stage, and operative urgency). Confidence intervals (CIs) and a P value for trend were fitted using the multilevel logistic regression model with the number of hospital facilities and all confounders as covariates.

	Hospital facility level	Hospital number	Patient number	Adjusted capacity to rescue (95% CI)	Odds ratio	P
All cancers	10-11	43	366	84.7 (81 to 88.4)	Ref	
	8-9	65	283	72.8 (67.6 to 78)	0.48 (0.33 to 0.71)	<0.001
	≤7	62	227	75.3 (69.7 to 81)	0.55 (0.36 to 0.84)	0.005
Colorectal and gastric cancer	10-11	34	189	71.5 (68.6 to 74.4)	Ref	
	8-9	61	195	71.2 (68.4 to 74)	0.99 (0.64 to 1.55)	1
	≤7	53	165	60.4 (56.6 to 64.2)	0.62 (0.39 to 0.96)	0.033

Table 10-34. Absolute risk for 30-day mortality associated with four or more hospital facilities within each income group stratified by cancer type and gender. Estimates for age 60 years, ECOG performance status 1, ASA grade II, cancer stage III, and elective surgery.

Hospital facility level	WB income (tertile)	Cancer type	Sex	Predicted probability of death	Absolute risk difference
>3	Low/lower middle	Colorectal	Male	0.036 (0.020 to 0.055)	-
≤3	Low/lower middle	Colorectal	Male	0.060 (0.034 to 0.095)	0.024 (0.005 to 0.051, P=0.011)
>3	Upper middle	Colorectal	Male	0.018 (0.009 to 0.029)	-
≤3	Upper middle	Colorectal	Male	0.031 (0.015 to 0.053)	0.012 (0.002 to 0.029, P=0.009)
>3	High	Colorectal	Male	0.009 (0.004 to 0.015)	-
≤3	High	Colorectal	Male	0.015 (0.007 to 0.028)	0.006 (0.001 to 0.015, P=0.010)
>3	Low/lower middle	Colorectal	Female	0.028 (0.016 to 0.044)	-
≤3	Low/lower middle	Colorectal	Female	0.048 (0.025 to 0.076)	0.019 (0.004 to 0.040, P=0.010)
>3	Upper middle	Colorectal	Female	0.014 (0.007 to 0.023)	-
≤3	Upper middle	Colorectal	Female	0.024 (0.011 to 0.042)	0.010 (0.002 to 0.023, P=0.011)
>3	High	Colorectal	Female	0.007 (0.003 to 0.012)	-
≤3	High	Colorectal	Female	0.012 (0.005 to 0.022)	0.005 (0.001 to 0.012, P=0.013)
>3	Low/lower middle	Gastric	Male	0.044 (0.024 to 0.070)	-
≤3	Low/lower middle	Gastric	Male	0.074 (0.041 to 0.117)	0.028 (0.006 to 0.060, P=0.009)
>3	Upper middle	Gastric	Male	0.022 (0.011 to 0.038)	-
≤3	Upper middle	Gastric	Male	0.038 (0.018 to 0.069)	0.015 (0.003 to 0.036, P=0.016)
>3	High	Gastric	Male	0.011 (0.005 to 0.020)	-
≤3	High	Gastric	Male	0.019 (0.008 to 0.037)	0.007 (0.001 to 0.020, P=0.014)
>3	Low/lower middle	Gastric	Female	0.035 (0.018 to 0.057)	-
≤3	Low/lower middle	Gastric	Female	0.059 (0.030 to 0.093)	0.023 (0.005 to 0.048, P=0.008)
>3	Upper middle	Gastric	Female	0.017 (0.008 to 0.030)	-
≤3	Upper middle	Gastric	Female	0.030 (0.014 to 0.053)	0.011 (0.002 to 0.028, P=0.015)
>3	High	Gastric	Female	0.009 (0.004 to 0.016)	-
≤3	High	Gastric	Female	0.015 (0.006 to 0.029)	0.006 (0.001 to 0.016, P=0.014)

Figure 10-6. Absolute risk for 30-day mortality in hospitals with more than three facilities within each income group stratified by cancer type and gender.

Estimates for age 60 years, performance status 1, ASA grade 2, cancer stage III, and elective surgery.

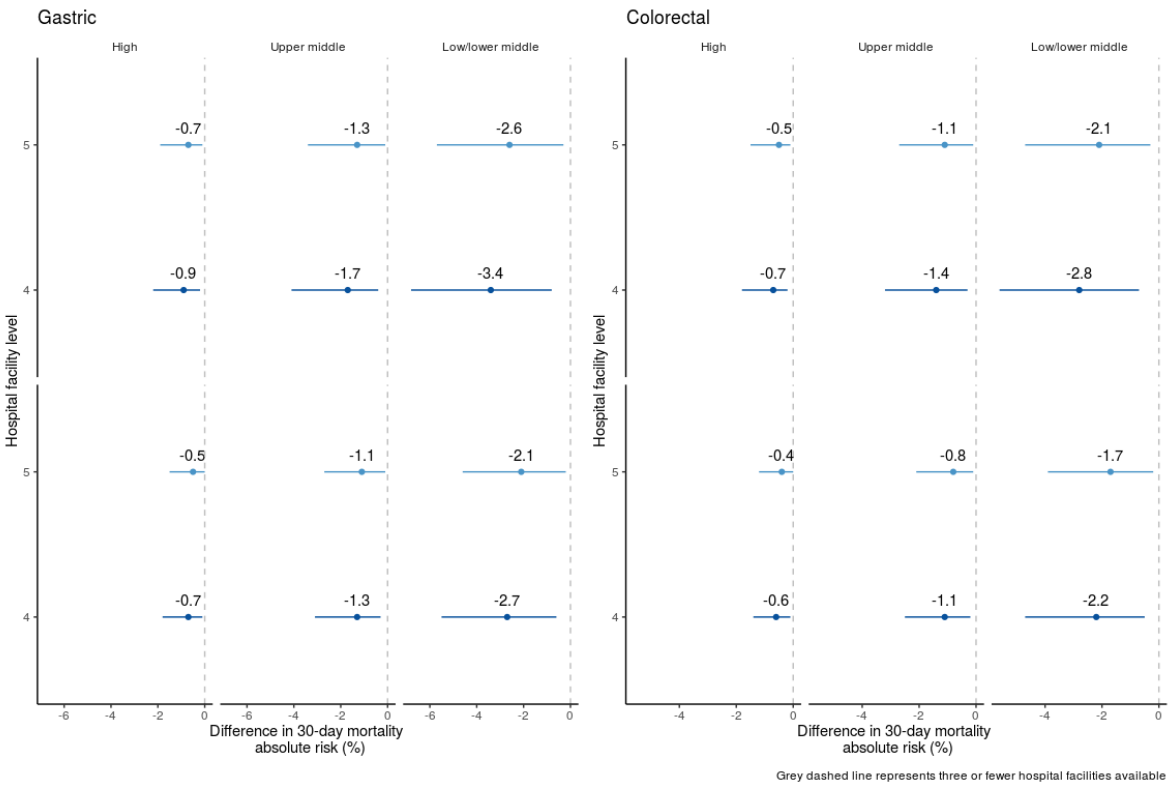


Table 10-35. **Absolute risk for 30-day mortality in hospitals with more than three facilities within each income group stratified by cancer type and gender.**

Estimates for age 60 years, performance status 1, ASA grade 2, cancer stage III, and elective surgery.

Hospital facility level	WB income (tertile)	Cancer type	Sex	Predicted probability of death	Absolute risk difference
5	Low/lower middle	Colorectal	Male	0.037 (0.021 to 0.058)	-
4	Low/lower middle	Colorectal	Male	0.030 (0.015 to 0.052)	-0.007 (-0.022 to 0.009, P=0.368)
≤3	Low/lower middle	Colorectal	Male	0.060 (0.033 to 0.095)	0.022 (0.003 to 0.049, P=0.025)
5	Upper middle	Colorectal	Male	0.019 (0.010 to 0.030)	-
4	Upper middle	Colorectal	Male	0.015 (0.007 to 0.028)	-0.003 (-0.011 to 0.004, P=0.378)
≤3	Upper middle	Colorectal	Male	0.030 (0.014 to 0.052)	0.011 (0.001 to 0.027, P=0.030)
5	High	Colorectal	Male	0.009 (0.005 to 0.016)	-
4	High	Colorectal	Male	0.008 (0.003 to 0.014)	-0.002 (-0.006 to 0.002, P=0.375)
≤3	High	Colorectal	Male	0.015 (0.007 to 0.029)	0.005 (0.001 to 0.016, P=0.023)
5	Low/lower middle	Colorectal	Female	0.029 (0.016 to 0.046)	-
4	Low/lower middle	Colorectal	Female	0.024 (0.011 to 0.041)	-0.005 (-0.018 to 0.007, P=0.368)
≤3	Low/lower middle	Colorectal	Female	0.047 (0.025 to 0.076)	0.017 (0.002 to 0.039, P=0.024)
5	Upper middle	Colorectal	Female	0.015 (0.007 to 0.024)	-
4	Upper middle	Colorectal	Female	0.012 (0.005 to 0.021)	-0.003 (-0.009 to 0.003, P=0.348)
≤3	Upper middle	Colorectal	Female	0.024 (0.011 to 0.041)	0.008 (0.001 to 0.022, P=0.031)
5	High	Colorectal	Female	0.007 (0.004 to 0.012)	-
4	High	Colorectal	Female	0.006 (0.002 to 0.011)	-0.001 (-0.005 to 0.002, P=0.362)
≤3	High	Colorectal	Female	0.012 (0.005 to 0.023)	0.004 (0.000 to 0.012, P=0.029)
5	Low/lower middle	Gastric	Male	0.046 (0.025 to 0.073)	-
4	Low/lower middle	Gastric	Male	0.038 (0.017 to 0.067)	-0.008 (-0.027 to 0.011, P=0.361)
≤3	Low/lower middle	Gastric	Male	0.073 (0.039 to 0.116)	0.026 (0.003 to 0.057, P=0.025)
5	Upper middle	Gastric	Male	0.023 (0.011 to 0.040)	-

4	Upper middle	Gastric	Male	0.019 (0.007 to 0.037)	-0.004 (-0.014 to 0.006, P=0.377)
≤3	Upper middle	Gastric	Male	0.037 (0.017 to 0.066)	0.013 (0.001 to 0.034, P=0.030)
5	High	Gastric	Male	0.012 (0.005 to 0.021)	-
4	High	Gastric	Male	0.009 (0.004 to 0.019)	-0.002 (-0.008 to 0.003, P=0.364)
≤3	High	Gastric	Male	0.019 (0.008 to 0.036)	0.007 (0.000 to 0.019, P=0.033)
5	Low/lower middle	Gastric	Female	0.036 (0.019 to 0.059)	-
4	Low/lower middle	Gastric	Female	0.030 (0.013 to 0.054)	-0.006 (-0.022 to 0.009, P=0.393)
≤3	Low/lower middle	Gastric	Female	0.058 (0.031 to 0.096)	0.021 (0.002 to 0.047, P=0.028)
5	Upper middle	Gastric	Female	0.018 (0.009 to 0.031)	-
4	Upper middle	Gastric	Female	0.015 (0.006 to 0.028)	-0.003 (-0.011 to 0.005, P=0.370)
≤3	Upper middle	Gastric	Female	0.029 (0.013 to 0.053)	0.010 (0.001 to 0.027, P=0.026)
5	High	Gastric	Female	0.009 (0.004 to 0.016)	-
4	High	Gastric	Female	0.007 (0.003 to 0.015)	-0.001 (-0.006 to 0.002, P=0.377)
≤3	High	Gastric	Female	0.015 (0.006 to 0.030)	0.005 (0.000 to 0.016, P=0.029)

Figure 10-7. Absolute risk for 30-day mortality associated with four or more hospital facilities within each income group stratified by cancer type and gender for higher risk surgical patients.

Estimates for age 70 years, performance status 3 or 4, ASA grade ≥3, cancer stage III, and elective surgery.

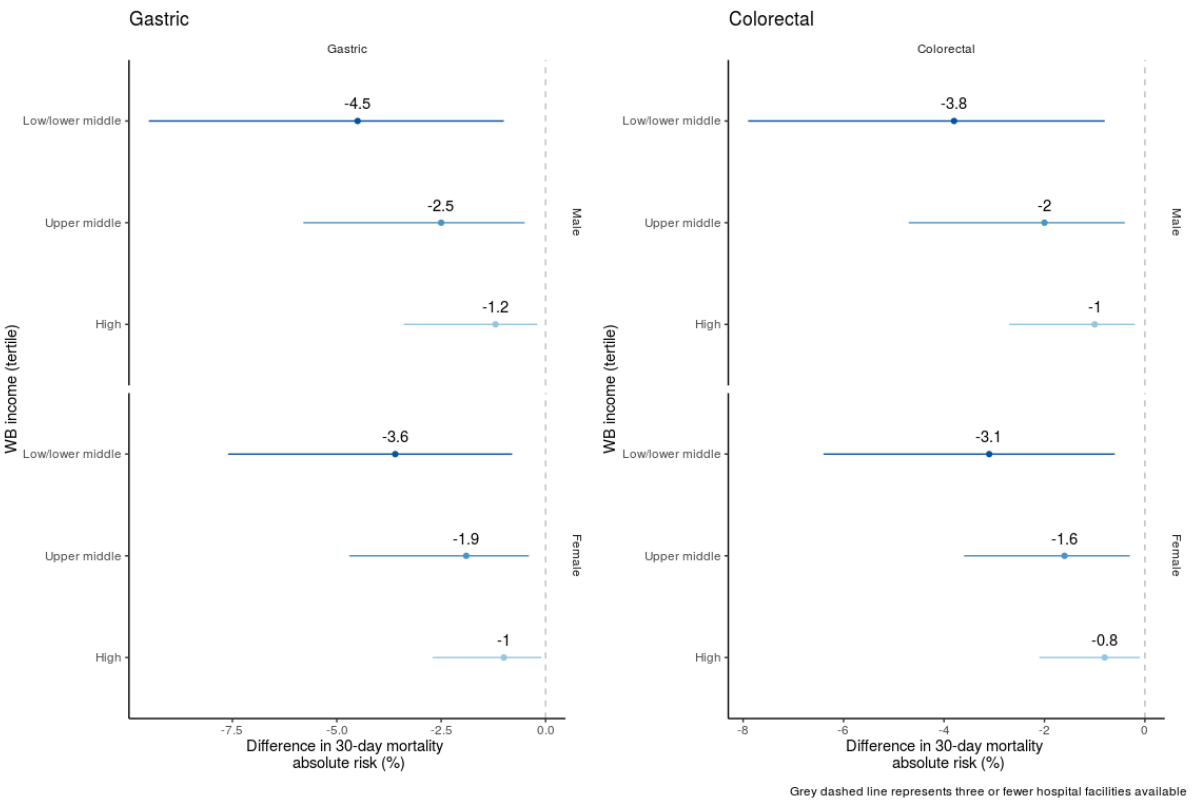


Table 10-36. Absolute risk for 30-day mortality associated with four or more hospital facilities within each income group stratified by cancer type and gender for higher risk surgical patients undergoing elective surgery.

Estimates for age 70 years, performance status 3/4, ASA grade ≥3, and cancer stage III.

Hospital facility level	WB income (tertile)	Cancer type	Sex	ASA (≥3)	Predicted probability of death	Absolute risk difference
>3	Low/lower middle	Colorectal	Male	Yes	0.323 (0.183 to 0.485)	-
≤3	Low/lower middle	Colorectal	Male	Yes	0.418 (0.251 to 0.594)	0.093 (-0.005 to 0.185, P=0.061)
>3	Upper middle	Colorectal	Male	Yes	0.201 (0.107 to 0.329)	-
≤3	Upper middle	Colorectal	Male	Yes	0.275 (0.147 to 0.430)	0.069 (-0.002 to 0.151, P=0.058)
>3	High	Colorectal	Male	Yes	0.109 (0.054 to 0.183)	-
≤3	High	Colorectal	Male	Yes	0.156 (0.072 to 0.277)	0.044 (-0.001 to 0.113, P=0.058)
>3	Low/lower middle	Colorectal	Female	Yes	0.271 (0.147 to 0.423)	-
≤3	Low/lower middle	Colorectal	Female	Yes	0.359 (0.205 to 0.534)	0.084 (0.000 to 0.171, P=0.050)
>3	Upper middle	Colorectal	Female	Yes	0.164 (0.085 to 0.272)	-
≤3	Upper middle	Colorectal	Female	Yes	0.228 (0.116 to 0.371)	0.061 (-0.003 to 0.141, P=0.061)
>3	High	Colorectal	Female	Yes	0.087 (0.043 to 0.153)	-
≤3	High	Colorectal	Female	Yes	0.126 (0.057 to 0.232)	0.037 (-0.000 to 0.097, P=0.054)
>3	Low/lower middle	Gastric	Male	Yes	0.379 (0.218 to 0.551)	-
≤3	Low/lower middle	Gastric	Male	Yes	0.478 (0.294 to 0.650)	0.096 (-0.000 to 0.192, P=0.050)
>3	Upper middle	Gastric	Male	Yes	0.243 (0.125 to 0.406)	-
≤3	Upper middle	Gastric	Male	Yes	0.326 (0.174 to 0.516)	0.080 (-0.001 to 0.171, P=0.053)
>3	High	Gastric	Male	Yes	0.135 (0.064 to 0.237)	-
≤3	High	Gastric	Male	Yes	0.191 (0.086 to 0.343)	0.054 (0.000 to 0.134, P=0.048)
>3	Low/lower middle	Gastric	Female	Yes	0.322 (0.176 to 0.494)	-
≤3	Low/lower middle	Gastric	Female	Yes	0.417 (0.245 to 0.594)	0.093 (-0.003 to 0.188, P=0.054)
>3	Upper middle	Gastric	Female	Yes	0.201 (0.101 to 0.335)	-
≤3	Upper middle	Gastric	Female	Yes	0.274 (0.139 to 0.438)	0.071 (-0.001 to 0.155, P=0.052)
>3	High	Gastric	Female	Yes	0.109 (0.050 to 0.204)	-
≤3	High	Gastric	Female	Yes	0.155 (0.068 to 0.298)	0.043 (-0.001 to 0.119, P=0.054)

10.5 Supplementary material for Chapter 7

Table 10-37. Summary of missing data for 30-day mortality.

		Available	Missing
Nutritional Status	No/Moderate Malnutrition	3786 (99.4)	24 (0.6)
	Severe Malnutrition	1874 (98.7)	25 (1.3)
WB income level (tertile)	High	3590 (99.4)	22 (0.6)
	Upper middle	1121 (98.8)	14 (1.2)
	Low/lower middle	949 (98.6)	13 (1.4)
Cancer Type	Colorectal (colon or rectum)	4559 (99.3)	34 (0.7)
	Gastric (stomach)	1101 (98.7)	15 (1.3)
ASA (>3)	No	5450 (99.2)	46 (0.8)
	Yes	210 (98.6)	3 (1.4)
ECOG performance status	0	2898 (99.4)	18 (0.6)
	1	1685 (99.1)	16 (0.9)
	2	690 (99.0)	7 (1.0)
	3/4	280 (97.9)	6 (2.1)
Age (years)	Mean (SD)	64.7 (13.5)	65.8 (12.1)
Sex	Female	2414 (99.3)	18 (0.7)
	Male	3242 (99.1)	31 (0.9)
Stage	I	1754 (99.5)	9 (0.5)
	II	1206 (99.5)	6 (0.5)
	III	2071 (99.1)	19 (0.9)
	IV	590 (97.7)	14 (2.3)
Treatment intent	Palliative	449 (96.4)	17 (3.6)
	Curative	5211 (99.4)	32 (0.6)
Approach	Open	3063 (98.7)	40 (1.3)
	Minimally invasive	2577 (99.7)	8 (0.3)

Table 10-38. Summary of missing data for 30-day major complication.

		Not missing	Missing
Nutritional Status	No/Moderate Malnutrition	3808 (99.9)	2 (0.1)
	Severe Malnutrition	1897 (99.9)	2 (0.1)
WB income level (tertile)	High	3611 (100.0)	1 (0.0)
	Upper middle	1134 (99.9)	1 (0.1)
	Low/lower middle	960 (99.8)	2 (0.2)
Cancer Type	Colorectal (colon or rectum)	4591 (100.0)	2 (0.0)
	Gastric (stomach)	1114 (99.8)	2 (0.2)
ASA (>3)	No	5492 (99.9)	4 (0.1)
	Yes	213 (100.0)	0 (0.0)
ECOG performance status	0	2914 (99.9)	2 (0.1)
	1	1699 (99.9)	2 (0.1)
	2	697 (100.0)	0 (0.0)
	3/4	286 (100.0)	0 (0.0)
Age (years)	Mean (SD)	64.7 (13.5)	68.8 (17.4)
Sex	Female	2432 (100.0)	0 (0.0)
	Male	3269 (99.9)	4 (0.1)
Stage	I	1763 (100.0)	0 (0.0)
	II	1212 (100.0)	0 (0.0)
	III	2086 (99.8)	4 (0.2)
	IV	604 (100.0)	0 (0.0)
Treatment intent	Palliative	465 (99.8)	1 (0.2)
	Curative	5240 (99.9)	3 (0.1)
Approach	Open	3100 (99.9)	3 (0.1)
	Minimally invasive	2585 (100.0)	1 (0.0)

Table 10-39. Missing data for nutritional status stratified by World Bank tertile.

		High	Upper middle	Low/lower middle	Total
Nutritional Status	No/Moderate Malnutrition	2818 (65.2)	631 (51.5)	361 (33.6)	3810 (57.5)
	Severe Malnutrition	794 (18.4)	504 (41.1)	601 (56.0)	1899 (28.7)
	(Missing)	713 (16.5)	90 (7.3)	111 (10.3)	914 (13.8)

Table 10-40. Distribution of individual major complications by nutritional state.

Major complication defined as Clavien-Dindo grade 3 or 4.

Complication	No/Moderate Malnutrition	Severe Malnutrition	Total
Readmission	292 (7.7)	155 (8.2)	447 (7.8)
Surgical Site Infection (SSI)	488 (12.8)	362 (19.1)	850 (14.9)
Postoperative Bleeding	198 (5.2)	111 (5.8)	309 (5.4)
Anastomotic Leak	200 (5.2)	119 (6.3)	319 (5.6)
Abscess	204 (5.4)	105 (5.5)	309 (5.4)

Table 10-41. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for 30-day mortality.

Dependent: 30-day mortality		Alive	Dead	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	2766 (98.6)	38 (1.4)	-	-	-
	Upper middle No/moderate malnutrition	616 (98.7)	8 (1.3)	0.95 (0.41-1.93, P=0.886)	1.22 (0.52-2.52, P=0.624)	1.41 (0.57-3.47, P=0.460)
	Low/lower middle No/moderate malnutrition	348 (97.2)	10 (2.8)	2.09 (0.98-4.07, P=0.040)	3.83 (1.67-7.94, P=0.001)	4.47 (1.81-11.03, P=0.001)
	High Severe malnutrition	761 (96.8)	25 (3.2)	2.39 (1.42-3.96, P=0.001)	1.93 (1.13-3.24, P=0.014)	1.96 (1.14-3.37, P=0.015)
	Upper middle Severe malnutrition	478 (96.2)	19 (3.8)	2.89 (1.62-5.00, P<0.001)	3.30 (1.80-5.87, P<0.001)	3.05 (1.45-6.42, P=0.003)
	Low/lower middle Severe malnutrition	546 (92.4)	45 (7.6)	6.00 (3.86-9.37, P<0.001)	12.04 (7.23-20.19, P<0.001)	11.57 (5.87-22.80, P<0.001)
Cancer Type	Colorectal (colon or rectum)	4460 (97.8)	99 (2.2)	-	-	-
	Gastric (stomach)	1055 (95.8)	46 (4.2)	1.96 (1.36-2.79, P<0.001)	1.49 (1.01-2.17, P=0.039)	1.53 (1.01-2.30, P=0.043)
Age (years)	Mean (SD)	64.6 (13.5)	70.4 (13.2)	1.04 (1.02-1.05, P<0.001)	1.07 (1.05-1.09, P<0.001)	1.07 (1.05-1.08, P<0.001)
Sex	Male	2367 (98.1)	47 (1.9)	-	-	-
	Female	3144 (97.0)	98 (3.0)	1.57 (1.11-2.25, P=0.012)	1.54 (1.08-2.23, P=0.020)	1.59 (1.09-2.32, P=0.016)
Stage	I	1720 (98.1)	34 (1.9)	-	-	-
	II	1180 (97.8)	26 (2.2)	1.11 (0.66-1.86, P=0.680)	0.90 (0.52-1.52, P=0.693)	0.97 (0.56-1.69, P=0.924)
	III	2025 (97.8)	46 (2.2)	1.15 (0.74-1.81, P=0.543)	0.91 (0.57-1.46, P=0.687)	1.01 (0.62-1.64, P=0.975)
	IV	552 (93.6)	38 (6.4)	3.48 (2.17-5.61, P<0.001)	2.73 (1.65-4.53, P<0.001)	3.07 (1.80-5.24, P<0.001)

Table 10-42. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for 30-day major complication.

Dependent: Major complications		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	2461 (87.3)	357 (12.7)	-	-	-
	Upper middle No/moderate malnutrition	588 (93.2)	43 (6.8)	0.50 (0.36-0.69, P<0.001)	0.53 (0.37-0.73, P<0.001)	0.54 (0.35-0.84, P=0.006)
	Low/lower middle No/moderate malnutrition	304 (84.2)	57 (15.8)	1.29 (0.95-1.74, P=0.098)	1.49 (1.07-2.04, P=0.016)	1.42 (0.92-2.20, P=0.114)
	High Severe malnutrition	675 (85.0)	119 (15.0)	1.22 (0.97-1.52, P=0.088)	1.15 (0.91-1.44, P=0.230)	1.17 (0.92-1.47, P=0.199)
	Upper middle Severe malnutrition	448 (88.9)	56 (11.1)	0.86 (0.63-1.15, P=0.329)	0.88 (0.64-1.19, P=0.431)	0.83 (0.55-1.25, P=0.382)
	Low/lower middle Severe malnutrition	497 (82.7)	104 (17.3)	1.44 (1.13-1.83, P=0.003)	1.75 (1.35-2.27, P<0.001)	1.51 (1.02-2.25, P=0.041)
Cancer Type	Colorectal (colon or rectum)	3999 (87.1)	594 (12.9)	-	-	-
	Gastric (stomach)	974 (87.3)	142 (12.7)	0.98 (0.80-1.19, P=0.852)	0.94 (0.77-1.15, P=0.576)	0.96 (0.77-1.18, P=0.684)
Age (years)	Mean (SD)	64.5 (13.6)	66.6 (12.8)	1.01 (1.01-1.02, P<0.001)	1.02 (1.01-1.02, P<0.001)	1.02 (1.01-1.02, P<0.001)
Sex	Male	2161 (88.9)	271 (11.1)	-	-	-
	Female	2808 (85.8)	465 (14.2)	1.32 (1.13-1.55, P=0.001)	1.31 (1.12-1.55, P=0.001)	1.33 (1.13-1.57, P=0.001)
Stage	I	1569 (89.0)	194 (11.0)	-	-	-
	II	1050 (86.6)	162 (13.4)	1.25 (1.00-1.56, P=0.051)	1.24 (0.99-1.56, P=0.063)	1.28 (1.02-1.62, P=0.034)
	III	1813 (86.7)	277 (13.3)	1.24 (1.02-1.50, P=0.034)	1.24 (1.01-1.51, P=0.038)	1.29 (1.05-1.58, P=0.016)
	IV	503 (83.3)	101 (16.7)	1.62 (1.25-2.10, P<0.001)	1.64 (1.25-2.14, P<0.001)	1.70 (1.29-2.24, P<0.001)

Table 10-43. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for 30-day major complication in patients with colorectal cancer.

Dependent: Major complications		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	2130 (87.5)	303 (12.5)	-	-	-
	Upper middle No/moderate malnutrition	487 (92.9)	37 (7.1)	0.53 (0.37-0.75, P=0.001)	0.55 (0.38-0.78, P=0.001)	0.56 (0.35-0.90, P=0.018)
	Low/lower middle No/moderate malnutrition	231 (82.5)	49 (17.5)	1.49 (1.06-2.06, P=0.018)	1.70 (1.18-2.39, P=0.003)	1.53 (0.93-2.50, P=0.092)
	High Severe malnutrition	499 (84.7)	90 (15.3)	1.27 (0.98-1.63, P=0.068)	1.20 (0.92-1.55, P=0.163)	1.21 (0.93-1.57, P=0.153)
	Upper middle Severe malnutrition	308 (87.7)	43 (12.3)	0.98 (0.69-1.37, P=0.914)	0.99 (0.69-1.39, P=0.961)	0.92 (0.58-1.46, P=0.720)
	Low/lower middle Severe malnutrition	344 (82.7)	72 (17.3)	1.47 (1.10-1.94, P=0.007)	1.77 (1.30-2.39, P<0.001)	1.46 (0.92-2.31, P=0.110)
Age (years)	Mean (SD)	64.9 (13.5)	66.5 (13.1)	1.01 (1.00-1.02, P=0.009)	1.01 (1.01-1.02, P<0.001)	1.01 (1.01-1.02, P<0.001)
Sex	Male	1765 (88.8)	222 (11.2)	-	-	-
	Female	2230 (85.7)	372 (14.3)	1.33 (1.11-1.59, P=0.002)	1.32 (1.11-1.58, P=0.002)	1.34 (1.12-1.60, P=0.002)
Stage	I	1230 (88.8)	155 (11.2)	-	-	-
	II	880 (86.3)	140 (13.7)	1.26 (0.99-1.61, P=0.062)	1.26 (0.98-1.62, P=0.067)	1.29 (1.00-1.66, P=0.049)
	III	1441 (86.9)	217 (13.1)	1.20 (0.96-1.49, P=0.112)	1.19 (0.95-1.49, P=0.130)	1.23 (0.98-1.55, P=0.079)
	IV	419 (83.8)	81 (16.2)	1.53 (1.14-2.05, P=0.004)	1.56 (1.15-2.10, P=0.004)	1.57 (1.16-2.13, P=0.003)

Table 10-44. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for 30-day major complication in patients with gastric cancer.

Dependent: Major complications		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	331 (86.0)	54 (14.0)	-	-	-
	Upper middle No/moderate malnutrition	101 (94.4)	6 (5.6)	0.36 (0.14-0.81, P=0.023)	0.39 (0.14-0.87, P=0.036)	0.36 (0.13-0.99, P=0.048)
	Low/lower middle No/moderate malnutrition	73 (90.1)	8 (9.9)	0.67 (0.29-1.40, P=0.320)	0.74 (0.29-1.66, P=0.492)	0.73 (0.28-1.95, P=0.533)
	High Severe malnutrition	176 (85.9)	29 (14.1)	1.01 (0.61-1.63, P=0.968)	0.89 (0.53-1.46, P=0.639)	0.86 (0.51-1.47, P=0.591)
	Upper middle Severe malnutrition	140 (91.5)	13 (8.5)	0.57 (0.29-1.05, P=0.083)	0.56 (0.28-1.05, P=0.085)	0.47 (0.21-1.04, P=0.064)
	Low/lower middle Severe malnutrition	153 (82.7)	32 (17.3)	1.28 (0.79-2.06, P=0.308)	1.52 (0.88-2.61, P=0.134)	1.40 (0.71-2.77, P=0.331)
Age (years)	Mean (SD)	62.5 (13.8)	67.3 (11.6)	1.03 (1.01-1.04, P<0.001)	1.03 (1.02-1.05, P<0.001)	1.03 (1.01-1.05, P<0.001)
Sex	Male	396 (89.0)	49 (11.0)	-	-	-
	Female	578 (86.1)	93 (13.9)	1.30 (0.90-1.89, P=0.163)	1.29 (0.89-1.89, P=0.189)	1.35 (0.90-2.01, P=0.148)
Stage	I	339 (89.7)	39 (10.3)	-	-	-
	II	170 (88.5)	22 (11.5)	1.12 (0.64-1.94, P=0.677)	1.19 (0.66-2.09, P=0.558)	1.30 (0.70-2.40, P=0.402)
	III	372 (86.1)	60 (13.9)	1.40 (0.92-2.17, P=0.123)	1.46 (0.93-2.31, P=0.103)	1.62 (0.99-2.64, P=0.053)
	IV	84 (80.8)	20 (19.2)	2.07 (1.13-3.70, P=0.016)	2.14 (1.11-4.02, P=0.020)	2.42 (1.21-4.83, P=0.012)

Table 10-45. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for all complications.

Dependent: All complications		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	1550 (55.0)	1267 (45.0)	-	-	-
	Upper middle No/moderate malnutrition	400 (63.4)	231 (36.6)	0.71 (0.59-0.84, P<0.001)	0.74 (0.62-0.89, P=0.001)	0.89 (0.57-1.40, P=0.623)
	Low/lower middle No/moderate malnutrition	184 (51.1)	176 (48.9)	1.17 (0.94-1.46, P=0.161)	1.28 (1.02-1.62, P=0.033)	1.23 (0.77-1.95, P=0.388)
	High Severe malnutrition	434 (54.7)	360 (45.3)	1.01 (0.87-1.19, P=0.856)	1.00 (0.85-1.18, P=0.963)	1.05 (0.88-1.25, P=0.610)
	Upper middle Severe malnutrition	270 (53.7)	233 (46.3)	1.06 (0.87-1.28, P=0.577)	1.08 (0.89-1.32, P=0.433)	1.38 (0.88-2.15, P=0.157)
	Low/lower middle Severe malnutrition	269 (44.8)	331 (55.2)	1.51 (1.26-1.80, P<0.001)	1.71 (1.41-2.07, P<0.001)	1.42 (0.91-2.20, P=0.122)
Cancer Type	Colorectal (colon or rectum)	2497 (54.4)	2094 (45.6)	-	-	-
	Gastric (stomach)	610 (54.8)	504 (45.2)	0.99 (0.86-1.12, P=0.825)	0.94 (0.82-1.08, P=0.380)	0.93 (0.79-1.09, P=0.363)
Age (years)	Mean (SD)	64.3 (13.4)	65.3 (13.6)	1.01 (1.00-1.01, P=0.003)	1.01 (1.01-1.01, P<0.001)	1.01 (1.01-1.02, P<0.001)
Sex	Male	1380 (56.7)	1052 (43.3)	-	-	-
	Female	1724 (52.7)	1545 (47.3)	1.18 (1.06-1.31, P=0.003)	1.17 (1.06-1.31, P=0.003)	1.19 (1.06-1.34, P=0.003)
Stage	I	988 (56.0)	775 (44.0)	-	-	-
	II	668 (55.1)	544 (44.9)	1.04 (0.90-1.20, P=0.618)	1.02 (0.88-1.19, P=0.788)	1.17 (0.99-1.38, P=0.071)
	III	1122 (53.8)	964 (46.2)	1.10 (0.96-1.24, P=0.162)	1.07 (0.94-1.22, P=0.297)	1.13 (0.98-1.32, P=0.094)
	IV	309 (51.2)	295 (48.8)	1.22 (1.01-1.46, P=0.038)	1.19 (0.98-1.44, P=0.072)	1.31 (1.06-1.62, P=0.013)

Table 10-46. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for all complications in patients with colorectal cancer.

Dependent: All complications		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	1341 (55.1)	1092 (44.9)	-	-	-
	Upper middle No/moderate malnutrition	341 (65.1)	183 (34.9)	0.66 (0.54-0.80, P<0.001)	0.69 (0.56-0.84, P<0.001)	0.83 (0.52-1.33, P=0.444)
	Low/lower middle No/moderate malnutrition	137 (49.1)	142 (50.9)	1.27 (0.99-1.63, P=0.057)	1.39 (1.07-1.80, P=0.013)	1.41 (0.85-2.35, P=0.184)
	High Severe malnutrition	310 (52.6)	279 (47.4)	1.11 (0.92-1.32, P=0.277)	1.08 (0.90-1.30, P=0.390)	1.11 (0.90-1.35, P=0.330)
	Upper middle Severe malnutrition	197 (56.1)	154 (43.9)	0.96 (0.77-1.20, P=0.723)	0.97 (0.77-1.22, P=0.805)	1.22 (0.76-1.97, P=0.402)
	Low/lower middle Severe malnutrition	171 (41.2)	244 (58.8)	1.75 (1.42-2.17, P<0.001)	2.01 (1.61-2.53, P<0.001)	1.80 (1.11-2.93, P=0.017)
Age (years)	Mean (SD)	64.7 (13.3)	65.6 (13.6)	1.00 (1.00-1.01, P=0.027)	1.01 (1.00-1.01, P<0.001)	1.01 (1.01-1.02, P<0.001)
Sex	Male	1127 (56.7)	860 (43.3)	-	-	-
	Female	1367 (52.6)	1233 (47.4)	1.18 (1.05-1.33, P=0.005)	1.19 (1.05-1.34, P=0.005)	1.23 (1.08-1.41, P=0.002)
Stage	I	776 (56.0)	609 (44.0)	-	-	-
	II	561 (55.0)	459 (45.0)	1.04 (0.89-1.23, P=0.616)	1.04 (0.88-1.23, P=0.614)	1.19 (0.99-1.43, P=0.070)
	III	888 (53.6)	768 (46.4)	1.10 (0.95-1.27, P=0.184)	1.09 (0.94-1.26, P=0.259)	1.16 (0.98-1.37, P=0.089)
	IV	256 (51.2)	244 (48.8)	1.21 (0.99-1.49, P=0.063)	1.23 (0.99-1.52, P=0.056)	1.31 (1.04-1.66, P=0.023)

Table 10-47. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for all complications in patients with gastric cancer.

Dependent: All complications		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	209 (54.4)	175 (45.6)	-	-	-
	Upper middle No/moderate malnutrition	59 (55.1)	48 (44.9)	0.97 (0.63-1.49, P=0.896)	1.03 (0.66-1.61, P=0.885)	0.98 (0.42-2.26, P=0.958)
	Low/lower middle No/moderate malnutrition	47 (58.0)	34 (42.0)	0.86 (0.53-1.40, P=0.554)	0.94 (0.56-1.55, P=0.798)	0.88 (0.41-1.92, P=0.756)
	High Severe malnutrition	124 (60.5)	81 (39.5)	0.78 (0.55-1.10, P=0.158)	0.76 (0.53-1.08, P=0.122)	0.76 (0.50-1.14, P=0.181)
	Upper middle Severe malnutrition	73 (48.0)	79 (52.0)	1.29 (0.89-1.88, P=0.181)	1.31 (0.88-1.94, P=0.184)	1.82 (0.83-3.97, P=0.133)
	Low/lower middle Severe malnutrition	98 (53.0)	87 (47.0)	1.06 (0.75-1.51, P=0.744)	1.13 (0.77-1.67, P=0.531)	0.89 (0.45-1.75, P=0.732)
Age (years)	Mean (SD)	62.3 (13.7)	64.1 (13.4)	1.01 (1.00-1.02, P=0.033)	1.01 (1.00-1.02, P=0.016)	1.02 (1.00-1.03, P=0.010)
Sex	Male	253 (56.9)	192 (43.1)	-	-	-
	Female	357 (53.4)	312 (46.6)	1.15 (0.90-1.47, P=0.252)	1.14 (0.89-1.46, P=0.295)	1.08 (0.81-1.44, P=0.586)
Stage	I	212 (56.1)	166 (43.9)	-	-	-
	II	107 (55.7)	85 (44.3)	1.01 (0.71-1.44, P=0.936)	1.00 (0.70-1.43, P=0.999)	1.19 (0.77-1.84, P=0.431)
	III	234 (54.4)	196 (45.6)	1.07 (0.81-1.41, P=0.635)	1.06 (0.80-1.42, P=0.674)	1.13 (0.80-1.61, P=0.491)
	IV	53 (51.0)	51 (49.0)	1.23 (0.79-1.90, P=0.353)	1.18 (0.74-1.87, P=0.481)	1.24 (0.72-2.13, P=0.437)

Table 10-48. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for anastomotic leak.

Dependent: Anastomotic leak		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	2659 (94.6)	153 (5.4)	-	-	-
	Upper middle No/moderate malnutrition	603 (96.6)	21 (3.4)	0.61 (0.37-0.94, P=0.034)	0.63 (0.38-0.98, P=0.051)	0.78 (0.43-1.41, P=0.407)
	Low/lower middle No/moderate malnutrition	329 (92.7)	26 (7.3)	1.37 (0.87-2.08, P=0.149)	1.40 (0.87-2.18, P=0.153)	1.38 (0.76-2.50, P=0.291)
	High Severe malnutrition	741 (93.6)	51 (6.4)	1.20 (0.86-1.65, P=0.283)	1.27 (0.90-1.76, P=0.160)	1.27 (0.90-1.79, P=0.174)
	Upper middle Severe malnutrition	469 (95.1)	24 (4.9)	0.89 (0.56-1.36, P=0.602)	0.96 (0.60-1.49, P=0.871)	1.08 (0.62-1.90, P=0.782)
	Low/lower middle Severe malnutrition	543 (92.5)	44 (7.5)	1.41 (0.98-1.98, P=0.054)	1.45 (0.97-2.13, P=0.064)	1.26 (0.72-2.21, P=0.417)
Cancer Type	Colorectal (colon or rectum)	4300 (94.3)	261 (5.7)	-	-	-
	Gastric (stomach)	1044 (94.7)	58 (5.3)	0.92 (0.68-1.22, P=0.553)	0.86 (0.63-1.15, P=0.325)	0.88 (0.64-1.22, P=0.455)
Age (years)	Mean (SD)	64.8 (13.6)	64.7 (12.8)	1.00 (0.99-1.01, P=0.941)	1.00 (0.99-1.01, P=0.728)	1.00 (0.99-1.01, P=0.774)
Sex	Male	2297 (95.2)	115 (4.8)	-	-	-
	Female	3043 (93.7)	204 (6.3)	1.34 (1.06-1.70, P=0.015)	1.38 (1.09-1.76, P=0.008)	1.40 (1.09-1.78, P=0.008)
Stage	I	1659 (94.6)	94 (5.4)	-	-	-
	II	1134 (93.9)	74 (6.1)	1.15 (0.84-1.57, P=0.378)	1.14 (0.83-1.57, P=0.419)	1.15 (0.83-1.60, P=0.407)
	III	1949 (94.2)	120 (5.8)	1.09 (0.82-1.44, P=0.558)	1.06 (0.80-1.41, P=0.684)	1.07 (0.80-1.44, P=0.647)
	IV	569 (95.6)	26 (4.4)	0.81 (0.51-1.24, P=0.343)	0.91 (0.55-1.45, P=0.691)	0.90 (0.54-1.49, P=0.681)

Table 10-49. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for anastomotic leak in patients with colorectal cancer.

Dependent: Anastomotic leak		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	2295 (94.5)	133 (5.5)	-	-	-
	Upper middle No/moderate malnutrition	500 (96.3)	19 (3.7)	0.66 (0.39-1.04, P=0.091)	0.66 (0.39-1.06, P=0.100)	0.78 (0.43-1.42, P=0.423)
	Low/lower middle No/moderate malnutrition	254 (92.4)	21 (7.6)	1.43 (0.86-2.25, P=0.145)	1.42 (0.84-2.31, P=0.167)	1.32 (0.70-2.47, P=0.389)
	High Severe malnutrition	547 (93.2)	40 (6.8)	1.26 (0.87-1.80, P=0.212)	1.30 (0.89-1.87, P=0.162)	1.33 (0.92-1.92, P=0.135)
	Upper middle Severe malnutrition	329 (95.4)	16 (4.6)	0.84 (0.48-1.39, P=0.518)	0.85 (0.48-1.42, P=0.554)	0.94 (0.51-1.74, P=0.837)
	Low/lower middle Severe malnutrition	375 (92.1)	32 (7.9)	1.47 (0.97-2.17, P=0.059)	1.37 (0.87-2.12, P=0.163)	1.12 (0.61-2.06, P=0.712)
Age (years)	Mean (SD)	65.2 (13.5)	64.7 (12.9)	1.00 (0.99-1.01, P=0.551)	1.00 (0.99-1.01, P=0.738)	1.00 (0.99-1.01, P=0.605)
Sex	Male	1880 (95.2)	95 (4.8)	-	-	-
	Female	2416 (93.6)	166 (6.4)	1.36 (1.05-1.77, P=0.020)	1.40 (1.08-1.82, P=0.013)	1.41 (1.09-1.83, P=0.010)
Stage	I	1299 (94.3)	78 (5.7)	-	-	-
	II	959 (94.1)	60 (5.9)	1.04 (0.73-1.47, P=0.816)	1.05 (0.74-1.49, P=0.782)	1.05 (0.74-1.49, P=0.791)
	III	1547 (94.2)	95 (5.8)	1.02 (0.75-1.39, P=0.887)	1.00 (0.73-1.37, P=0.983)	1.01 (0.73-1.39, P=0.957)
	IV	470 (94.9)	25 (5.1)	0.89 (0.55-1.39, P=0.608)	0.86 (0.53-1.36, P=0.541)	0.86 (0.54-1.39, P=0.547)

Table 10-50. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for anastomotic leak in patients with gastric cancer.

Dependent: Anastomotic leak		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	364 (94.8)	20 (5.2)	-	-	-
	Upper middle No/moderate malnutrition	103 (98.1)	2 (1.9)	0.35 (0.06-1.24, P=0.165)	0.37 (0.06-1.32, P=0.191)	0.44 (0.06-3.13, P=0.411)
	Low/lower middle No/moderate malnutrition	75 (93.8)	5 (6.2)	1.21 (0.39-3.11, P=0.708)	1.14 (0.31-3.31, P=0.824)	1.33 (0.29-6.07, P=0.713)
	High Severe malnutrition	194 (94.6)	11 (5.4)	1.03 (0.47-2.16, P=0.935)	1.00 (0.45-2.13, P=0.993)	0.89 (0.36-2.23, P=0.807)
	Upper middle Severe malnutrition	140 (94.6)	8 (5.4)	1.04 (0.42-2.33, P=0.927)	1.15 (0.46-2.65, P=0.757)	1.18 (0.32-4.42, P=0.802)
	Low/lower middle Severe malnutrition	168 (93.3)	12 (6.7)	1.30 (0.60-2.69, P=0.486)	1.51 (0.64-3.45, P=0.335)	1.83 (0.53-6.32, P=0.338)
Age (years)	Mean (SD)	63.0 (13.7)	64.8 (12.2)	1.01 (0.99-1.03, P=0.321)	1.02 (0.99-1.04, P=0.161)	1.00 (0.98-1.03, P=0.787)
Sex	Male	417 (95.4)	20 (4.6)	-	-	-
	Female	627 (94.3)	38 (5.7)	1.26 (0.73-2.24, P=0.409)	1.25 (0.71-2.26, P=0.442)	1.23 (0.62-2.42, P=0.553)
Stage	I	360 (95.7)	16 (4.3)	-	-	-
	II	175 (92.6)	14 (7.4)	1.80 (0.85-3.78, P=0.119)	1.70 (0.79-3.65, P=0.171)	1.73 (0.70-4.29, P=0.234)
	III	402 (94.1)	25 (5.9)	1.40 (0.74-2.71, P=0.306)	1.31 (0.68-2.62, P=0.426)	1.30 (0.58-2.91, P=0.517)
	IV	99 (99.0)	1 (1.0)	0.23 (0.01-1.13, P=0.153)	0.19 (0.01-1.01, P=0.119)	0.20 (0.02-2.20, P=0.189)

Table 10-51. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for surgical site infection.

Dependent: SSI		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	2473 (89.2)	300 (10.8)	-	-	-
	Upper middle No/moderate malnutrition	520 (83.3)	104 (16.7)	1.65 (1.29-2.09, P<0.001)	1.67 (1.30-2.14, P<0.001)	1.51 (0.95-2.40, P=0.085)
	Low/lower middle No/moderate malnutrition	268 (76.1)	84 (23.9)	2.58 (1.96-3.38, P<0.001)	2.59 (1.93-3.45, P<0.001)	2.77 (1.70-4.51, P<0.001)
	High Severe malnutrition	687 (88.0)	94 (12.0)	1.13 (0.88-1.44, P=0.339)	1.17 (0.91-1.50, P=0.210)	1.16 (0.90-1.50, P=0.261)
	Upper middle Severe malnutrition	390 (78.6)	106 (21.4)	2.24 (1.75-2.86, P<0.001)	2.35 (1.81-3.03, P<0.001)	2.30 (1.46-3.62, P<0.001)
	Low/lower middle Severe malnutrition	424 (72.4)	162 (27.6)	3.15 (2.53-3.91, P<0.001)	3.16 (2.48-4.02, P<0.001)	3.00 (1.90-4.74, P<0.001)
Cancer Type	Colorectal (colon or rectum)	3809 (84.4)	704 (15.6)	-	-	-
	Gastric (stomach)	953 (86.7)	146 (13.3)	0.83 (0.68-1.00, P=0.055)	0.70 (0.57-0.86, P=0.001)	0.62 (0.50-0.78, P<0.001)
Age (years)	Mean (SD)	65.1 (13.5)	62.8 (13.7)	0.99 (0.98-0.99, P<0.001)	1.00 (0.99-1.01, P=0.979)	1.00 (0.99-1.01, P=0.776)
Sex	Male	2021 (84.4)	374 (15.6)	-	-	-
	Female	2738 (85.2)	475 (14.8)	0.94 (0.81-1.09, P=0.390)	0.98 (0.84-1.14, P=0.761)	0.95 (0.81-1.12, P=0.570)
Stage	I	1511 (87.1)	223 (12.9)	-	-	-
	II	1021 (85.4)	174 (14.6)	1.15 (0.93-1.43, P=0.187)	0.97 (0.78-1.21, P=0.792)	1.10 (0.87-1.40, P=0.404)
	III	1701 (82.7)	355 (17.3)	1.41 (1.18-1.70, P<0.001)	1.14 (0.94-1.38, P=0.178)	1.24 (1.01-1.52, P=0.039)
	IV	502 (85.2)	87 (14.8)	1.17 (0.90-1.53, P=0.239)	0.91 (0.69-1.19, P=0.500)	1.04 (0.77-1.39, P=0.815)

Table 10-52. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for surgical site infection in patients with colorectal cancer.

Dependent: SSI		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	2123 (88.8)	268 (11.2)	-	-	-
	Upper middle No/moderate malnutrition	435 (83.7)	85 (16.3)	1.55 (1.18-2.01, P=0.001)	1.53 (1.16-1.99, P=0.002)	1.55 (0.94-2.55, P=0.087)
	Low/lower middle No/moderate malnutrition	200 (73.3)	73 (26.7)	2.89 (2.14-3.87, P<0.001)	2.74 (1.99-3.73, P<0.001)	2.85 (1.66-4.89, P<0.001)
	High Severe malnutrition	503 (87.0)	75 (13.0)	1.18 (0.89-1.55, P=0.233)	1.17 (0.88-1.53, P=0.270)	1.15 (0.87-1.54, P=0.330)
	Upper middle Severe malnutrition	280 (80.7)	67 (19.3)	1.90 (1.40-2.53, P<0.001)	1.81 (1.33-2.44, P<0.001)	1.82 (1.10-3.02, P=0.020)
	Low/lower middle Severe malnutrition	268 (66.3)	136 (33.7)	4.02 (3.15-5.12, P<0.001)	3.76 (2.88-4.89, P<0.001)	3.51 (2.11-5.83, P<0.001)
Age (years)	Mean (SD)	65.5 (13.4)	62.9 (13.8)	0.99 (0.98-0.99, P<0.001)	1.00 (0.99-1.01, P=0.998)	1.00 (0.99-1.01, P=0.787)
Sex	Male	1641 (83.9)	315 (16.1)	-	-	-
	Female	2165 (84.8)	388 (15.2)	0.93 (0.79-1.10, P=0.406)	0.99 (0.84-1.17, P=0.895)	0.98 (0.83-1.17, P=0.855)
Stage	I	1188 (87.3)	173 (12.7)	-	-	-
	II	858 (85.2)	149 (14.8)	1.19 (0.94-1.51, P=0.144)	1.05 (0.82-1.33, P=0.715)	1.14 (0.88-1.47, P=0.313)
	III	1330 (81.6)	299 (18.4)	1.54 (1.26-1.89, P<0.001)	1.26 (1.02-1.56, P=0.032)	1.35 (1.08-1.69, P=0.009)
	IV	414 (84.8)	74 (15.2)	1.23 (0.91-1.64, P=0.172)	1.03 (0.75-1.38, P=0.870)	1.12 (0.81-1.55, P=0.479)

Table 10-53. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for surgical site infection in patients with gastric cancer.

Dependent: SSI		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	350 (91.6)	32 (8.4)	-	-	-
	Upper middle No/moderate malnutrition	85 (81.7)	19 (18.3)	2.44 (1.30-4.49, P=0.004)	2.69 (1.42-4.99, P=0.002)	1.44 (0.54-3.88, P=0.467)
	Low/lower middle No/moderate malnutrition	68 (86.1)	11 (13.9)	1.77 (0.82-3.59, P=0.127)	2.00 (0.90-4.20, P=0.075)	2.51 (0.93-6.73, P=0.068)
	High Severe malnutrition	184 (90.6)	19 (9.4)	1.13 (0.61-2.03, P=0.689)	1.20 (0.65-2.18, P=0.553)	1.21 (0.63-2.35, P=0.567)
	Upper middle Severe malnutrition	110 (73.8)	39 (26.2)	3.88 (2.32-6.52, P<0.001)	4.42 (2.58-7.62, P<0.001)	4.71 (2.10-10.57, P<0.001)
	Low/lower middle Severe malnutrition	156 (85.7)	26 (14.3)	1.82 (1.04-3.16, P=0.033)	1.95 (1.05-3.60, P=0.033)	1.96 (0.84-4.57, P=0.118)
Age (years)	Mean (SD)	63.2 (13.7)	62.3 (13.5)	0.99 (0.98-1.01, P=0.422)	1.00 (0.99-1.02, P=0.746)	1.00 (0.99-1.02, P=0.797)
Sex	Male	380 (86.6)	59 (13.4)	-	-	-
	Female	573 (86.8)	87 (13.2)	0.98 (0.69-1.40, P=0.902)	0.95 (0.66-1.37, P=0.763)	0.88 (0.58-1.33, P=0.540)
Stage	I	323 (86.6)	50 (13.4)	-	-	-
	II	163 (86.7)	25 (13.3)	0.99 (0.58-1.64, P=0.972)	0.81 (0.47-1.38, P=0.447)	0.99 (0.53-1.84, P=0.971)
	III	371 (86.9)	56 (13.1)	0.98 (0.65-1.47, P=0.904)	0.81 (0.52-1.25, P=0.330)	0.91 (0.55-1.51, P=0.721)
	IV	88 (87.1)	13 (12.9)	0.95 (0.48-1.79, P=0.889)	0.67 (0.32-1.31, P=0.260)	0.72 (0.33-1.56, P=0.401)

Table 10-54. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for major complication after multiple imputation for missing data.

Dependent: Major complications		OR (multivariable imputation)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	-
	Upper middle No/moderate malnutrition	0.54 (0.39-0.75, P<0.001)
	Low/lower middle No/moderate malnutrition	1.43 (1.04-1.95, P=0.026)
	High Severe malnutrition	1.22 (0.79-1.88, P=0.352)
	Upper middle Severe malnutrition	0.90 (0.64-1.26, P=0.536)
	Low/lower middle Severe malnutrition	1.70 (1.27-2.28, P<0.001)
Cancer Type	Colorectal (colon or rectum)	-
	Gastric (stomach)	0.96 (0.79-1.16, P=0.661)
Age (years)	Mean (SD)	1.02 (1.01-1.02, P<0.001)
Sex	Male	-
	Female	0.80 (0.69-0.93, P=0.004)
Stage	I	-
	II	1.19 (0.97-1.47, P=0.101)
	III	1.23 (1.01-1.48, P=0.035)
	IV	1.57 (1.21-2.02, P=0.001)

Table 10-55. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for all complications after multiple imputation for missing data.

Dependent: Any complications		OR (multivariable imputation)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	-
	Upper middle No/moderate malnutrition	0.75 (0.63-0.90, P=0.002)
	Low/lower middle No/moderate malnutrition	1.28 (1.02-1.60, P=0.032)
	High Severe malnutrition	0.99 (0.75-1.31, P=0.967)
	Upper middle Severe malnutrition	1.11 (0.90-1.37, P=0.310)
	Low/lower middle Severe malnutrition	1.66 (1.34-2.05, P<0.001)
Cancer Type	Colorectal (colon or rectum)	-
	Gastric (stomach)	0.95 (0.83-1.08, P=0.419)
Age (years)	Mean (SD)	1.01 (1.01-1.01, P<0.001)
Sex	Male	-
	Female	0.87 (0.79-0.96, P=0.006)
Stage	I	-
	II	1.02 (0.89-1.17, P=0.780)
	III	1.07 (0.95-1.21, P=0.270)
	IV	1.17 (0.97-1.39, P=0.095)

Table 10-56. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for surgical site infection after multiple imputation for missing data.

Dependent: SSI		OR (multivariable imputation)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	-
	Upper middle No/moderate malnutrition	1.65 (1.28-2.14, P<0.001)
	Low/lower middle No/moderate malnutrition	2.48 (1.79-3.44, P<0.001)
	High Severe malnutrition	1.29 (0.78-2.13, P=0.299)
	Upper middle Severe malnutrition	2.32 (1.74-3.09, P<0.001)
	Low/lower middle Severe malnutrition	3.28 (2.54-4.25, P<0.001)
Cancer Type	Colorectal (colon or rectum)	-
	Gastric (stomach)	0.71 (0.59-0.86, P<0.001)
Age (years)	Mean (SD)	1.00 (1.00-1.01, P=0.792)
Sex	Male	-
	Female	1.06 (0.92-1.21, P=0.447)
Stage	I	-
	II	0.94 (0.76-1.15, P=0.536)
	III	1.09 (0.92-1.30, P=0.324)
	IV	0.91 (0.71-1.18, P=0.495)

Table 10-57. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for 30-day mortality after imputation of missing GLIM criteria.

Imputation of all missing GLIM criteria with severe malnutrition status (highest prevalence).

Dependent: 30-day mortality		Alive	Dead	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	2766 (98.6)	38 (1.4)	-	-	-
	Upper middle No/moderate malnutrition	616 (98.7)	8 (1.3)	0.95 (0.41-1.93, P=0.886)	1.21 (0.52-2.51, P=0.625)	1.48 (0.59-3.69, P=0.401)
	Low/lower middle No/moderate malnutrition	348 (97.2)	10 (2.8)	2.09 (0.98-4.07, P=0.040)	3.73 (1.64-7.69, P=0.001)	4.76 (1.91-11.87, P=0.001)
	High Severe malnutrition	1446 (97.0)	44 (3.0)	2.21 (1.43-3.45, P<0.001)	1.90 (1.21-2.98, P=0.005)	1.90 (1.19-3.01, P=0.007)
	Upper middle Severe malnutrition	563 (96.1)	23 (3.9)	2.97 (1.73-4.99, P<0.001)	3.29 (1.86-5.70, P<0.001)	3.28 (1.59-6.79, P=0.001)
	Low/lower middle Severe malnutrition	640 (92.8)	50 (7.2)	5.69 (3.71-8.79, P<0.001)	10.88 (6.68-17.85, P<0.001)	11.63 (5.91-22.88, P<0.001)
Cancer Type	Colorectal (colon or rectum)	5199 (97.7)	121 (2.3)	-	-	-
	Gastric (stomach)	1180 (95.8)	52 (4.2)	1.89 (1.35-2.62, P<0.001)	1.51 (1.05-2.13, P=0.022)	1.47 (1.01-2.15, P=0.044)
Age (years)	Mean (SD)	64.8 (13.4)	70.2 (13.2)	1.03 (1.02-1.05, P<0.001)	1.06 (1.05-1.08, P<0.001)	1.06 (1.04-1.08, P<0.001)
Sex	Male	3639 (97.0)	113 (3.0)	-	-	-
	Female	2734 (97.9)	59 (2.1)	0.69 (0.50-0.95, P=0.025)	0.70 (0.50-0.97, P=0.033)	0.68 (0.49-0.96, P=0.028)
Stage	I	2032 (97.8)	45 (2.2)	-	-	-
	II	1372 (98.1)	27 (1.9)	0.89 (0.54-1.43, P=0.631)	0.72 (0.43-1.17, P=0.187)	0.78 (0.47-1.30, P=0.340)
	III	2286 (97.7)	55 (2.3)	1.09 (0.73-1.62, P=0.683)	0.90 (0.59-1.36, P=0.607)	0.99 (0.64-1.52, P=0.955)
	IV	647 (93.6)	44 (6.4)	3.07 (2.00-4.70, P<0.001)	2.49 (1.58-3.91, P<0.001)	2.74 (1.70-4.42, P<0.001)

Imputation of all missing GLIM criteria with no/moderate malnutrition status (lowest prevalence)

Dependent: 30-day mortality		Alive	Dead	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	3451 (98.4)	57 (1.6)	-	-	-
	Upper middle No/moderate malnutrition	701 (98.3)	12 (1.7)	1.04 (0.53-1.87, P=0.911)	1.26 (0.61-2.34, P=0.501)	1.51 (0.67-3.44, P=0.322)
	Low/lower middle No/moderate malnutrition	442 (96.7)	15 (3.3)	2.05 (1.11-3.56, P=0.014)	3.86 (1.99-7.07, P<0.001)	5.02 (2.26-11.13, P<0.001)
	High Severe malnutrition	761 (96.8)	25 (3.2)	1.99 (1.21-3.17, P=0.005)	1.68 (1.01-2.71, P=0.039)	1.69 (1.02-2.81, P=0.043)
	Upper middle Severe malnutrition	478 (96.2)	19 (3.8)	2.41 (1.38-4.00, P=0.001)	2.81 (1.58-4.82, P<0.001)	2.86 (1.37-6.00, P=0.005)
	Low/lower middle Severe malnutrition	546 (92.4)	45 (7.6)	4.99 (3.33-7.44, P<0.001)	9.87 (6.17-15.77, P<0.001)	10.84 (5.48-21.43, P<0.001)
Cancer Type	Colorectal (colon or rectum)	5199 (97.7)	121 (2.3)	-	-	-
	Gastric (stomach)	1180 (95.8)	52 (4.2)	1.89 (1.35-2.62, P<0.001)	1.50 (1.05-2.13, P=0.024)	1.47 (1.01-2.15, P=0.046)
Age (years)	Mean (SD)	64.8 (13.4)	70.2 (13.2)	1.03 (1.02-1.05, P<0.001)	1.06 (1.05-1.08, P<0.001)	1.06 (1.04-1.08, P<0.001)
Sex	Male	3639 (97.0)	113 (3.0)	-	-	-
	Female	2734 (97.9)	59 (2.1)	0.69 (0.50-0.95, P=0.025)	0.71 (0.51-0.98, P=0.041)	0.69 (0.49-0.96, P=0.030)
Stage	I	2032 (97.8)	45 (2.2)	-	-	-
	II	1372 (98.1)	27 (1.9)	0.89 (0.54-1.43, P=0.631)	0.72 (0.44-1.18, P=0.202)	0.79 (0.47-1.32, P=0.371)
	III	2286 (97.7)	55 (2.3)	1.09 (0.73-1.62, P=0.683)	0.89 (0.59-1.35, P=0.582)	0.98 (0.64-1.51, P=0.931)
	IV	647 (93.6)	44 (6.4)	3.07 (2.00-4.70, P<0.001)	2.52 (1.60-3.96, P<0.001)	2.76 (1.71-4.47, P<0.001)

Table 10-58. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for major complication after imputation of missing GLIM criteria.

Imputation of all missing GLIM criteria with severe malnutrition status (highest prevalence).

Dependent: Major complications		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	3083 (87.3)	448 (12.7)	-	-	-
	Upper middle No/moderate malnutrition	671 (93.1)	50 (6.9)	0.51 (0.37-0.69, P<0.001)	0.53 (0.38-0.72, P<0.001)	0.55 (0.37-0.82, P=0.003)
	Low/lower middle No/moderate malnutrition	402 (85.2)	70 (14.8)	1.20 (0.91-1.56, P=0.193)	1.36 (1.01-1.81, P=0.038)	1.30 (0.88-1.92, P=0.192)
	High Severe malnutrition	675 (85.0)	119 (15.0)	1.21 (0.97-1.50, P=0.083)	1.16 (0.92-1.44, P=0.196)	1.17 (0.93-1.46, P=0.185)
	Upper middle Severe malnutrition	448 (88.9)	56 (11.1)	0.86 (0.63-1.15, P=0.317)	0.89 (0.65-1.19, P=0.431)	0.85 (0.58-1.26, P=0.415)
	Low/lower middle Severe malnutrition	497 (82.7)	104 (17.3)	1.44 (1.14-1.81, P=0.002)	1.73 (1.34-2.23, P<0.001)	1.53 (1.05-2.22, P=0.026)
Cancer Type	Colorectal (colon or rectum)	4681 (87.2)	688 (12.8)	-	-	-
	Gastric (stomach)	1095 (87.3)	159 (12.7)	0.99 (0.82-1.19, P=0.898)	0.96 (0.79-1.15, P=0.644)	0.96 (0.79-1.17, P=0.704)
Age (years)	Mean (SD)	64.7 (13.5)	66.7 (12.7)	1.01 (1.01-1.02, P<0.001)	1.02 (1.01-1.02, P<0.001)	1.02 (1.01-1.02, P<0.001)
Sex	Male	3269 (86.2)	525 (13.8)	-	-	-
	Female	2501 (88.6)	321 (11.4)	0.80 (0.69-0.93, P=0.003)	0.80 (0.69-0.93, P=0.004)	0.80 (0.69-0.93, P=0.004)
Stage	I	1865 (88.9)	232 (11.1)	-	-	-
	II	1226 (86.9)	185 (13.1)	1.21 (0.99-1.49, P=0.066)	1.20 (0.97-1.48, P=0.091)	1.24 (1.00-1.54, P=0.045)
	III	2050 (86.8)	312 (13.2)	1.22 (1.02-1.47, P=0.029)	1.23 (1.02-1.48, P=0.030)	1.27 (1.05-1.54, P=0.013)
	IV	592 (83.9)	114 (16.1)	1.55 (1.21-1.97, P<0.001)	1.56 (1.21-2.00, P<0.001)	1.61 (1.25-2.08, P<0.001)

Imputation of all missing GLIM criteria with no/moderate malnutrition status (lowest prevalence)

Dependent: Major complications		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	3083 (87.3)	448 (12.7)	-	-	-
	Upper middle No/moderate malnutrition	671 (93.1)	50 (6.9)	0.51 (0.37-0.69, P<0.001)	0.53 (0.38-0.72, P<0.001)	0.55 (0.37-0.82, P=0.003)
	Low/lower middle No/moderate malnutrition	402 (85.2)	70 (14.8)	1.20 (0.91-1.56, P=0.193)	1.36 (1.01-1.81, P=0.038)	1.30 (0.88-1.92, P=0.192)
	High Severe malnutrition	675 (85.0)	119 (15.0)	1.21 (0.97-1.50, P=0.083)	1.16 (0.92-1.44, P=0.196)	1.17 (0.93-1.46, P=0.185)
	Upper middle Severe malnutrition	448 (88.9)	56 (11.1)	0.86 (0.63-1.15, P=0.317)	0.89 (0.65-1.19, P=0.431)	0.85 (0.58-1.26, P=0.415)
	Low/lower middle Severe malnutrition	497 (82.7)	104 (17.3)	1.44 (1.14-1.81, P=0.002)	1.73 (1.34-2.23, P<0.001)	1.53 (1.05-2.22, P=0.026)
Cancer Type	Colorectal (colon or rectum)	4681 (87.2)	688 (12.8)	-	-	-
	Gastric (stomach)	1095 (87.3)	159 (12.7)	0.99 (0.82-1.19, P=0.898)	0.96 (0.79-1.15, P=0.644)	0.96 (0.79-1.17, P=0.704)
Age (years)	Mean (SD)	64.7 (13.5)	66.7 (12.7)	1.01 (1.01-1.02, P<0.001)	1.02 (1.01-1.02, P<0.001)	1.02 (1.01-1.02, P<0.001)
Sex	Male	3269 (86.2)	525 (13.8)	-	-	-
	Female	2501 (88.6)	321 (11.4)	0.80 (0.69-0.93, P=0.003)	0.80 (0.69-0.93, P=0.004)	0.80 (0.69-0.93, P=0.004)
Stage	I	1865 (88.9)	232 (11.1)	-	-	-
	II	1226 (86.9)	185 (13.1)	1.21 (0.99-1.49, P=0.066)	1.20 (0.97-1.48, P=0.091)	1.24 (1.00-1.54, P=0.045)
	III	2050 (86.8)	312 (13.2)	1.22 (1.02-1.47, P=0.029)	1.23 (1.02-1.48, P=0.030)	1.27 (1.05-1.54, P=0.013)
	IV	592 (83.9)	114 (16.1)	1.55 (1.21-1.97, P<0.001)	1.56 (1.21-2.00, P<0.001)	1.61 (1.25-2.08, P<0.001)

Table 10-59. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for all complications after imputation of missing GLIM criteria.

Imputation of all missing GLIM criteria with severe malnutrition status (highest prevalence).

Dependent: All complications		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	1958 (55.5)	1572 (44.5)	-	-	-
	Upper middle No/moderate malnutrition	454 (63.1)	266 (36.9)	0.73 (0.62-0.86, P<0.001)	0.76 (0.64-0.90, P=0.002)	0.91 (0.60-1.37, P=0.637)
	Low/lower middle No/moderate malnutrition	248 (52.8)	222 (47.2)	1.11 (0.92-1.35, P=0.269)	1.23 (1.01-1.51, P=0.044)	1.11 (0.73-1.68, P=0.623)
	High Severe malnutrition	434 (54.7)	360 (45.3)	1.03 (0.88-1.21, P=0.679)	1.03 (0.88-1.20, P=0.751)	1.06 (0.89-1.26, P=0.518)
	Upper middle Severe malnutrition	270 (53.7)	233 (46.3)	1.07 (0.89-1.30, P=0.450)	1.10 (0.91-1.34, P=0.320)	1.38 (0.91-2.10, P=0.134)
	Low/lower middle Severe malnutrition	269 (44.8)	331 (55.2)	1.53 (1.29-1.82, P<0.001)	1.73 (1.43-2.09, P<0.001)	1.40 (0.93-2.11, P=0.107)
Cancer Type	Colorectal (colon or rectum)	2942 (54.8)	2423 (45.2)	-	-	-
	Gastric (stomach)	691 (55.2)	561 (44.8)	0.99 (0.87-1.12, P=0.820)	0.94 (0.83-1.07, P=0.357)	0.92 (0.79-1.07, P=0.305)
Age (years)	Mean (SD)	64.5 (13.4)	65.5 (13.5)	1.01 (1.00-1.01, P=0.003)	1.01 (1.01-1.01, P<0.001)	1.01 (1.01-1.02, P<0.001)
Sex	Male	2023 (53.4)	1766 (46.6)	-	-	-
	Female	1605 (56.9)	1216 (43.1)	0.87 (0.79-0.96, P=0.005)	0.87 (0.79-0.96, P=0.005)	0.85 (0.76-0.95, P=0.003)
Stage	I	1182 (56.4)	915 (43.6)	-	-	-
	II	780 (55.3)	630 (44.7)	1.04 (0.91-1.20, P=0.540)	1.02 (0.89-1.17, P=0.791)	1.16 (1.00-1.36, P=0.055)
	III	1279 (54.2)	1079 (45.8)	1.09 (0.97-1.23, P=0.154)	1.07 (0.94-1.21, P=0.299)	1.13 (0.98-1.29, P=0.086)
	IV	368 (52.1)	338 (47.9)	1.19 (1.00-1.41, P=0.050)	1.16 (0.97-1.38, P=0.096)	1.26 (1.03-1.53, P=0.021)

Imputation of all missing GLIM criteria with no/moderate malnutrition status (lowest prevalence)

Dependent: All complications		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	1958 (55.5)	1572 (44.5)	-	-	-
	Upper middle No/moderate malnutrition	454 (63.1)	266 (36.9)	0.73 (0.62-0.86, P<0.001)	0.76 (0.64-0.90, P=0.002)	0.91 (0.60-1.37, P=0.637)
	Low/lower middle No/moderate malnutrition	248 (52.8)	222 (47.2)	1.11 (0.92-1.35, P=0.269)	1.23 (1.01-1.51, P=0.044)	1.11 (0.73-1.68, P=0.623)
	High Severe malnutrition	434 (54.7)	360 (45.3)	1.03 (0.88-1.21, P=0.679)	1.03 (0.88-1.20, P=0.751)	1.06 (0.89-1.26, P=0.518)
	Upper middle Severe malnutrition	270 (53.7)	233 (46.3)	1.07 (0.89-1.30, P=0.450)	1.10 (0.91-1.34, P=0.320)	1.38 (0.91-2.10, P=0.134)
	Low/lower middle Severe malnutrition	269 (44.8)	331 (55.2)	1.53 (1.29-1.82, P<0.001)	1.73 (1.43-2.09, P<0.001)	1.40 (0.93-2.11, P=0.107)
Cancer Type	Colorectal (colon or rectum)	2942 (54.8)	2423 (45.2)	-	-	-
	Gastric (stomach)	691 (55.2)	561 (44.8)	0.99 (0.87-1.12, P=0.820)	0.94 (0.83-1.07, P=0.357)	0.92 (0.79-1.07, P=0.305)
Age (years)	Mean (SD)	64.5 (13.4)	65.5 (13.5)	1.01 (1.00-1.01, P=0.003)	1.01 (1.01-1.01, P<0.001)	1.01 (1.01-1.02, P<0.001)
Sex	Male	2023 (53.4)	1766 (46.6)	-	-	-
	Female	1605 (56.9)	1216 (43.1)	0.87 (0.79-0.96, P=0.005)	0.87 (0.79-0.96, P=0.005)	0.85 (0.76-0.95, P=0.003)
Stage	I	1182 (56.4)	915 (43.6)	-	-	-
	II	780 (55.3)	630 (44.7)	1.04 (0.91-1.20, P=0.540)	1.02 (0.89-1.17, P=0.791)	1.16 (1.00-1.36, P=0.055)
	III	1279 (54.2)	1079 (45.8)	1.09 (0.97-1.23, P=0.154)	1.07 (0.94-1.21, P=0.299)	1.13 (0.98-1.29, P=0.086)
	IV	368 (52.1)	338 (47.9)	1.19 (1.00-1.41, P=0.050)	1.16 (0.97-1.38, P=0.096)	1.26 (1.03-1.53, P=0.021)

Table 10-60. Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status for surgical site infection after imputation of missing GLIM criteria.

Imputation of all missing GLIM criteria with severe malnutrition status (highest prevalence).

Dependent: SSI		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	2415 (85.7)	403 (14.3)	-	-	-
	Upper middle No/moderate malnutrition	515 (81.6)	116 (18.4)	1.35 (1.07-1.69, P=0.010)	1.36 (1.08-1.71, P=0.008)	1.42 (0.93-2.18, P=0.106)
	Low/lower middle No/moderate malnutrition	264 (73.1)	97 (26.9)	2.20 (1.70-2.83, P<0.001)	2.15 (1.63-2.80, P<0.001)	2.16 (1.39-3.35, P=0.001)
	High Severe malnutrition	1257 (83.4)	250 (16.6)	1.19 (1.00-1.41, P=0.045)	1.22 (1.03-1.45, P=0.024)	1.21 (1.01-1.45, P=0.040)
	Upper middle Severe malnutrition	458 (77.1)	136 (22.9)	1.78 (1.43-2.21, P<0.001)	1.85 (1.47-2.31, P<0.001)	2.01 (1.34-3.02, P=0.001)
	Low/lower middle Severe malnutrition	515 (72.3)	197 (27.7)	2.29 (1.88-2.78, P<0.001)	2.29 (1.85-2.84, P<0.001)	1.99 (1.33-2.98, P=0.001)
Cancer Type	Colorectal (colon or rectum)	4373 (81.4)	996 (18.6)	-	-	-
	Gastric (stomach)	1051 (83.8)	203 (16.2)	0.85 (0.72-1.00, P=0.051)	0.74 (0.63-0.88, P=0.001)	0.69 (0.57-0.84, P<0.001)
Age (years)	Mean (SD)	65.3 (13.4)	63.6 (13.5)	0.99 (0.99-1.00, P<0.001)	1.00 (0.99-1.00, P=0.735)	1.00 (0.99-1.00, P=0.399)
Sex	Male	3107 (81.9)	687 (18.1)	-	-	-
	Female	2311 (81.9)	511 (18.1)	1.00 (0.88-1.13, P=1.000)	0.96 (0.84-1.09, P=0.527)	0.96 (0.84-1.10, P=0.574)
Stage	I	1760 (83.9)	337 (16.1)	-	-	-
	II	1161 (82.3)	250 (17.7)	1.12 (0.94-1.35, P=0.200)	1.00 (0.83-1.20, P=0.966)	1.08 (0.89-1.32, P=0.419)
	III	1885 (79.8)	477 (20.2)	1.32 (1.13-1.54, P<0.001)	1.14 (0.97-1.33, P=0.108)	1.19 (1.01-1.41, P=0.042)
	IV	584 (82.7)	122 (17.3)	1.09 (0.87-1.37, P=0.453)	0.91 (0.72-1.14, P=0.413)	0.97 (0.76-1.25, P=0.838)

Imputation of all missing GLIM criteria with no/moderate malnutrition status (lowest prevalence)

Dependent: SSI		No	Yes	OR (univariable)	OR (multivariable)	OR (multilevel)
Nutritional Status:WB income level (tertile)	High No/moderate malnutrition	3005 (85.1)	526 (14.9)	-	-	-
	Upper middle No/moderate malnutrition	587 (81.4)	134 (18.6)	1.30 (1.05-1.60, P=0.013)	1.32 (1.06-1.63, P=0.011)	1.39 (0.92-2.10, P=0.117)
	Low/lower middle No/moderate malnutrition	353 (74.8)	119 (25.2)	1.93 (1.53-2.41, P<0.001)	1.90 (1.49-2.42, P<0.001)	1.85 (1.21-2.81, P=0.004)
	High Severe malnutrition	667 (84.0)	127 (16.0)	1.09 (0.88-1.34, P=0.435)	1.13 (0.91-1.39, P=0.278)	1.13 (0.90-1.41, P=0.295)
	Upper middle Severe malnutrition	386 (76.6)	118 (23.4)	1.75 (1.39-2.18, P<0.001)	1.81 (1.43-2.28, P<0.001)	2.03 (1.34-3.09, P=0.001)
	Low/lower middle Severe malnutrition	426 (70.9)	175 (29.1)	2.35 (1.92-2.86, P<0.001)	2.33 (1.87-2.90, P<0.001)	2.06 (1.36-3.10, P=0.001)
Cancer Type	Colorectal (colon or rectum)	4373 (81.4)	996 (18.6)	-	-	-
	Gastric (stomach)	1051 (83.8)	203 (16.2)	0.85 (0.72-1.00, P=0.051)	0.74 (0.62-0.88, P=0.001)	0.69 (0.57-0.84, P<0.001)
Age (years)	Mean (SD)	65.3 (13.4)	63.6 (13.5)	0.99 (0.99-1.00, P<0.001)	1.00 (0.99-1.00, P=0.769)	1.00 (0.99-1.00, P=0.420)
Sex	Male	3107 (81.9)	687 (18.1)	-	-	-
	Female	2311 (81.9)	511 (18.1)	1.00 (0.88-1.13, P=1.000)	0.96 (0.84-1.09, P=0.545)	0.96 (0.84-1.10, P=0.581)
Stage	I	1760 (83.9)	337 (16.1)	-	-	-
	II	1161 (82.3)	250 (17.7)	1.12 (0.94-1.35, P=0.200)	1.00 (0.83-1.20, P=0.990)	1.09 (0.89-1.32, P=0.409)
	III	1885 (79.8)	477 (20.2)	1.32 (1.13-1.54, P<0.001)	1.14 (0.97-1.33, P=0.111)	1.19 (1.00-1.41, P=0.045)
	IV	584 (82.7)	122 (17.3)	1.09 (0.87-1.37, P=0.453)	0.91 (0.72-1.15, P=0.436)	0.98 (0.77-1.25, P=0.862)

Table 10-61. Three-way decomposition mediation model of the effect of country income group on 30-day mortality mediated by nutritional state after imputation of missing GLIM criteria.

Imputation of all missing GLIM criteria with severe malnutrition status (highest prevalence)

	Pathway	Odds ratio	95% CI	Percentage mediated
Upper middle	Direct	1.44	0.88-2.34	71
	Indirect	1.12	1.06-1.19	29
Low/lower middle	Direct	5.21	3.37-8.06	74
	Indirect	1.28	1.16-1.42	26

Imputation of all missing GLIM criteria with no/moderate malnutrition status (lowest prevalence)

	Pathway	Odds ratio	95% CI	Percentage mediated
Upper middle	Direct	1.35	0.83-2.21	57
	Indirect	1.19	1.09-1.36	43
Low/lower middle	Direct	5.08	3.26-7.91	71
	Indirect	1.33	1.16-1.53	29

Table 10-62. Three-way decomposition mediation model of the effect of country income group on 30-day mortality mediated by nutritional state after imputation of missing GLIM criteria.

Imputation of all missing GLIM criteria with severe malnutrition status (highest prevalence)

	Pathway	Odds ratio	95% CI	Percentage mediated
Upper middle	Direct	1.83	1.52-2.21	94
	Indirect	1.03	1.01-1.05	6
Low/lower middle	Direct	2.64	2.16-3.23	90
	Indirect	1.07	1.02-1.12	10

Imputation of all missing GLIM criteria with no/moderate malnutrition status (lowest prevalence)

	Pathway	Odds ratio	95% CI	Percentage mediated
Upper middle	Direct	1.81	1.50-2.18	90
	Indirect	1.05	1.01-1.09	10
Low/lower middle	Direct	2.61	2.13-3.21	88
	Indirect	1.09	1.02-1.16	12