THE IMPACT OF THE COVID-19 PANDEMIC ON PERIOPERATIVE SAFETY AND SURGICAL ACTIVITY

by

DMITRI NEPOGODIEV

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SUPERVISORS

Professor Kate Jolly

Professor of Public Health and Primary Care, Institute of Applied Heath Research, College of Medical and Dental Sciences, University of Birmingham, UK.

Professor Richard Lilford

Professor of Public Health, Institute of Applied Heath Research, College of Medical and Dental Sciences, University of Birmingham, UK.

Professor Dion Morton

Barling Chair of Surgery, Institute of Cancer and Genomic Sciences, College of Medical and Dental Sciences, University of Birmingham, UK.

ABSTRACT

Early reports from hospitalised medical patients indicated that severe COVID-19 was associated with high mortality rates. In March 2020 there was no high-quality evidence to inform surgical practice during the pandemic. This thesis reports four studies investigating the impact of the COVID-19 pandemic on perioperative safety and surgical activity.

To characterise the outcomes of surgery in patients with perioperative SARS-CoV-2 infection, an international cohort study of 1,128 patients who underwent surgery during the first COVID-19 wave (January to March 2022) was undertaken. It identified that perioperative SARS-CoV-2 infection was associated with increased risk of both 30-day postoperative pulmonary complications and mortality. These data indicated that whenever possible, surgery should be avoided in patients with acute SARS-CoV-2 infection.

To determine the optimal timing of surgery following SARS-CoV-2 infection an international, prospective cohort study was undertaken. This included 140,231 patients in October 2020. Whereas patients operated 0–2 weeks, 3–4 weeks, and 5–6 weeks after a SARS-CoV-2 diagnosis were at increased risk of adverse events, patients operated ≥7 weeks after SARS-CoV-2 diagnosis were not at increased risk compared to patients who had not had a SARS-CoV-2 infection. Subsequent to this study SARS-CoV-2 vaccines were rolled out and the Omicron SARS-CoV-2 variant emerged.

To characterize the applicability of the previous findings to the period of Omicron SARS-CoV-2 variant dominance a further international, prospective cohort study was undertaken to capture surgical outcomes for 19,684 patients with perioperative SARS-CoV-2 infection (December 2021 to February 2022). This found that mortality and 30-day postoperative pulmonary complications had substantially reduced compared to outcomes during the first COVID-19 wave. The findings support initiatives to relax some COVID-19 mitigations measures.

To inform planning of strategies to address pandemic elective care backlogs, the need for elective care in England was modelled and forecast forward to 2030. This estimated that in March 2022 4.3 million people needed elective procedures in England. Even in the most optimistic scenario, 2.6 million people would still be on waiting lists for elective procedures in 2030.

DEDICATION

This thesis is dedicated to my parents and brother.

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THESIS FORMAT

This thesis is formatted in accordance with the University of Birmingham alternative format thesis guidelines; Regulation 7.4.1(g).

As a result, published (chapters 3-4) and manuscripts under preparation (chapters 5-6) have been incorporated into the thesis. I have outlined my role and that of my co-authors at the start of each chapter.

The two published manuscripts are included in the Appendix.

PUBLICATIONS RELATED TO THIS THESIS

Two peer-reviewed articles and one pre-print manuscript have been published from data presented in this thesis:

- **Nepogodiev D** (first author), CovidSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet*. 2020;396(10243):27-38.
- **Nepogodiev D** (first and corresponding author), CovidSurg Collaborative, GlobalSurg Collaborative. Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. *Anaesthesia*. 2021;76(6):748-58.
  Awarded prize "Anaesthesia Paper of the Year 2021" by the Anaesthesia editorial board.
- **Nepogodiev D** (corresponding author), Acharya R, Chaudhry D, Glasbey JC, Harris B, Li E, et al. Forecasting waiting lists for elective procedures and surgery in England: a modelling study. *medRxiv*. 2022:2022.06.20.22276651.

Additional publications arising from the body of research presented in this thesis are listed below:

- **Nepogodiev D**, Martin J, Biccard B, Makupe A, Bhangu A. Global burden of postoperative death. *Lancet*. 2019 Feb 2;393(10170):401.
- **Nepogodiev D** (first author), 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;106(2):e113-e20.
- **Nepogodiev D** (corresponding author), CovidSurg Collaborative. Global guidance for surgical care during the COVID-19 pandemic. *Br J Surg*. 2020;107(9):1097-103.
- **Nepogodiev D** (first and corresponding author), CovidSurg Collaborative. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans. Br J Surg. 2020;107(11):1440-9.
- **Nepogodiev D** (first and corresponding author), CovidSurg Collaborative. Projecting COVID-19 disruption to elective surgery. *Lancet*. 2022;399(10321):233-4.
- **Nepogodiev D** (first and corresponding author), CovidSurg Collaborative, GlobalSurg Collaborative. SARS-CoV-2 vaccination modelling for safe surgery to save lives: data from an international prospective cohort study. *Br J Surg*. 2021;108(9):1056-63.

PRESENTATIONS FROM THIS THESIS

Four national oral presentations arising from the body of research presented in this thesis are listed below:

- *"SARS-CoV-2 vaccination modelling for safe surgery to save lives: data from an international prospective cohort study"*
  PHE Public Health Research and Science Conference 2020 (online), May 2021.
- *"Impact of the COVID-19 pandemic on surgery and the winter ahead"*
  Association of Upper Gastrointestinal Surgeons (AUGIS) 2021 (online), October 2021.
- *"Timing of surgery after SARS-CoV-2 infection"*
  Association of Anaesthetists (AAGBI) Winter Scientific Meeting (online), January 2022.
- *"Timing of surgery after SARS-CoV-2 infection: update"*
  Association of Anaesthetists (AAGBI) Winter Scientific Meeting (Belfast), September 2022.

ABBREVIATIONS

ARDS	Acute respiratory distress syndrome
COVID-19	Coronavirus disease 2019
CRF	Case report form
CT	Computed tomography
GSU	Global surgery unit
HES	Hospital Episode Statistics
HIC	High income countries
ICU	Intensive care unit
LMIC	Low- and middle-income countries
NHS	National Health Service
NIHR	National Institute for Health and Care Research
OPCS	Office of Population Censuses and Surveys (Classification of Interventions and Procedures)
PHEIC	Public health emergency of international concern
REDCap	Research Electronic Data Capture
RT-PCR	Reverse transcription polymerase chain reaction
RCT	Randomised controlled trial
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
UK	United Kingdom
US	United States
WHO	World Health Organisation

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1 INTRODUCTION

1.1 Synopsis

The first part of this chapter provides an overview of the pandemic as it emerged and treatments and preventative measures as they were developed. The second part of this chapter describes the impact of previous pandemics on surgical outcomes and activity. This overview of the previous literature provides context for the research undertaken in this thesis and justification for the research questions. The evolving nature of the pandemic means that the research findings should be interpreted in the context of clinical practice and the data available in the relevant phase of the pandemic.

1.2 Coronavirus disease 2019 (COVID-19)

1.2.1 First COVID-19 wave

1.2.1.1 Emergence of the severe acute respiratory syndrome coronavirus 2

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus that causes Coronavirus disease 2019 (COVID-19). It is unknown when SARS-CoV-2 transmission first occurred to humans; some analyses suggest that the virus may have emerged as early as October 2019[1]. The earliest known cases of SARS-CoV-2 were identified in Wuhan in China[2]. The Wuhan Municipal Health Commission issued an emergency notice to local hospitals on 30 December 2019 reporting recent cases of unexplained pneumonia[2]. The onset of illness in the first known case may have been as early as 8 December 2019[2].

There are several hypotheses for how this virus was first transmitted to humans. These include the possibility of a spill over from either wild or farmed animals, transmission through contaminated food, or transmission following escape of the virus from a laboratory[3]. An investigation by the World Health Organisation (WHO) in

Wuhan in early 2021 pointed towards transmission having first occurred in animal markets[4]. Analysis of genetic sequencing of viral samples from the earliest known cases suggest that multiple separate spill over events may have occurred[2]. However, a subsequent report by a different WHO committee in June 2022 stated that no definitive origin for SARS-CoV-2 has yet been proven and that further research is needed, including in to the possibility of a lab-leak[5].

1.2.1.2 COVID-19 timeline

A timeline of the COVID-19 pandemic is presented in Table 1.1. The Wuhan Municipal Health Commission first publicly announced clusters of unexplained pneumonias on 31 December 2019[2]. On 13 January 2020, the first SARS-CoV-2 infection outside of China had been detected in Thailand[6]. By the end of January 2020, a total of 7,818 SARS-CoV-2 cases had been confirmed worldwide, including 82 cases in 18 countries outside China[6]. On 30 January 2020 the WHO declared COVID-19 a Public Health Emergency of International Concern (PHEIC)[7]. This was the sixth PHEIC declared since updated international health regulations came in to force in 2007; previous PHEICs related to H1N1 pandemic influenza (2009), Poliovirus (2014), Ebola virus in West Africa (2014), Zika (2016), and Ebola virus in the Democratic Republic of Congo (2019)[8].

As of 1 July 2022, a total of 545 million SARS-CoV-2 infections had been confirmed worldwide as well as 6.3 million COVID-19-related deaths[9]. The highest COVID-19-related death tolls are reported in the United States, Brazil, Russia, Mexico, and Peru[10]. However, it is thought that some countries have significantly under-reported COVID-19 deaths. This could occur as a result of limited SARS-CoV-2 testing capacity or due to a lack of reliable death registration systems. An analysis by the Institute for Health Metrics and Evaluation has estimated that by 31 December 2021

there had been 18.2 million excess deaths worldwide[11]. A more recent estimate by *The Economist* was of a total of 21.5 million excess deaths by 3 July 2022[10].

The first two known individuals with SARS-CoV-2 infection the United Kingdom were identified on 29 January 2020; an individual had flown to the UK from Wuhan on 23 January 2020 and had infected another person in the UK[12]. By the end of February 2020, 73 SARS-CoV-2 cases had been identified in the UK, and the first COVID-19-related death occurred on 2 March 2020[13]. As of 30 June 2022, 19,144,946 SARS-CoV-2 infections and 157,037 deaths within 28 days of a positive SARS-CoV-2 test result had occurred in the UK[13]. The number of SARS-CoV-2 infections is likely to be significantly underestimated as a result of both insufficient testing capacity at the start of the pandemic, and the end of mass testing in April 2022[14,15].

Table 1.1: Timeline of the COVID-19 pandemic

Date	Development
31 Dec 2019	Wuhan Municipal Health Commission publicly announces clusters of unexplained pneumonias in Wuhan
10 Jan 2020	SARS-CoV-2 genome sequence publicly released
13 Jan 2020	First SARS-CoV-2 infection detected outside of China
23 Jan 2020	Wuhan lockdown starts
28 Jan 2020	100 SARS-CoV-2 related deaths confirmed
30 Jan 2020	WHO declares COVID-19 a Public Health Emergency of International Concern
6 Mar 2020	100,000 SARS-CoV-2 cases confirmed worldwide
19 Mar 2020	10,000 SARS-CoV-2 related deaths confirmed worldwide
2 Apr 2020	1 million SARS-CoV-2 cases confirmed worldwide
28 June 2020	10 million SARS-CoV-2 cases confirmed worldwide
19 Sept 2020	1 million SARS-CoV-2 related deaths confirmed worldwide
9 Dec 2020	Administration of the first SARS-CoV-2 vaccine in a clinical setting
25 Jan 2021	100 million SARS-CoV-2 cases confirmed worldwide
30 Oct 2021	5 million SARS-CoV-2 related deaths confirmed worldwide
11 Apr 2022	500 million SARS-CoV-2 cases confirmed worldwide

Figures for SARS-CoV-2 cases and deaths are taken from the Our World in Data dataset[16]

1.2.1.3 SARS-CoV-2 transmission

The SARS-CoV-2 virus is transmitted through both direct close contact (droplet), indirect contact, and airborne transmission (aerosol)[17,18]. Droplets and aerosols are

formed when an infected person talks, coughs, or sneezes. Large droplets can travel up to two metres, so the greatest risk of transmission is within two metres of an infected person. Fine aerosols disperse over distances greater than two metres and may persist in the environment for a period of hours. Indirect contact occurs when a person touches a fomite surface that has been contaminated by respiratory secretions from an infected individual. Fomite surfaces are commonly touchpoints such as door handles.

The incubation period for SARS-CoV-2 is around 5-6 days[19]. Individuals are most infectious when viral shedding peaks; typically, this occurs at the time of symptom onset and then reduces over time[20]. People are most infectious in the two days before and up to ten days after symptom onset. However, in around 20-30% of cases there are no symptoms and these individuals can infect other people (asymptomatic transmission)[21,22]. The significance of asymptomatic transmission is disputed. Although transmission appears to be less frequent in asymptomatic than symptomatic individuals[22-24], some modelling studies suggest that up to 50% of infections are the result of asymptomatic transmission[25].

1.2.1.4 SARS-CoV-2 reproduction number

R0 is the basic reproduction number, a measure of the transmissibility of an infectious disease in a susceptible population who have not previously been infected with that disease and are not vaccinated against it[26]. The R0 value is the number of other people that an infectious individual will infect on average. A R0 value of greater than 1 is associated with exponential growth of infection, whereas a R0 value of less than 1 indicates that infection rates are decreasing[27].

Factors that contribute to the R0 value include the duration of the infectious period, the contact rate, and mode of transmission (airborne diseases typically have higher R0 values)[26]. Behavioural changes as a result of awareness of the risk of infection, for example social distancing or self-isolation of infected individuals, will reduce R0. Therefore, R0 can differ between different settings and change over time. As R0 is based on the susceptible population, immunity from prior infection and vaccination does not directly change R0[26]. The effective reproduction number (R) measures transmissibility of an infectious disease without the assumption of complete susceptibility.

Two early analyses based on data from the Wuhan outbreak up to mid-January 2020, estimated R0 for SARS-CoV-2 to be either 2.2 or 2.6[19,27]. Subsequent meta-analyses of published R0 values from the first COVID-19 wave suggested higher R0 values of 3.2 to 3.3[28,29].

1.2.1.5 COVID-19 symptoms

Early reports from hospitalised patients in China suggested that the most frequent symptoms with COVID-19 were fever, cough, sputum production, and fatigue[30]. The International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) study of hospitalised patients in the UK found the most common symptoms to be cough, fever, and shortness of breath[31]. During the first wave most studies focused on hospitalised patients so there was limited data from non-hospitalised patients. The PRINCIPLE platform trial recruited UK patients in the community (non-hospitalised) aged either ≥65 years or ≥50 years with comorbidities to evaluate possible COVID-19 treatments. In this population, 80% experienced cough, 69% experienced muscle ache, 58% experienced shortness of breath, and 53% experienced fever[32]. Although not identified as a key symptom in early studies, meta-

analysis subsequently found that 31-67% of patients develop loss of smell or taste, depending on disease severity[33].

1.2.1.6 Diagnosis of SARS-CoV-2 infection

In the early pandemic diagnosis of COVID-19 was based on clinical, radiological, or laboratory criteria. The earliest WHO guidance defined possible COVID-19 as hospitalised patients with a history of recent onset of fever and cough, and either travel history from Wuhan or contact with a known SARS-CoV-2 case[34]. No consistent clinical criteria were adopted globally for clinical diagnosis of COVID-19. During the first wave, the UK Government publicised the main symptoms of COVID-19 as being fever, new onset continuous cough, or loss of taste or smell[35]; but this definition was rarely implemented in research studies. Importantly, clinical diagnoses were associated with low specificity; a study of Dutch healthcare works found symptom-based diagnostic scores to have specificity of 55%[36]. This means that COVID-19 outcomes studies that enrolled patients solely based on symptoms included significant numbers of patients who did not in fact have COVID-19, reducing the reliability of their findings.

SARS-CoV-2 is a single-stranded RNA virus. Its genome was sequenced in China and released publicly as early as 10 January 2020[37]. This enabled the development of primers and probes required for Reverse Transcription-Polymerase Chain Reaction (RT-PCR)[38]. RT-PCR testing using nasal and/or throat samples became established as the gold standard for SARS-CoV-2 diagnosis. There are methodological challenges to precisely establishing the diagnostic accuracy of RT-PCR, including the lack of a reference standard for assessing test performance in asymptomatic patients[39]. Nonetheless, there is evidence that false negatives do occur with RT-PCR testing, either as a result of poor sampling technique, or testing

patients either too early or too late[40-43]. If samples are taken too early in infection, this may be before significant viral shedding has started; if samples are taken too late in infection, viral shedding may have reduced[20]. As viral shedding is greatest at the time of symptom onset[20], this is the point at which the likelihood of false negative results is lowest, although even at around the time of symptom onset the false negative rate may be up to 20%[20]. False positive results can also occur with RT-PCR due to contamination at the time of sampling or in the laboratory, but the frequency of this is much lower than of false negative results[40]. A further challenge, is that in some individuals viral shedding may continue for a period of months, resulting in persistent positive RT-PCR results, although the virus is rarely viable beyond two weeks[44].

RT-PCR testing requires a sophisticated infrastructure for safe sample collection and transportation, and analysis in laboratories using specialist equipment and staff[45]. The logistics of transporting and analysing RT-PCR samples is time consuming and test results may take 24 hour or longer to return. This is particularly problematic for the purposes of screening, since an individual may have an accurate negative test result based on the sample that was taken, but may become exposed to SARS-CoV-2 in the period between sample collection and receiving their result. Finally, RT-PCR testing is expensive; a single test provided to international travel arrivals by the UK Government cost £68 in August 2021[46].

COVID-19 rapid antigen tests (also known as lateral flow tests) were developed to overcome some of the drawbacks of RT-PCR testing. These tests detect antigens (specific proteins) on the viral surface; a large number of assays have been developed by over 130 different suppliers[47]. Rapid antigen tests can be used by patients at home, with a result available within around 30 minutes. However, their

major disadvantage is that their sensitivity is lower than that of RT-PCR[47,48]. Sensitivity is highest when viral shedding is high, so these tests perform best in symptomatic people, particularly during the first few days of symptoms[48].

Serological testing was developed to test for SARS-CoV-2 immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies. These are not considered appropriate tests for acute infection, since the IgM antibody response takes several days[38], meaning that testing for these would be associated with a high false negative rate in early infections. However, serological testing has had a range of research applications, including monitoring serological prevalence and defining risk factors for infection[49,50].

Early case series from China suggested that computed tomography (CT) chest imaging had close to 100% sensitivity for COVID-19[51,52]. A later meta-analysis of 60 studies found both sensitivity and specificity for CT chest imaging to be below 90% when compared to RT-PCR[53]. However, these studies were performed in hospitalised patients with severe COVID-19, so their findings are not generalisable to the patients with asymptomatic SARS-CoV-2 infection. The diagnostic accuracy of CT chest imaging is likely to be substantially lower than RT-PCR and requires exposure to ionising radiation, so CT is not recommended as a screening test in asymptomatic patients[54].

Whilst RT-PCR testing is considered the gold standard for detecting SARS-CoV-2 infection, it has not always been readily available in all settings. Many less severe infections were not detected in the first wave when access to RT-PCR was limited[15]. In order to meet the demand for RT-PCR test capacity, the UK Government established large-scale Lighthouse laboratories[55]. However, many LMICs lacked the infrastructure and personnel to establish equivalent facilities[56] and so were restricted to diagnosing COVID-19 clinically. It is estimated that as a result up to 85% of

infections were not detected in Africa[57]. Although access to testing increased when rapid antigen testing became widely available, these tests still attract a substantial cost; for example, up to £7 in South Africa[58].

1.2.1.7 Covid-19 treatment

In the early stages of the pandemic there were no specific treatments available for COVID-19. If patients developed respiratory compromise they were hospitalised for respiratory support. This could range from supplemental oxygenation to invasive ventilation depending on COVID-19 severity and resource availability[59].

The urgency to identify treatments for COVID-19 led to two distinct responses. Some individuals promoted drug treatments to prevent or treat COVID-19 such as hydroxychloroquine and ivermectin. The proponents of these drugs argued that although there was no robust evidence to support the efficacy of these drugs for COVID-19, it would be unethical to deny potentially beneficial treatment, particularly to severely unwell patients. A contrasting response was based on the principles of evidence-based medicine, that patients should only be receive treatment which have been robustly demonstrated to be both safe and effective. Ensuring patients were only exposed to experimental treatments within strictly controlled trial settings would reduce the risk of harming patients and ensure that there would be a clear evidence-base to inform the treatment of future patients.

The most robust methodology to generate new evidence regarding COVID-19 treatment efficacy and safety is by testing these treatments in randomised controlled trials (RCTs). By randomly allocating patient to two or more treatment groups, RCTs ensure that baseline characteristics of patients receiving each treatment are broadly similar, allowing a fair comparison of patient outcomes between these groups. This

minimises selection bias which is common in cohort studies, whereby the treatment that patients receive may be influenced by patient or disease factors. This can result in spurious associations being identified between an exposure (e.g. treatment type) and outcome due to confounding factors which influence both the exposures patients receive and their outcome. For example, age may be a confounding factor if younger patients are both more likely to receive a particular treatment and also more likely to have a more favourable outcome; this could result in a spurious finding that the treatment is associated with improved outcomes.

The two-arm parallel RCT is the simplest RCT design which either determines the effectiveness of a treatment versus a placebo, or compares effectiveness of two treatments head-to-head. Many drugs were proposed as having a potential benefit in COVID-19 treatment. Establishing separate RCTs to evaluate each possible treatment would be both time consuming and very costly. As a result, several groups utilised novel platform trial methodologies to efficiently evaluate multiple treatment simultaneously. One specific RCT design that was utilised was the multi-arm multi-stage (MAMS) trial methodology; this evaluates multiple interventions simultaneously against a common control group, with flexibility to analyse trial results at multiple stages allowing effective interventions to be identified early and ineffective interventions to be dropped, as well as for new interventions to be added or the treatment protocol of the control group to be updated based on emerging evidence[60].

The largest COVID-19 platform trial is RECOVERY. It enrolled its first patient on 19 March 2020. By 10 July 2022, RECOVERY had enrolled over 47,500 patients hospitalised with COVID-19. In June 2020, RECOVERY data demonstrated that dexamethasone reduced mortality in patients with severe COVID-19 by a third[61], whereas hydroxychloroquine and lopinavir-ritonavir did not improve outcomes[62,63].

Subsequent data found no clinical benefit with azithromycin, convalescent plasma, colchicine, or aspirin, whereas there were benefits identified with tocilizumab (February 2021), monoclonal antibody combinations (June 2021), and baricitinib (March 2022)[64]. Another key COVID-19 platform trial is PRINCIPLE; whereas RECOVERY focuses on patients hospitalised with COVID-19, PRINCIPLE is based in the community. It enrols patients aged ≥65 years, or ≥50 years with comorbidities who are unwell with COVID-19 in the community. PRINCIPLE has identified benefits with the use of inhaled budesonide[65], but not doxycycline[32], azithromycin[66], or colchicine[67].

The impact of well-designed RCTs is illustrated by the estimate that adoption of dexamethasone in COVID-19 treatment prevented over 1 million deaths worldwide[68]. RCT evidence is important even if a trial result is nominally 'negative', as this identifies treatments that are not only ineffective, but also potentially harmful. In contrast to small, under-powered, and poorly conducted RCTs that had suggested a possible benefit to hydroxychloroquine, RECOVERY found hydroxychloroquine to not only be ineffective but also to be associated with a small increase in frequency of invasive mechanical ventilation and cardiac deaths[62].

1.2.1.8 SARS-CoV-2 infection outcomes

The severity of SARS-CoV-2 infection can range from asymptomatic infection to organ failure and death. Characterisation of SARS-CoV-2 infection outcomes and identification of high-risk patient groups have been key research areas during the pandemic in order to inform both individual patient care and also broad areas of public policy, including the need for lockdowns.

Reports of asymptomatic infection and transmission emerged in February 2020; for example, the *Journal of the American Medical Association* published a report of a cluster of five SARS-CoV-2 infections which were apparently related to a single asymptomatic index case[69]. A key early event that demonstrated the extent of asymptomatic infection was the SARS-CoV-2 outbreak that started aboard the cruise ship *Diamond Princess* in late January 2020, which has been extensively documented[70-73]. The passengers and crew were unable to leave the ship, so the population at-risk of infection was well defined, facilitating contact tracing and testing of contacts. The significance of the *Diamond Princess* outbreak was that it was one of the first outbreaks to have comprehensive mass testing. Of 696 confirmed cases, 410 were asymptomatic at the time of testing positive[72]. An estimated 17.9% of individuals who tested positive for SARS-CoV-2 aboard *Diamond Princess* never developed symptoms[73].

Asymptomatic infection poses an important methodological challenge when characterising SARS-CoV-2 infection outcomes because if it is not possible to identify all patients with asymptomatic infection, this will lead to an over-estimate of mortality. Moreover, results from different studies will not be directly comparable if these studies vary in their case ascertainment of patients with asymptomatic infection. This was a particularly important consideration during the early pandemic when access to testing was limited. As a result, most early report focused on SARS-CoV-2 outcomes in hospitalised (tested) patients rather than on population-level outcomes.

Amongst the earliest reports from the initial outbreak in Wuhan was a report of two patients published in the *New England Journal of Medicine* on 24 January 2020; of these two patients, one had died[74]. Although this report provided little data, it

confirmed that severe SARS-CoV-2 infection could result in death. The same day *The Lancet* published a series of 41 patients with confirmed SARS-CoV-2 infection from a hospital in Wuhan. This study found that all patients had abnormal CT chest findings, 29% of patients developed adult respiratory distress syndrome (ARDS), and 15% of patients died[75]. On 29 January 2020 *The Lancet* published a further series of 99 patients with confirmed COVID-19 from another hospital in Wuhan. In this series 17% of patients developed ARDS and 11% died[76]. On 7 February 2020 the *Journal of the American Medical Association* published a single-centre case series of 138 COVID-19 patients from Wuhan which found that 26% of patients required intensive care and 4% died[77]. Hospital acquired infection was suspected in 41% of patients. The authors of these studies focussed on rapidly releasing data and did not wait for all patients to complete 30-day follow-up. As the authors did not censor patients who had not reached 30-day follow-up, it is likely that these early reports underestimated the true mortality in hospitalised COVID-19 patients.

The *New England Journal of Medicine* published a further report in late February 2020 with data for 1,099 patients with confirmed SARS-CoV-2 infection from 552 hospitals in China[78]. In this study, 86% of patients CT chest abnormalities in their chest, but ARDS (3.4%) and mortality (1.4%) were considerably lower than in earlier studies. Although this study included patients from across China and therefore had greater generalisability than earlier studies, a key weakness was that 94% of patients remained in hospital at the time of follow-up. Therefore, it is likely that the study significantly underestimated final complication and mortality rates.

The first large population-level study was published on 24 February 2020 using data for 72,314 SARS-CoV-2 cases from the Chinese Center for Disease Control and Prevention[79]. Most cases (81%) were found to be mild, defined as no or mild

pneumonia only. Overall mortality was 2.3%. However, over a third of patients in this dataset were included based on clinical diagnosis only (not tested for SARS-CoV-2), so it is possible that some were misdiagnosed. Secondly, although this study included non-hospitalised patients, only 1% of cases were asymptomatic; this is lower than the proportion of infections expected to be asymptomatic and could indicate an over-estimation of mortality.

Early multicentre data from New York, US was published in April 2020. This found that amongst 2,634 hospitalised patients with RT-PCR confirmed SARS-CoV-2 who had been discharged or had died at the study end point, 12.2% had needed invasive mechanical ventilation and 21% had died[80]. The first UK multicentre data was published in May 2020, reporting on 20,133 RT-PCR confirmed hospitalised patients with SARS-CoV-2, from across 208 hospitals[31]. The authors reported that 16% of patients required non-invasive ventilation, whilst 10% required invasive ventilation. At the time of follow-up, 41% of patients had been discharged, 26% had died, and 34% remained in hospital.

Although it is difficult to synthesis the early SARS-CoV-2 outcomes data, there was a clear signal that a substantial proportion of patients developed severe lung injury necessitating mechanical ventilation and that this was associated with high mortality. Subsequent studies have suggested that overall mortality, including the full spectrum of disease from asymptomatic to hospitalised patients, may be 1-2%, with mortality significantly increasing with age; mortality in people aged ≥80 years may be over 10%[81-83].

1.2.1.9 Self-isolation of SARS-CoV-2 cases and contacts

The key aim of public health measures during the pandemic was to reduce the burden of SARS-CoV-2-related illness and mortality by breaking the chain of SARS-CoV-2 transmission in the community. Potentially infectious individuals were advised to stay at home and avoid mixing with other people (self-isolation) to reduce the likelihood of virus transmission to other people. However, a significant proportion of patients who are infectious are not aware of this because they are either asymptomatic (section 1.1.1.7) or pre-symptomatic in the 48 hours before symptoms develop (section 1.1.1.3); such individuals are unlikely to get tested or to self-isolate and may therefore infect other people[84].

Tracing of individuals who had close contact within the infectious period of known positive cases was intended to identify individuals who may have been infected at the earliest possible time, to get them tested. Such test, trace, and isolate strategies are only effective if there is a high level of population compliance with testing and isolation requirements[85]. Over the course of 2020 several countries developed contact tracing apps to automate detection of close contacts based on the proximity of an individual's mobile phone to the mobile phone of someone else who subsequently tests positive. In the early pandemic many countries introduced legal requirements for close contacts of known cases to self-isolate, to prevent further onward transition. These self-isolation requirements for contacts were loosened over the course of the pandemic[14], partly because increases in infection rates were mirrored by increases in the numbers of close contacts who might need to self-isolate, resulting in significant impact on the operation of businesses and public services[86].

1.2.1.10 Non-pharmaceutical interventions

Non-pharmaceutical interventions utilised during the pandemic have included the wearing of face masks (principally intended to reduce droplet transmission), social distancing of two metres between individuals (to reduce droplet transmission), and hand hygiene and touchpoint cleaning (to reduce indirect spread)[87,88]. As it was not possible to identify and self-isolate all infectious individuals promptly, public health authorities promoted non-pharmaceutical interventions as additional measures to reduce SARS-CoV-2 transmission. However, some authorities initially overestimated the role of indirect spread and underestimated the role of aerosol spread resulting in greater prominence being given to hand hygiene and less prominence being given to mask wearing than later in the pandemic.

1.2.1.11 COVID-19 lockdowns

Tracing, testing, and isolation of contacts of known SARS-CoV-2 cases and non-pharmaceutical interventions such as mask wearing and social distancing can all reduce R. However, despite these measures, R may remain greater than 1, resulting in sustained outbreaks. This is particularly likely to occur if population compliance with public health measures is incomplete; fewer than half of people in the UK asked to self-isolate self-reported compliance.

If a government may consider that increasing high SARS-CoV-2 case rates are likely to place unsustainable pressures on health systems, with the number of people developing severe COVID-19 exceeding available hospital bed, intensive care, equipment (ventilators), or drug (oxygen) availability. In such circumstances governments may consider introducing more stringent measures to reduce social mixing and transmission (R).

Lockdowns apply social restrictions to the whole population. In situations when it is not possible to identify and promptly isolate all infected individuals, this whole-population approach ensures that contacts between infected individuals and individuals susceptible to infection are reduced.

The specific restrictions imposed during lockdowns have differed between different countries[89], but common features were cancellation of public events, closure of public transport and restrictions on internal and international travel, school closure, limits on public gatherings, workplace closure, and stay-at-home orders[89]. In many countries restrictions were gradually relaxed in order to monitor the impact of each stage of reopening, with the effect that lockdowns represent a continuum of measures rather than a binary state[89]. Whilst there is evidence from multiple settings that lockdowns were effective in reducing infection rates, the optimal combination of restrictions to be imposed in lockdown is unknown[90]. The most robust methodology to evaluate the impact of different restrictions on SARS-CoV-2 transmission would be in cluster randomised trials, but randomisation would be highly unlikely to be acceptable to the public. Consequently, there is only limited evidence from observational studies. These suggest that school closure, workplace closure, and stay-at-home orders do reduce transmission[91].

The first lockdown was introduced in Wuhan on 23 January 2020 and lasted approximately 12 weeks. The lockdown was successful in controlling the Wuhan outbreak, with modelled estimates of R declining from 2.35 to 1.05 within a week of the start of lockdown[92]. Additional modelling studies suggest that the lockdown was effective in preventing further spread across China[93]. One year on from the lockdown, China had recorded under 100,000 SARS-CoV-2 infections and under 5,000 COVID-19 deaths in total[94]. Although infections were likely to be under

detected in the early pandemic, per capita China has had fewer infections and deaths than most high-income countries[95].

Most countries initiated their first lockdown between late February 2020 and mid-March 2020. The circumstances of initiation of lockdowns varied significantly. For example, lockdown started on 26 March 2020 in New Zealand when the country had recorded just 283 SARS-CoV-2 cases in total[16]. In contrast, restrictions were announced on 23 March 2020 in the UK when the country's health system was already coming under significant pressure; by 27 March 2020 (first available data) there were 7,267 patients admitted in hospital with COVID-19[13]. Subsequent modelling suggested that commencing the lockdown two weeks earlier could have prevented between 26,000 and 43,000 deaths[96]. A report from the House of Commons Health and Social Care, and Science and Technology Committees was critical of delay in implementation of social restrictions by the UK Government, whilst recognising uncertainty in what would have been the impact of an earlier lockdown on infection rates later in 2020[97].

Although lockdowns were effective in reducing SARS-CoV-2 infection[98,99], these had to be traded off against disruption of normal social patterns by lockdowns can cause significant social and economic harms. Whilst lockdowns are intended to protect hospitals from being overwhelmed by COVID-19 admissions, they can also result in severe disruption to elective treatment, including cancer care[100-102]. People may be hesitant to seek medical care for non-COVID conditions during lockdowns, resulting in delayed presentations with advanced disease. Closure of non-essential businesses results in economic losses; UK gross domestic product decreased by 9.9% in 2020, whilst the unemployment rate increased from 3.8% to 5.1%. Lockdowns may also have unintended negative impacts on health behaviours, for

example, lockdowns have been associated with decreased exercise[103] and increased alcohol consumption[104].

1.2.2 SARS-CoV-2 variants

The SARS-CoV-2 virus has a ribonucleic acid (RNA) genome. During the replication process viruses can develop mutations in the RNA, producing variants of the original virus. Some mutations may provide a particular variant with advantage over previous variants, with the result that this new variant becomes dominant.

Variants can develop characteristics that increase population risk such as increased transmissibility, immune evasion (both natural and vaccine derived immunity), and increased severity. Therefore, variants have the potential to both increase the number of people who get infected and also to increase disease severity.

Public health agencies can designate new variants as variants of interest (mutations that could result in increased population risk) or variants of concern (variants for which there is real-world evidence of increased population risk)[105]. To date, the World Health Organisation has designated five variants of concern: Alpha (designated in December 2020), Beta (December 2020), Gamma (January 2021), Delta (May 2021), and Omicron (November 2021)[106].

The Alpha variant was first identified in the UK in late 2020 and it was found to be 43-90% more transmissible than the original SARS-CoV-2 virus. Transmissibility of the Beta variant was similar to Alpha, but it was associated with moderate evasion of vaccine-derived immunity and high evasion of naturally-acquired immunity[107]. The Delta variant was found to be around 64% more transmissible than Alpha and to have increased disease severity compared to Alpha[108].

In some countries the emergence of these variants can be distinguished as separate waves of infection. For example, in South Africa there had been four well defined COVID-19 waves by January 2022[109], with each attributable to a different variant. Differences in when variants became dominant in different geographic areas, as well as differences in the application of lockdowns and other control measures, explain why different countries have experienced COVID-19 waves at different points in time.

1.2.2.1 Omicron variant

The Omicron variant was first identified in Botswana in November 2021[110]. It rapidly spread across the world, with countries across all continents reporting a majority of sequenced SARS-CoV-2 samples to be Omicron in the two weeks to 27 December 2021: South Africa (99% of all sequenced samples were Omicron), Canada (75%), Thailand (74%), UK (71%), Colombia (68%), Australia (53%)[16]. In the two weeks to 7 February 2022, Omicron accounted for >90% of all SARS-CoV-2 infections in all countries reporting on SARS-CoV-2 variants except for Kazakhstan (42% of all sequenced samples were Omicron) and Vietnam (56%)[16].

Omicron was found to have increased immune evasion compared to Delta[111]. A review of estimates for R0 for the initial Omicron strain (subsequently termed BA.1) reported a mean value of 9.5[112]. The subsequent BA.2 and BA.4/5 sub lineages have also been determined to have growth advantages over BA.1, meaning that that there is likely to be a further increase in the rate of spread of SARS-CoV-2 infection[113].

Early data on Omicron severity was collected in South Africa, which was first to experience a major Omicron wave. A cohort study based on linked national datasets

from South Africa found that patients with S-gene target failure (SGTF, a proxy for identifying the Omicron variant) had significantly lower odds of severe disease than patients treated during the earlier Delta wave (62.5% versus 23.4%)[114]. A further study from South Africa confirmed that the Omicron variant was associated with a lower rate of severe disease, lower rate of hospitalization, and lower case fatality rate than the previous variants[115]. These findings were supported by an analysis of ZOE app data from the UK which found lower hospital admission rates during the Omicron wave than the Delta wave (1.9% versus 2.6%)[116].

Further sub lineages have emerged within the Omicron 'family'. Aside from BA.1 the most widespread sub lineage is BA.2[117]; data from South Africa suggests that there is no significant difference in severe illness or hospitalization between BA.1 and BA.2[118].

1.2.2.2 Future variants

Evolution of further SARS-CoV-2 variants is thought to be likely[119,120]. The UK Scientific Advisory Group for Emergencies (SAGE) published a report exploring the possibilities for future SARS-CoV-2 virus evolution[119]. Although it is not possible to precisely predict the characteristics of future variants, SAGE outlined several scenarios and rated their likelihood and potential impact (Table 1.2).

Table 1.2: SAGE scenarios for future SARS-CoV-2 variant evolution

Scenario	Likelihood	Impact
A variant that causes severe disease in a greater proportion of the population	Possible	High
A variant that evades current vaccines (e.g. antigenic shift or drift)	Likely	Medium
Variant resistant to anti-viral drug treatments	Likely	Medium
Variants with decreasing virulence	Possible in the long-term	Reduced harm

Source: Scientific Advisory Group for Emergencies[119]

Based on the SAGE scenarios it seems that new SARS-CoV-2 variant are likely to continue to emerge for the foreseeable future, with the potential that some may acquire characteristics that result in increased severe disease and mortality, perhaps to levels observed during the first COVID-19 wave.

1.2.3 SARS-CoV-2 vaccines

The aim of SARS-CoV-2 vaccination is to achieve vaccine derived immunity which reduces the risk of severe COVID-19 and death. An ideal vaccine would also provide sterilising immunity, meaning that they would prevent not only severe disease but also infection and therefore eliminate the possibility of transmission.

As of 12 July 2022, nine SARS-CoV-2 vaccines have been approved by a regulatory authority recognised by the WHO and have completed the WHO Emergency Use Listing (EUL) Procedure (Table 1.3)[121]. There are several additional vaccines in use globally that have not yet completed the WHO EUL procedure, such as the Sputnik vaccine[122].

Table 1.3: Vaccines approved under the WHO Emergency Use Listing Procedure

Company	Vaccine (Trade name)	Vaccine type	Number of doses in a full course	Date WHO EUL procedure finalised
Pfizer–BioNTech	BNT162b2 (Comirnaty)	mRNA	2	December 2020
Oxford–AstraZeneca	ChAdOx1 (Covishield)	Viral vector	2	February 2021
Moderna	mRNA-1273 (Spikevax)	mRNA	2	April 2021
Sinopharm	BBIBP-CorV	Inactivated	2	May 2021
Janssen	Ad26.CoV2.S (Jcovden)	Viral vector	1	June 2021
Sinovac	CoronaVac	Inactivated	2	June 2021
Bharat Biotech	Covaxin	Inactivated	2	November 2021
Novavax	Nuvaxovid (Covovax)	Inactivated	2	December 2021
CanSino	AD5-nCOV (Convidecia)	Viral vector	1	May 2022

Broadly, the vaccine types are messenger RNA (mRNA) vaccines, viral vector vaccines, and inactivated vaccines. The mRNA vaccines contain SARS-CoV-2

antigen-encoding mRNA that is delivered into immune cells[123]. This mRNA is used by the cells to produce protein (antigen) derived from the SARS-CoV-2 virus and this elicits an immune response. The Pfizer-BioNTech and Moderna vaccines are based on mRNA encoding the SARS-CoV-2 spike protein.

Viral vector vaccines are viruses that are able to infect human cells that have been genetically engineered to include deoxyribonucleic acid (DNA) encoding SARS-CoV-2 antigens[123]. Following inoculation, the viral vector infects human cells and the DNA is transcribed in to SARS-CoV-2-derived proteins that elicit an immune response. For example, the Oxford-AstraZeneca vaccine is based on the chimpanzee adenovirus ChAdOx1 and contained the coding sequence of SARS-CoV-2 spike protein[124]. The Janssen and CanSino vaccines also target the spike protein[123].

Inactivated vaccines contain either the whole SARS-CoV-2 virus (whole pathogen inactivated vaccine) or a part of the SARS-CoV-2 virus required to elicit an immune response (subunit vaccine). For example, the Sinopharm vaccine is based on the 19nCoV-CDC-Tan-HB02 viral strain which was inactivated[125].

Several SARS-CoV-2 variants have emerged with mutations to the spike proteins, including Delta[126] . Future mutations to the spike protein could result in immune escape, but it may be possible to redesign mRNA vaccines to target these new variants[127].

1.2.3.1 Evidence base for SARS-CoV-2 vaccination

The effectiveness of SARS-CoV-2 vaccines was initially evaluated within RCTs. A large number of trials have been completed evaluating the different vaccines. For example, 23,848 participants were enrolled across four RCTs evaluating the Oxford-AstraZeneca vaccine; an interim analysis found overall vaccine effectiveness to be

70.4%[128]. A total of 43,548 people were randomised to a RCT evaluating the Pfizer-BioNTech vaccine (two doses administered 21 days apart)[129]. This trial found the vaccine to be 95% effective in preventing COVID-19. A RCT evaluating the Moderna vaccine enrolled 44,325 participants found vaccine effectiveness against severe to critical COVID-19 to be 76.7% at 14-days following vaccination (single dose) and onwards[130]. A key insight from these early studies was that the protective effect of vaccination was only observed after around 14 days following the second dose[129,130].

Although well conducted RCTs provided robust evidence for the effectiveness of the various vaccines, RCTs have several disadvantages. Firstly, there are important subgroups (e.g. immunosuppressed patients, pregnant patients) for whom evidence from RCTs in the general population may not be generalisable. Secondly, RCTs are conducted in specific geographic locations at a point in time, so there may be uncertainties over how generalisable such data are to other settings which may have different levels of previous SARS-CoV-2 infection, different baseline SARS-CoV-2 prevalence rates, or different non-pharmaceutical interventions in place. In particular, most RCTs were conducted when either the original SARS-CoV-2 virus or the Alpha variant were dominant, so such data may not be valid in the period of Omicron dominance. Thirdly, the primary endpoints in RCTs are based on relatively short follow-up, in order to release data as rapidly as possible; longer-term follow-up is required to address issues around immune waning and the benefits of booster vaccinations. Fourthly, as the pandemic progresses new hypotheses may be identified, such as the benefit of mix-and-matching different vaccines for initial and booster vaccinations. Due to logistical and financial constraints, it would be difficult to conduct adequately powered RCTs to address these wide-ranging evidence gaps.

When RCTs are either impractical or unavailable, insights may be gained from real-world observational evidence. Such analyses can be based on routinely collected data by public health agencies. For example, although increasing age is associated with increased risk of severe COVID-19, under 10% in the initial Oxford-AstraZeneca trials were aged 70 years and over, making sub-group analysis of vaccine effectiveness for this high-risk group difficult[128]. However, this evidence gap was addressed by using UK National Immunisation Management System data for 156,930 adults aged 70 years and over[131]. In this analysis both the Pfizer-BioNTech and Oxford-AstraZeneca vaccines were found to be effective in older adults.

Other observational studies have provided insights in to immune waning and the role of vaccine booster doses. A meta-analysis of predominantly observational data determined that the effectiveness of vaccines begins diminished from one to six months after vaccination[132]. Analyses of ZOE app data in the UK found that vaccine booster doses significantly increased vaccine effectiveness[133]. A limitation of the ZOE data is that the dataset is based on symptom and test data crowd-sourced from the public, so this data is not independently verified.

The UK Health Security Agency (UKHSA) published consensus vaccine effectiveness estimates for the Oxford-AstraZeneca, PfizerBioNTech, and Moderna vaccines, based on both UK and international data[134]. These estimates suggest that vaccines are more effective in preventing severe COVID-19 requiring hospitalisation than overall symptomatic infections. No vaccines have achieved fully sterilising immunity, as they only reduce all infections by 30-45% at most. Vaccine effectiveness wanes over time, and although administration of a booster vaccine temporarily increases effectiveness, this may also wane (Table 1.4).

Table 1.4: Summary of UKHSA consensus vaccine effectiveness estimates

Outcome	Full course (two doses)			Booster dose		
	0-3 months	4-6 months	>6 months	0-3 months	4-6 months	>6 months
All infection	30%	0-30%	0-30%	45%	15%	0%
Symptomatic infection	40-55%	20-30%	5-15%	60-65%	40-45%	10%
Hospitalisation	85-90%	70-80%	55-90%	85-95%	85%	70%

The table shows range of UKHSA central estimates for the Oxford-AstraZeneca, PfizerBioNTech, and Moderna vaccine effectiveness[134]

1.2.3.2 SARS-CoV-2 vaccine global rollout

In early 2021, the Economist Intelligence Unit projected that vaccination of most adults in high-income countries would be achieved by mid-2022, but this would not be achieved in low-income countries until 2024, if at all[135]. The COVID-19 Vaccines Global Access (COVAX) initiative was established by the WHO alongside partners to provide economies of scale to support LMICs to procure SARS-CoV-2 vaccines[136,137]. By late 2020 COVAX had secured funding and contracts to procure 500 million vaccine doses[136]. By 14 July 2022, 1.4 billion doses has been shipped to LMICs[138]. Several logistical factors have determined which vaccines have been distributed to which global regions, including vaccine storage requirements; some vaccines require ultra-low temperature freezers (-70 degrees Celsius) whereas others Oxford-AstraZeneca can be stored in a refrigerator. In addition, the cost of different vaccines had varied widely; the Oxford-AstraZeneca vaccine was marketed at $6 per dose, whilst the Moderna vaccine was marketed at up to $74 per course[136]. These factors have resulted in Oxford-AstraZeneca being widely used in LMICs[137].

The UK approved the Pfizer/BioNTech vaccine on 2 December 2020, with the first-ever SARS-CoV-2 dose administered outside of a clinical trial setting on 8 December 2020 in Coventry, UK[139]. By 8 July 2022, 5.3 billion people (66.5% of the global population) had received at least one SARS-CoV-2 vaccine dose[16]. Despite the

COVAX initiative, there are significant global disparities in access to vaccination; whereas over 95% of people in Brunei, Qatar, and the United Arab Emirates have been vaccinated, 2% or fewer have been vaccinated in Burundi, Haiti, and Yemen[16]. Access to SARS-CoV-2 vaccines is lowest in low-income and lower-middle income countries (Table 1.5).

Table 1.5: Global distribution of SARS-CoV-2 vaccines and COVID-19 deaths prevented

Country income	Proportion of population that had received at least one vaccine dose		COVID-19 deaths averted by vaccination up to 8 Dec 2021	
	8 Dec 2021	8 Jul 2022	Total	Per 10000 people
Low	5.9%	19.1%*	0.2 million	2.7
Lower-middle	45.0%	61.7%	7.4 million	22.2
Upper-middle	75.9%	83.0%	4.2 million	37.0
High	73.3%	78.3%	8.0 million	66.2
World	55.2%	66.5%	19.8 million	31.2

*Data on proportion of population that had received at least one vaccine dose extracted from Our World in Data[16] and data on COVID-19 deaths averted by vaccination taken from Watson et al[140]. *Most recent available data for low-income countries is from 30 June 2022*

Inequalities in global SARS-CoV-2 vaccination distribution is reflected in the differential impact of vaccination on COVID-19 deaths; of the 19.8 million estimated COVID-19 deaths averted in the 12 months from the start of the global vaccination rollout, a majority were in high-income or upper-middle income countries (Table 1.5)[140]. On a per capita basis, the number of deaths averted in high-income countries was more than 20-fold greater than in low-income countries (66.2 versus 2.7 per 10,000 population).

Interpretation of global vaccination uptake statistics is complicated by the statistics not being age-adjusted. As SARS-CoV-2 case fatality rates increase with age[81], the number needed to vaccinate to prevent COVID-19 deaths is lower (more favourable) for older than younger people. This is illustrated in Table 1.6 based on a modelling

study I completed[141]. In order to maximise the number of lives saved through vaccination, countries such as the UK prioritised vaccination rollouts based on age, with older people being vaccinated first[142]. In addition, as severe COVID-19 is rare in children, there is debate whether the benefits of SARS-CoV-2 vaccination in children outweighs the associated risks and opportunity costs[143,144]. Consequently, SARS-CoV-2 vaccination uptake rates should be age-stratified to enable meaningful comparisons; however, these data are not readily available at a global level.

Table 1.6: Modelled estimates for number needed to vaccinate with SARS-CoV-2 vaccination to prevent one COVID-19 death over 1 year

SARS-CoV-2 incidence	Age		
	18–49 years	50–69 years	≥70 years
Low	3,378,555	222,028	31,692
Medium	196,131	12,889	1,840
High	43,088	2,832	404

The number needed to vaccinate is related to SARS-CoV-2 incidence; the number needed to vaccinate decreasing as SARS-CoV-2 incidence increases. For these estimates, countries were split into tertiles by overall SARS-CoV-2 incidence in 2020 and median SARS-CoV-2 incidence rates were calculated for each tertile (low, medium, high). Estimates were only produced for adults.

1.2.4 Summary of SARS-CoV-2 characteristics relevant to surgical care

Key characteristics of SARS-CoV-2 and their implications for surgical care are described in Table 1.7.

Table 1.7: Key characteristics of SARS-CoV-2 and relevance to surgical care

SARS-CoV-2 characteristic	Relevance to surgical care	Elaboration
Asymptomatic infection	Patients presenting to surgical services may be infected with SARS-CoV-2 even if they do not have symptoms	Routine preoperative assessment (history taking, examination, routine blood tests, radiological investigations) is insufficient to identify infected patients. The only sensitive test for SARS-CoV-2 infection is RT-PCR
Pre-symptomatic and asymptomatic transmission	Transmission is possible even if an infected person is not currently symptomatic	Individuals should be assumed to be potentially infectious unless they have been tested for SARS-CoV-2
High transmissibility (particularly of the Omicron variant)	There is a high risk of cross-infection between patients, and between patients and surgical staff	Mitigation measures are required to reduce the risk of cross-infection in surgical settings
Airborne transmission	Patients and staff in surgical settings are at risk of airborne transmission even if they are not close contacts of SARS-CoV-2 cases	Airborne mitigation measures are needed to reduce the risk of cross-infection in surgical settings
Emergence of new variants of concern	SARS-CoV-2 epidemiology may change over time	The transmissibility, immune evasiveness, and severity of new variants of concern may be different to current variants. All recommendations for management of SARS-CoV-2 in surgical care must be reviewed when new variants of concern emerge

1.3 Surgery during the COVID-19 pandemic

1.3.1 Evidence of impact of previous outbreaks on surgical services

In March 2020, Italian surgeons with early experience of managing surgical services during the SARS-CoV-2 pandemic identified several key challenges, including: disruption to elective care due to the cancellation of non-urgent surgeries and other activities such as cancer multidisciplinary meetings, a lack of data regarding the safety of surgery in patients with perioperative SARS-CoV-2 infection, and a lack of data regarding the risk of SARS-CoV-2 transmission during surgical procedures[145]. In the earliest stages of the pandemic some of the best available evidence to address these challenges was from previous infectious disease outbreaks. A

summary of the available evidence concerning surgical care during WHO designated Public Health Emergencies of International Concern is presented below. In addition, evidence is presented from previous coronavirus outbreaks that were not designated Public Health Emergencies of International Concern; these relate to Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-1) and Middle East respiratory syndrome–related coronavirus (MERS-CoV).

1.3.1.1 Severe Acute Respiratory Syndrome Coronavirus (2002)

The SARS-CoV-1 virus is a coronavirus that was first identified in April 2003 as being the agent responsible for Severe Acute Respiratory Syndrome (SARS)[146]. The first SARS outbreak started in Guangdong, China; the first case was retrospectively traced as having had onset of illness on 16 November 2002[147]. The SARS outbreak was characterised by febrile respiratory illness and atypical pneumonia[148]. The SARS-CoV-1 virus has a median incubation period of 4-5 days, with viral shedding maximal on day 10 after illness onset[149]. The main mode of transmission is by infected respiratory droplets and the estimated R0 value is 3[149].

By February 2003, cases were reported in Hong Kong. In March 2003 the WHO issued a global alert for SARS[150]. In total in 2002-3 there were 8,437 SARS cases across 32 countries and 813 deaths (9.6% case fatality rate)[148].

Clinical reports of perioperative SARS are limited to: a case report of a patient in Hong Kong who died after developing SARS following fracture surgery[151]; two case series from Hong Kong, each reporting two SARS patients who underwent surgical tracheostomy[152,153]; a case series from Canada of two SARS patients who underwent surgical tracheostomies and one SARS patient who died following an emergency laparotomy[154]; a case series from Singapore of ten SARS patients who

underwent surgery, of whom three required intensive care and two died[155]; and a report from Singapore of 41 SARS patients having undergone surgery, although clinical details were not provided[156].

The risks of SARS-CoV-1 transmission were particularly highlighted[154]. Several reports described the infection prevention and control measures that their units implemented to reduce the risk of SARS-CoV-1 spread, including the use of personal protective equipment and improvements to ventilation systems to reduce airborne viral spread[156,157]. One report described how an operating theatre complex was modified to ensure segregation of SARS and non-SARS patients to reduce the risk of cross-infection[156].

Several studies evaluated the impact of the SARS epidemic on provision of surgical services. A single centre study from a colorectal surgery unit in Hong Kong found that during the epidemic, emergency surgery volume was reduced by 45% and elective inpatient surgery volume was reduced by 58%, although cancer surgery was relatively spared with only a 16% reduction[158]. The waiting time for minor elective colorectal procedures increased from 11 months pre-epidemic to 18 months post-epidemic. Colonoscopy volume during the epidemic was also decreased by 48%, resulting in a nine week increase in waiting times for non-urgent colonoscopies. Another single centre study from an otolaryngology unit in Hong Kong found that clinic attendances were reduced by 59% and elective surgeries by 79% during the epidemic[159]. A regional population-level study from Greater Toronto, Canada found a 10% reduction in medical admission and a 22% reduction in elective surgeries during the early phase of the epidemic[160].

1.3.1.2 H1N1 influenza pandemic (2009)

The 2009 H1N1 influenza pandemic was the first influenza pandemic since the 1977-79 H1N1 "Russian flu" pandemic. It was first identified in Mexico. It is a respiratory infection that can result in severe complications such as ARDS. The 2009 H1N1 influenza strain had an estimated R0 of 1.5[161].

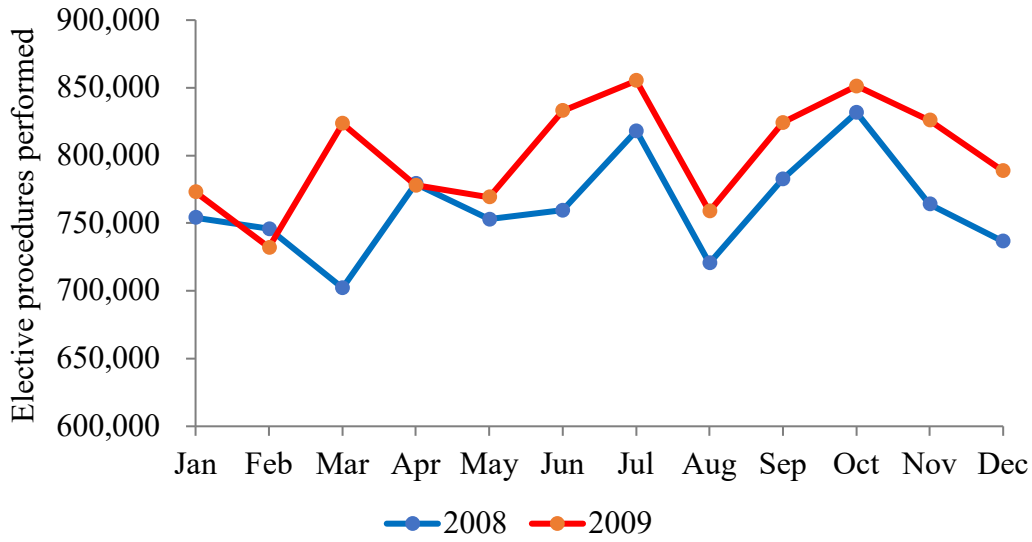
In the United States, in April 2009 to April 2010 there were an estimated 60.8 million cases and 274,304 H1N1 influenza hospitalisations. Globally, the pandemic was estimated to have resulted in around 200,000 respiratory deaths and 80,000 cardiovascular deaths[162,163], with half of these deaths occurring in southeast Asia and Africa. Overall, this was similar to the number of seasonal influenza deaths that would be expected in an average year[162].

Despite the high global prevalence of H1N1 influenza in 2019 there is little published literature on its impact on surgical care. The available evidence is mainly limited to case reports of single cases[164-167] and a case series of two perioperative H1N1 influenza cases[168].

The first two H1N1 influenza cases in the UK were identified on 27 April 2009[169]. In total, 19,995 lab-confirmed H1N1 influenza cases in England in 2009, resulting in 2,427 hospitalisations[170]. There were two peaks of cases and hospitalisations in mid-July 2009 and early November 2009. I have assessed the impact of the H1N1 influenza pandemic on surgical services in England by accessing monthly activity data from NHS Digital for 2008-2009[171]. The number of elective procedures (including surgery, endoscopy, interventional radiology, and medical procedures) completed by NHS England was higher in 2009 than 2008 each month from May to

December (Figure 1.1). This suggests that the H1N1 influenza pandemic did not substantially impact the ability of NHS England to deliver elective procedures.

Figure 1.1: Elective procedures completed in England in 2009-10



1.3.1.3 Middle East respiratory syndrome–related coronavirus (2012)

The MERS-CoV virus is a coronavirus that was first identified in Saudi Arabia in 2012[172]. MERS-CoV is the agent responsible for Middle East respiratory syndrome (MERS). MERS ranges from asymptomatic infection or mild flu-like symptoms to respiratory failure[172]. Most recorded cases have occurred in Saudi Arabia[173]. As of September 2019, there had been 2,468 confirmed MERS cases, and 851 deaths (a 34.5% case fatality rate)[173].

A report was published from Seoul, Republic of Korea, detailing the implementation of infection control protocols and preoperative testing during a hospital MERS-CoV outbreak[174]. The hospital was partially closed, resulting in a reduction in surgical activity. A case report from Bahrain reported the death of a patient who developed MERS following cardiac surgery[175]. A case series from Saudi Arabia reported a

MERS-CoV outbreak on a cardiac surgery ward which result in the deaths of five of six infected postoperative patients[176].

1.3.1.4 Poliovirus (2014)

Poliovirus is predominantly transmitted through the faeco-oral route. Poliovirus causes poliomyelitis, which can result in paralysis and death in a small proportion of cases. Although distribution of poliovirus vaccines has resulted in the eradication of poliovirus in most countries, prior to 2014 several countries remained infected with wild poliovirus: Cameroon, Ethiopia, Israel, Nigeria, Pakistan, and Syria[177]. Concerns regarding international spread of poliovirus from Pakistan to Afghanistan, from Syria to Iraq, and from Cameroon to Equatorial Guinea led the WHO to declare a Public Health Emergency of International Concern, which remains in place[177-179]. However, the absolute number of cases of poliovirus are low. In 2014-21 there were 3,275 cases of paralytic poliomyelitis worldwide[16]. In the period between poliovirus and SARS-CoV-2 being declared Public Health Emergencies of International Concern (2014-19) there are no published reports of poliovirus patients requiring or undergoing surgery.

1.3.1.5 Ebola in West Africa (2014) and the Democratic Republic of Congo (2019)

Ebola virus is transmitted through body fluids including urine, faeces, saliva, and semen, either through direct contact or indirect contact via contaminated objects. However, unlike with SARS-CoV-2 there is no asymptomatic or pre-symptomatic transmission; Ebola virus is only spread by symptomatic individuals. Estimates of R0 for Ebola virus range from 1.5 to 2.5[180]. Healthcare workers are at particular risk of infection, with an estimated 38% of disease transmission in Liberia occurring in hospitals[181] and 8% of Liberian healthcare workers having died by 2015 as a result

of Ebola virus disease[182]. The overall case fatality rate in West Africa in 2014 was 70.8%[183].In 2014-16 the WHO recorded 28,610 Ebola cases and 11,308 Ebola deaths in Guinea, Liberia, and Sierra Leone, and in 2018-20 a total of 3,665 Ebola cases and 2,387 Ebola deaths were recorded in the Democratic Republic of the Congo[184]. However, these are likely to be significant underestimates, as many patients did not seek medical care and died at home[185].

There are no international guidelines on surgical care during Ebola epidemics[186]. Emergency Ebola guidance published by the WHO in January 2015 did not offer any specific recommendations for surgical care[187]. The Spanish Association of Surgeons published a surgical protocol for Ebola in 2015 which focussed on infection prevention and control measures to reduce the risk of disease transmission to surgical staff[188]. For patients with Ebola virus disease, surgery was recommended to be restricted to emergencies where it is not possible to either offer a suitable alternative conservative management strategy or to delay surgery until the patient has recovered from Ebola virus disease.

There are no reports of surgical outcomes in patients who underwent surgery with perioperative Ebola virus disease. However, several reports have investigated the wider impact of Ebola on the provision of surgery. A study across 40 hospitals in Sierra Leone found that between May and October 2014 there was a 70% reduction in hospital admissions and a 50% reduction in major surgeries[189]. Another national survey across Sierra Leone found that in May 2014 to May 2015 there was a 20% reduction in the number of Caesarean sections performed[190]. A further study suggested that there was a shift in Caesarean sections from the private to the public sector[191]. The impact of Ebola was particularly marked at Sierra Leone's main referral hospital, Connaught Hospital; in December 2014 ward admission were 84%

lower and surgical volume 97% lower than in December 2013[192]. Factors contributing to the reduction in surgical volume included the deaths of two surgeons and the introduction of a requirement for preoperative Ebola testing.

A qualitative study evaluated the impact of the Ebola epidemic on surgical staff performing Caesarean sections in Sierra Leone[193]. Caesarean section was identified as the highest priority surgical procedure, but surgical teams often lacked resources, including personal protective equipment and access to Ebola testing to screen patients. This resulted in 'moral dilemma' with staff reporting that they continued to perform surgery despite significant risk of themselves becoming infected.

1.3.1.6 Zika (2016)

The Zika virus is primarily spread by mosquitoes, although it can also be spread through sexual contact, blood transfusion, and vertical mother-to-child transmission[194]. Most people experience asymptomatic or mild infection, though complications can occur such as Guillain-Barré syndrome[195]. The greatest concern with Zika virus is that infection during pregnancy can lead to birth defects such as microcephaly[196]. The declaration of a Public Health Emergency of International Concern was made following the rapid spread of Zika virus in the Americas in 2015 onwards.

There are no published reports presenting real-world data on the impact of zika on surgical care. One review article was published which noted the potential risks of transmission of Zika virus to surgical teams during surgery and also the risk of transmission to patients through perioperative blood transfusions[195].

1.3.1.7 Summary of literature from previous outbreaks

Information from previous outbreaks largely focused on infection prevention and control measures, including those that can be implemented in operating theatre and surgical ward settings to reduce the risk of both patient-patient and patient-staff transmission. This includes studies describing measures to reduce SARS-CoV-1 transmission, a virus presenting similar airborne transmission risks to SARS-CoV-2. However, there are no robust evaluations of the effectiveness of the various measures described in previous literature, and recommendations in previous outbreaks were based on expert opinion.

Data on the impact of perioperative infections in previous outbreaks is restricted to case reports and small case series. The largest study providing outcome data is a case series of ten patients who had perioperative SARS[155]. The methodological limitations of case reports make it impossible to generalise their findings in the context of a pandemic. Firstly, it is not possible to draw causal inference from a single uncontrolled observation[197]; for example, it would be difficult to determine from case reports whether perioperative infection had an impact on patients' postoperative outcomes. Secondly, there is a publication bias with authors choosing to submit and journals choosing to publish what they consider to be interesting, and therefore non-typical, cases. Surveys of case reports published in dental and dermatology journals found that case reports were overwhelmingly likely to present what the authors considered to be 'positive' results[198,199]. Thirdly, patients presented in case reports and small case series are unlikely to be representative of the diverse patient populations who undergo surgery, so any findings from these studies cannot be broadly generalised.

The lack of large, well conducted studies of patients with perioperative infection from previous outbreaks may reflect that most outbreaks did not exceed several tens of thousands of cases, meaning there would have been a relatively small number of infected patients who underwent surgery. The exception was the H1N1 influenza pandemic which caused hundreds of millions of infections globally. It is possible that because H1N1 influenza was not associated with significantly increased mortality compared to seasonal influenza[200], research into the impact of H1N1 influenza on surgical patients was not prioritised.

Data from Hong Kong and Canada (SARS-CoV-1) and Sierra Leone (Ebola virus) indicates that infectious disease outbreaks place significant burdens on health services which can substantially disrupt the provision of both elective and emergency surgery.

1.3.2 Surgical practice during the first COVID-19 wave

1.3.2.1 Early data on safety of surgery in patients with SARS-CoV-2 infection

In the first three months of the pandemic (January to March 2020) three case reports, eight single centre case series, and three multicentre studies were published reporting the management of patients with perioperative SARS-CoV-2 (Table 1.8). These publications were identified by a hand search of reference lists in published systematic reviews of the outcomes of perioperative SARS-CoV-2 infection[201-205].

Table 1.8: Reports of surgery in patients with perioperative SARS-CoV-2 published in January to March 2020

Author	Location & dates[1]	Patients	Postoperative mortality
Single patient case reports			
Wang[206]	Suzhou, China 8 Feb 2020	1 patient (confirmed SARS-CoV-2) who underwent Caesarean section	Patient discharged alive
Qin[207]	Wuhan, China 21 Jan 2020	1 patient (confirmed SARS-CoV-2) who underwent liver transplant	Patient discharged alive
Xia[208]	Wuhan, China 24 Jan 2020	1 patient (confirmed SARS-CoV-2) who underwent Caesarean section	Patient discharged alive
Single centre case series with 2 or more patients			
Aminian[209]	Qom, Iran 8-24 Feb 2020	4 patients (2 confirmed, 2 suspected SARS-CoV-2) who underwent general surgery (n=3) or hysterectomy (n=1)	75% (3/4)
Chen[210]	Wuhan, China 20-30 Jan 2020	9 patients (all confirmed SARS-CoV-2) who underwent Caesarean section	0% (0/9)
Chen[211]	Wuhan, China 30 Jan - 23 Feb 2020	17 patients who underwent Caesarean section. Unclear how many patients had confirmed SARS-CoV-2	0% (0/17)
He[212]	Wuhan, China Dates not reported	4 patients (2 confirmed, 2 suspected SARS-CoV-2) who underwent aortic dissection repair	Not reported
Li[213]	Wuhan, China 1 Jan - 20 Feb 2020	13 patients (12 confirmed, 1 suspected SARS-CoV-2) who underwent thoracic surgery	39% (5/13)
Liu[214]	Wuhan, China 29 Jan - 15 Feb 2020	10 patients (confirmed SARS-CoV-2) who underwent Caesarean section	0% (0/10)
Tian[215]	Wuhan, China Dates not reported	2 patients (1 confirmed, 1 suspected SARS-CoV-2) who underwent lung lobectomies	50% (1/2)
Zhong[216]	Wuhan, China 1 Jan - 14 Feb 2020	49 patients (13 confirmed, 36 suspected SARS-CoV-2) who underwent Caesarean section (n=45) or lower limb surgery (n=4)	0% (0/49)
Multicentre case series			
Zhao[217]	Four hospitals in Wuhan, China 23-32 Jan 2020	37 patients (5 confirmed, 32 suspected SARS-CoV-2) who underwent emergency surgery	Not reported
Zhang[218]	Three hospitals in Hubei, China 1 Jan – 20 Mar 2020	89 patients (all confirmed SARS-CoV-2) who underwent Caesarean section	Not reported
Zhu[219]	Five hospitals in Hubei, China 20 Jan - 5 Feb 2020	10 patients (all confirmed SARS-CoV-2) who underwent Caesarean section	0% (0/7)

Patients classified as having confirmed SARS-CoV-2 if they had a positive RT-PCR test result for SARS-CoV-2. [1]Dates of surgery presented if available, otherwise dates of hospital admission, or patient inclusion window dates are recorded as presented by authors.

Of the reports available up to the end of March 2020, 13 of 14 were from China, limiting generalisability of the data to other countries. The largest study providing mortality data included only 49 patients[216]. Of the 14 reports, eight focussed on Caesarean section, possibly reflecting that this is a common emergency procedure that cannot be delayed. However, data dominated by Caesarean section may not be generalisable to all types of surgery, as compared to other emergency surgeries, Caesarean section is a low-risk procedure, even in low resource settings[220].

Mortality ranged from 0% to 75% in individual reports. The pooled mortality from the available reports was 7.9% (9/114), with a 95% confidence interval that indicates that mortality could be between 3.7% and 14.5%. Such a wide range makes it difficult to draw firm conclusions about the safety of surgery in patients with SARS-CoV-2 infection. This uncertainty may result from several factors. Firstly, there may be a publication bias, with a tendency for authors to choose to publish reports with either very low or very high mortality. Secondly, whilst some studies only included patients with RT-PCR confirmed SARS-CoV-2, others included patients with suspected SARS-CoV-2 who may not have a positive RT-PCR test result. If some suspected SARS-CoV-2 cases were misdiagnoses, this could lead to underestimation of mortality in some studies by inflating the denominator for total SARS-CoV-2 cases with patients who do not have SARS-CoV-2. Thirdly, there is variability in how perioperative SARS-CoV-2 exposure is defined. I have tried to only include studies presenting data for patients with a positive SARS-CoV-2 diagnosis within 30 days of surgery, but timing of diagnosis is not clearly reported in all studies; some studies have included postoperative SARS-CoV-2 cases where a SARS-CoV-2 diagnosis was made several months after the date of surgery. Fourthly, there is variability in the duration of follow-up. Some studies have limited follow-up to inpatient outcomes, some have reported 30-day outcomes, and some have not clearly explained the duration of follow-up. Since mortality increases with length of follow-up, this may explain some differences in outcomes between studies.

In April to May 2020 a further seven multicentre studies were published (Table 1.9). Although China accounted for the largest share of these studies (3 of 7), four other countries also contributed data (France, Italy, Spain, United States). Amongst the studies I identified, four of seven related to fracture surgery. In individual reports,

mortality ranges from 0% to 33%. The pooled mortality was 20.6% (28/136) with a 95% confidence interval of 14.1% to 28.4%.

Table 1.9: Multicenter reports of surgery in patients with perioperative SARS-CoV-2 published in April to May 2020

Author	Location & dates[1]	Patients	Postoperative mortality
Dai[221]	14 hospitals in Wuhan, China 1 Jan – 24 Feb	8 patients (all confirmed SARS-CoV-2) undergoing cancer surgery	25% (2/8)
Egol[222]	7 hospitals in New York City, United States 1 Feb – 15 Apr 2020	14 patients (all suspected SARS-CoV-2) who underwent hip fracture surgery[2]	14% (2/14)
Lei[223]	4 hospitals in Wuhan, China 1 Jan - 5 Feb 2020	34 patients who underwent surgery. Unclear how many patients had confirmed SARS-CoV-2	21% (7/34)
Luong-Nguyen[224]	3 hospitals in Paris, France 1 Mar - 3 Apr 2020	5 patients (all confirmed SARS-CoV-2) who underwent gastrointestinal surgery	0% (0/5)
Maniscalco[225]	2 hospitals in Italy 22 Feb - 18 Apr 2020	64 patients (32 confirmed, 32 suspected SARS-CoV-2) who underwent proximal femoral fracture surgery	2% (14/64)
Mi[226]	8 hospitals in Hubei, China 9 Jan – 21 Jan 2020	3 patients (2 confirmed, 1 suspected SARS-CoV-2) who underwent fracture surgery	33% (1/3)
Muñoz Vives[227]	13 hospitals in Spain 14 Mar - 4 Apr 2020	18 patients (all confirmed SARS-CoV-2) who underwent surgery for proximal hip fracture[3]	11% (2/18)

Patients classified as having confirmed SARS-CoV-2 if they had a positive RT-PCR test result for SARS-CoV-2. Some studies included either non-operated or historical comparator data, so there may be fewer patients reported as having surgery with perioperative SARS-CoV-2 than the number of participating hospitals. Where possible, data were only extracted for patients with SARS-CoV-2 infection within 30 days of surgery. [1]Dates of surgery presented if available, otherwise dates of hospital admission, or patient inclusion window dates as presented by authors are recorded. [2]The study included 17 patients with confirmed SARS-CoV-2 infection but it was not possible to extract data for the patients with confirmed infection who underwent surgery. [3]The denominator for patients who underwent surgery and tested positive for SARS-CoV-2 is taken as 16 based on the data presented, although it is not clarified by the authors that all patients who tested positive and survived had undergone surgery

Although the multicentre studies published in April to May 2020 from five different countries should provide more generalisable data than the earlier, predominantly single centre, reports from China, the absolute number of patients included was low, resulting in a wide confidence interval when data were pooled. These studies were

still subject to many of the methodological shortcomings of earlier reports, for example, inclusion of patients who did not have RT-PCR confirmation of infection, and inconsistency of follow-up and outcome measurement.

I have focussed on summarising reporting of mortality because this is the most widely reported outcome. The studies are inconsistent in what other outcomes are reported. Outcomes such as pneumonia and ARDS are not defined in most studies, making their interpretation difficult. The utility of the available studies is further limited by a lack of information to inform identification of patients at high risk of complications or death. One study did analyse factors associated with major postoperative complications, but only found postoperative day 1 white blood cell count to be associated with complications[222]. This is likely to reflect the study's small sample size which resulted in analyses being underpowered.

Since I have not undertaken a formal systematic review, it is possible that I have missed high quality studies published in this period.

1.3.2.2 Early guidance for surgical practice during the pandemic

A large number of clinical guidance documents were published in January to March 2020. This included recommendations for how to arrange operating theatre infection control and prevention processes to minimise the risk of cross-infection[228], guidance on anaesthetic techniques for patients with SARS-CoV-2 infection[229], disease-specific treatment protocols for implementation during the pandemic[230,231], and procedure-specific recommendations[232]. Many early publications were by individual clinicians with early experience of management of surgical services during the COVID-19 pandemic[229-231,233]. In March 2020, national surgical associations and colleges began publishing clinical guidance[234-236]. However, given the lack of high

quality studies exploring the impact of COVID-19 on surgical care, most recommendations were based on expert opinion rather than robust evidence.

In response to requests from colleagues across the NIHR-GSU network (see section 2.1.2) for clearer guidance during the early pandemic, in mid-March 2020 I co-led the preparation of a global guideline for surgical care during the COVID-19 pandemic[203]. Whereas previous guidance published up until that time had been informed by single-centre experience, our guideline was informed by multiple data sources. This included a scoping review literature to identify on the impact of previous pandemics on surgical services, a scoping review of the COVID-19 literature available at the time, and key informant interviews with surgeons from Hong Kong, Italy, Republic of Korea, Singapore, and Spain who had had early experience of managing surgical services during the pandemic. The final recommendations we made are summarised in Table 1.10.

Table 1.10: Initial recommendations for surgical care during the pandemic

Domain	Recommendations
Prepare a pandemic response plan for surgical services	All hospitals should prepare context-specific pandemic plans that can be implemented as soon as COVID-19 cases are identified locally. Plans should include all surgical specialties and both elective and emergency services
Ensure staff are trained to deliver surgery safely during pandemic	Practice drills with experienced infection control teams, including: patient transfers between different areas of the hospital; donning and doffing personal protection equipment; recognizing and managing COVID-19 infection
Support hospital response to COVID-19	Reduce non-urgent activities, including outpatient clinics, endoscopy and non-cancer elective operations. Plan how to continue delivering urgent elective surgery safely, for example for patients with cancer
Agree a team-based approach for running emergency services	Anticipate increased pressure on emergency surgical services during the pandemic, with staff absence owing to illness or quarantine. Establish team structures that minimize cross-contamination and risk of nosocomial infection
Recognize and manage COVID-19 infection	Have a high index of suspicion for COVID-19 infection in both emergency surgical admissions and patients who develop postoperative respiratory complications. Ensure there are arrangements in place for patients with suspected COVID-19 to be isolated and tested

Table reproduced from: COVIDSurg Collaborative. *Global guidance for surgical care during the COVID-19 pandemic*. Br J Surg. 2020 Aug;107(9):1097-1103.

Although we took a more systematic approach to developing our guideline than other groups, by collaborating with surgeons across diverse international settings, our recommendations were based on expert opinion only. The guidance document highlighted that there were many uncertainties regarding the care of surgical patients during the pandemic and that there was a need for high-quality multicentre research to inform future recommendations. Key uncertainties included the need for research regarding the impact of perioperative SARS-CoV-2 infection on patient outcomes, strategies to safely provide elective surgery during the pandemic, and the role of non-operative management strategies to reduce the need for surgery during the pandemic.

Despite its limitations, when our guidance was published on 15 April 2020 in the *BJS*[203] it became a key resource for surgeons during the early pandemic; for several months it was the most read article on the *BJS* website and as of 17 July 2022 it had 545 citations on Google Scholar.

1.3.2.3 Impact of the first COVID-19 wave on surgical activity

Studies from regions impacted by the SARS and Ebola virus epidemics identified that large-scale infectious disease outbreaks were associated with a reduction in the provision of outpatient surgical clinics, diagnostic tests such as endoscopies, and elective surgeries. Early guidance in 2020 also recommended that non-urgent surgical activities should be reduced during the COVID-19 pandemic. The rationale for this was to both maintain patient safety and to support the wider hospital response to the pandemic.

During the early pandemic there was no robust evidence to inform the impact of perioperative SARS-CoV-2 on surgical patient outcomes (see section 1.2.2.2), but

reports of COVID-19 patient outcomes in medical patients suggested there might be substantial morbidity and mortality associated with infection. Admitting elective patients to hospitals treating medical patients for COVID-19 would place them at risk of hospital acquired SARS-CoV-2 and consequently increased risk of adverse events, including postoperative pulmonary complications and death.

Hospital capacity to deliver safe elective surgical services was further limited by the diversion of surgical resources to support the care of medical COVID-19 patients. For example, surgical ward and critical care beds were used in many hospitals to accommodate surges in admissions of COVID-19 patients and some hospitals repurposed theatre suites as overflow intensive care units. In some hospitals junior surgical staff were required to support emergency departments or medical wards, whilst anaesthetists and theatre staff were redeployed to support expanded intensive care units to care for COVID-19 patients with respiratory failure.

On 17 March the Chief Executive of NHS England wrote to all NHS hospitals in England to advise them stop all elective surgery in order to focus on the demands of an expected surge of COVID-19 medical admissions[237]. Similar mandates were issued by governments in other countries[238-240].

Cancelling elective surgery at scale would be likely to result in substantial impacts on patients, as delayed surgical treatment could result in worsening symptoms and quality of life, and potentially unnecessary deaths. Since few countries have access to real-time surgical volume data, it would be many months before the impact of the pandemic on surgical activity would become established. Therefore, to inform planning for post-pandemic surgical recovery, I led a team to estimate country-level figures for operations cancelled as a result of the pandemic[241]. Overall, we estimated that during elective surgical activity would be reduced by approximately 70% during

lockdowns. Based on a 12-week duration, we estimated that lockdowns would result in the cancellation of 28 million operations globally.

The estimate that there would be a 70% reduction in elective surgical activity in the first 12 weeks of the pandemic, was supported by study using a different modelling methodology. O'Reilly-Shah et al analysed the trend in usage of the "Anesthesiologist" mobile application from October 2018 to June 2020[242]. This is free application is used by over 100,000 anaesthesia providers for tasks such as drug dose calculation. Across 112 countries with available data they calculated a median reduction from baseline use of the application of 73.6%.

An analysis of surgical activity in public hospitals in Brazil found that in the period March to December 2020 there were 928,758 fewer elective operations (69% reduction) compared to what would be expected based on activity in 2019[243].

There was also a reduction in the volume of diagnostic tests performed during the pandemic. In England, the number of diagnostic endoscopies performed was 89% lower in April 2020 than in April 2019[244]. I accessed NHS England's Diagnostic Imaging Dataset to determine the reduction in imaging tests in England[245]. Compared to April 2019, in April 2020 there was a 43% reduction in CT imaging (Figure 1.2), a 57% reduction in magnetic resonance imaging (MRI, Figure 1.3), and a 67% reduction in ultrasound imaging (Figure 1.4). These diagnostic tests are required to diagnose patients with surgical conditions, so a reduction in the volume of diagnostic tests is likely to delay diagnosis and treatment of surgical disease.

Figure 1.2: Computed tomography imaging performed by NHS England in 2019-20

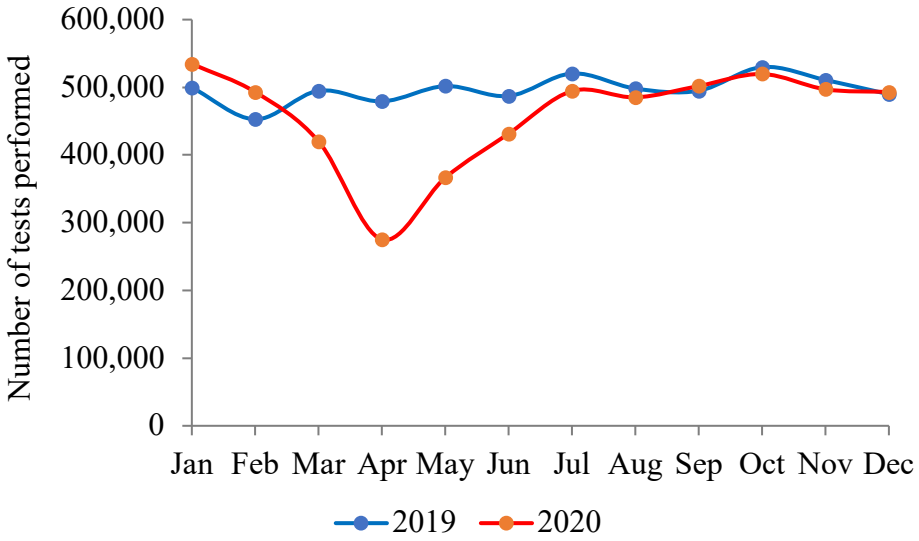


Figure 1.3: Magnetic resonance imaging performed by NHS England in 2019-20

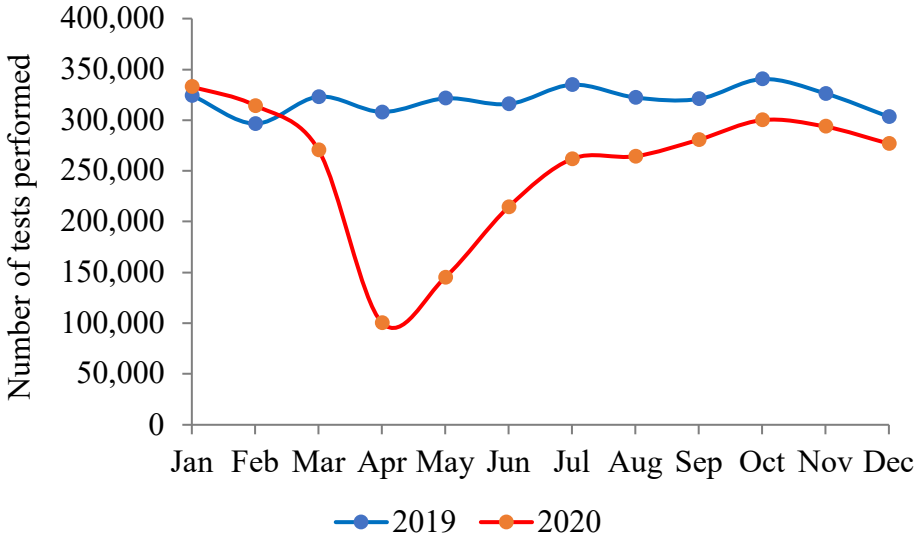
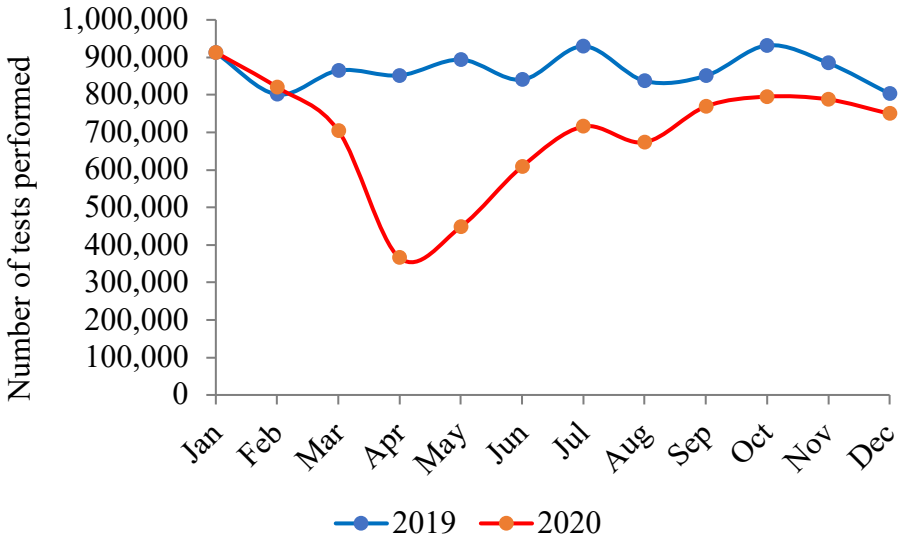


Figure 1.4: Ultrasound imaging performed by NHS England in 2019-20



1.3.3 Surgical research priorities during the first COVID-19 wave

During the first few months of the pandemic recommendations in guidelines were based on expert opinion. Evidence from previous infectious disease outbreaks such as SARS and Ebola virus suggested that pandemic-related disruption was likely to significantly impact surgical provision. Reports of poor outcomes of COVID-19 in medical admissions suggested that perioperative SARS-CoV-2 infection was likely to increase the risk of postoperative pulmonary complications and possibly mortality. However, up to May 2020 no large multicentre studies had been published to evaluate the safety of surgery during the pandemic; the only available evidence was from case reports and small case series (see section 1.2.2.1). Therefore, there was a need for high-quality multi-centre surgical outcomes studies to inform care during the pandemic.

An international Delphi consensus exercise in 2020 sought to identify surgical research priorities[246]. Key research gaps were identified relating to surgical outcomes associated with SARS-CoV-2 infection and risk prediction (Table 1.11).

Additional priorities related to the mechanisms, risk, and mitigation of SARS-CoV-2 transmission in surgical settings.

Table 1.11: Selected COVID-19 research questions in surgery

Research questions
• What is the impact of COVID-19 infection on surgical outcomes?
• What are the principal factors influencing mortality in COVID-19 surgical patients?
• Is there an increased incidence of perioperative complications in COVID-19 positive patients following surgery (e.g. surgical site infection, venous thromboembolism, pulmonary embolism)?
• Does the presence of SARS-CoV-2 antibodies confer protection from reinfection?

Source: Delphi consensus by Allan et al[246]

1.4 Thesis aims

1.4.1 Thesis hypothesis

Perioperative SARS-CoV-2 infection is associated with increased postoperative complications and mortality and decreased surgical activity.

1.4.2 Thesis aim

The aim of this thesis was to determine the impact of perioperative SARS-CoV-2 infection on the safety and delivery of surgery.

1.4.3 Thesis objectives

1. To determine whether perioperative SARS-CoV-2 infection was associated with increased mortality in the first COVID-19 wave.
2. To determine the optimal timing of surgery following SARS-CoV-2 infection in the first COVID-19 wave.
3. To determine whether perioperative SARS-CoV-2 infection was associated with increased postoperative complications and mortality in the period of Omicron variant dominance.

4. To determine the medium-term impact of the COVID-19 pandemic on the delivery of elective procedures in England.

1.5 Summary of chapter

This chapter has described the literature underpinning the research questions in relation to the COVID-19 pandemic and surgery. Chapter 2 describes the structure of the Global Surgery Unit which collected the data for the studies reported in Chapters 3-5, and the research methods of these studies.

2 METHODS

2.1 Synopsis

The first part of this chapter provides background to the NIHR Global Health Research Unit on Global Surgery (GSU) where this research was undertaken. The second part introduces the general principles of research collaboratives in relation to the conduct of cohort studies. The third part describes the methodology underpinning the three cohort studies reported in chapters 3-5.

2.2 Research setting

2.2.1 Global surgery

The greater part of the research in this thesis can be considered to belong to the field of global surgery. This field encompasses research, educational, and advocacy initiatives aimed at improving treatment of surgical disease and increasing access to safe surgery across all global settings[247]. This is a multidisciplinary research field with contributions from surgeons, anaesthetists, epidemiologists, and economists[247]. Global surgery came to prominence in 2015 with the publication of the Lancet Commission on Global Surgery[248]. The Lancet Commission demonstrated that the majority of world's population (4.8 billion) do not have access to safe, timely, affordable surgery. An estimated 14 million deaths occur annually that might be prevented if patients had access to safe surgery[248]; an additional 321 million operations per year would be needed to meet the global need for surgery[249]. Real-world studies have demonstrated that adults undergoing abdominal surgery in LMICs are three times and children seven times more likely to die after surgery[250,251]. Of the estimated 4.2 million annual postoperative deaths, a majority occur in LMICs[252]. Given the burden of surgical disease on population health, surgery is now recognised as an indispensable part of global health[248]. This is reflected by

governments committing to the development of National Surgical Obstetric Anaesthesia Plans (NSOAP) to prioritise development of surgical capacity[253].

Global surgery initiatives continue to principally focus on clinical service delivery, with few programmes aimed at delivering high-quality research across diverse global settings. Several high quality, practice changing trials in surgery and obstetrics have been completed[254,255], but most were limited projects that, whilst aiming to change clinical practice, did not seek to achieve a longer term legacy of high-quality LMIC-led research. Although multi-institutional projects increase research impact, there are very few platforms facilitating such initiatives in LMICs for surgery.

Most research is conducted in high-income settings[256], leading to several inequalities. Firstly, it is unknown how generalisable many key research findings are to diverse LMIC settings which have distinct clinical and financial constraints to high income settings. Moreover, there are clinical issues which are largely not applicable in high-income settings but are of intense interest in LMIC settings. As a result there is little or no robust evidence to inform some areas of LMIC clinical practice. For example, in most high-income countries laparoscopy has become the principal technique for appendicectomy, whereas in LMICs many surgeons perform open appendicectomies which present a different set of challenges[257]. Consequently, surgeons in LMIC settings lack the evidence needed to provide best care to their patients. Secondly, participation in research is associated with improved patient outcomes[258], so expansion of research in LMICs could support clinicians to address global disparities in patient outcomes.

2.2.2 NIHR Global Health Research Unit on Global surgery

The research for this thesis was undertaken within the framework of the NIHR Global Health Research Unit on Global Surgery (GSU). This is a multi-institutional research partnership funded in 2017 by the UK National Institute for Health and Care Research (NIHR) to develop a sustainable platform to prioritise and deliver surgical research in low- and middle-income countries (LMICs)[259]. The GSU is focused around Hub (university hospital) and Spoke (district hospital) surgical research networks in seven LMICs (Benin, Ghana, India, Mexico, Nigeria, Rwands, South Africa). Three UK higher educational institutions (University of Birmingham, University of Edinburgh, University of Warwick) provide methodological and research delivery expertise to the Hubs. I was embedded within the University of Birmingham team.

The philosophy underpinning the GSU's establishment is to support surgical teams in LMICs to develop local expertise in the delivery of robust practice-changing research and to establish sustainable long-term research capacity. These aims were in sharp contrast to prior global surgery research initiatives, which were typically led exclusively by high income researchers with no framework for the development of sustainable infrastructure in the LMICs where data was collected. Such initiatives often resembled “parachute research”, whereby local investigators in LMICs collect data, which is then analysed and published by high income country researchers, with little or no credit given to the LMIC collaborators[260,261].

The Hub and Spoke model is intended to overcome the risks of parachute research by empowering local research teams. Hubs are led by senior surgical researchers who are responsible for developing research infrastructure, such as training data managers and research nurses, and establishing diverse country wide Spoke

networks. In the period 2017-19 this network delivered a randomized controlled trial across 54 hospitals in the 7 Hub countries that evaluated interventions aimed at reducing surgical site infection[262]. In addition, the network delivered an international prospective cohort study (428 hospitals in 82 countries) exploring variation in outcomes after cancer surgery[263].

2.2.3 Research prioritisation

Hub leads drive the GSU's research prioritisation processes, engaging their Hub and Spokes to identify important clinical research questions. I led the facilitation of the GSU's initial prioritisation cycle in 2017, working with Hub leads to design and deliver a modified Delphi process[264]. The four-stage iterative process involved a combination of anonymous electronic voting, teleconferencing, and an in-person workshop. Overall, surgeons and methodologists from 60 countries contributed to this process. The final prioritised topics were related to increasing access to surgery, improving outcomes of cancer surgery, and improving perioperative care.

As the first COVID-19 wave spread to an increasing number of countries in early March 2020, Hub teams initiated discussions around what should be best practice for managing patients with peri-operative SARS-CoV-2 infection. This led to the development of an initial global guideline for surgical services during the COVID-19 pandemic (see 1.3.2.2) which identified significant evidence gaps. The CovidSurg-1 cohort study (see chapter 3) was developed to address these gaps.

The research studies forming this thesis were linked to the over-arching prioritised topic of improving perioperative care, however they also represented responsiveness to a public health emergency. This was possible because within the GSU

programme grant the NIHR had specifically allocated funding to respond to emerging priorities that were not foreseen when the GSU was initially established.

2.3 Surgical research collaboratives

Historically most clinical research in surgery was single-centre and at high-risk of bias[265]. High rates of research waste were observed in surgical research, for example, poor methodology, early discontinuation of studies due to failure to recruit patients, and non-publication of results[266,267]. Surgical research collaboratives were developed to increase the robustness of surgical research by providing a stable platform for multicentre research[268].

Research collaboratives are networks of individuals interested in surgical research who work together to design, deliver, and analyse multicentre research studies[268,269]. By running a standardised research protocol across multiple hospitals, collaboratives are able to rapidly enrol large numbers of patients rapidly, increasing study power, producing more broadly generalisable data than would be possible with a single-centre study[268,269]. Moreover, shifting from each researcher running their own single-centre study to a model where research activity is coordinated across multiple hospitals, reduces duplication of research activities and research waste[266-268]. Moreover, by centralising administrative tasks, collaboratives introduce efficiencies that decreases the burden on individuals, reducing the barriers to participation in research for frontline clinicians[269].

Research collaboratives provide a platform for medical students and junior researchers to gain experience in clinical research, within a supported environment. This increases research capacity by developing individuals' practical research skills and improving their confidence in participating in research[270,271].

2.3.1 Surgical research collaboratives in the United Kingdom

The first surgical research collaborative was the West Midlands Research Collaborative (WMRC), established in Birmingham, UK in 2007[272]. The WMRC was led by surgical trainees who formed a natural multicentre network across the West Midlands hospitals through which they rotated as trainees[268]. This model was successfully used to deliver both observational studies[273] and randomised controlled trials[274,275]. In order to increase the generalisability and power of its studies, this model was expanded across the UK, with 154 UK hospitals participating in a recent observational study[276]. By 2017, over 95% of UK hospitals had participated in at least on trainee research collaborative study[277].

2.3.2 Global surgical research collaboratives

The first major international collaborative research study in perioperative care was the European Surgical Outcomes Study (EuSOS) in 2012[278]. This study was led by anaesthetists and collected data on postoperative mortality across 498 hospitals in 28 countries. However, the first global collaborative research study in surgery with significant LMIC representation was GlobalSurg-1[250]. The GlobalSurg team expanded on their earlier experience of delivering collaborative studies in the UK by designing a study of emergency surgery outcomes that was open to any hospital worldwide. Of the 10,745 enrolled patients, 6,538 were from high-income countries, 2,889 were from middle-income countries, and 1,318 from low-income countries[250]. The study found that even after adjustment, mortality was three times higher in LMICs than high-income countries. The GlobalSurg team subsequently used the study's results to build the case for the NIHR to fund the GSU, with the leads from the top recruiting countries becoming Hub leads within the GSU structure[259].

2.4 CovidSurg Collaborative

The CovidSurg Collaborative was formed in March 2020 as a research platform to generate the best possible evidence to inform surgical care during the pandemic. The core of the CovidSurg Collaborative was the existing GSU network; the team structure is outlined in 2.4.1.

Activities undertaken by the CovidSurg Collaborative have included research studies, educational webinars aimed at disseminating best practice during the pandemic, open-access online educational modules, and co-production with patients of patient information resources[279]. In addition to the three cohort studies described in this thesis, another major research study was CovidSurg-Cancer. This was an international, multicentre cohort study which aimed to determine the impact of the pandemic on cancer surgery. In total, CovidSurg-Cancer enrolled 40,025 patients with cancer diagnoses across 776 hospitals in 78 countries[101,280].

2.4.1 Team structure

The structure of the CovidSurg Collaborative was multi-layered, with individuals leading study administration and data collection at international, national, and local levels:

- Operations Committee: a central team that coordinated the administration of the study including: development and dissemination of study resources (study protocol, case report forms, study approval documentation), running of the REDCap study database, data quality monitoring, and chasing of missing data.
- Dissemination Committee: a global team with representation from as many countries as possible. The Dissemination Committee provided broad global

input through online discussions and teleconferences into research question prioritisation and study design. This ensured that study design and documentation were tailored to the needs of different countries. Dissemination Committee members were research-active surgeons or anaesthetists. The nucleus of the Dissemination Committee was formed by international GSU members and they were supplemented by other individuals who had established leadership roles in previous collaborative studies. Further individuals were identified by either through personal recommendation by other Dissemination Committee members, or an open call on social media and through email lists for volunteers.

- Hospital Leads: individuals who coordinated local data collection team(s) at their hospital. They were responsible for securing local study approvals, recruiting local collaborators and providing training for them, ensuring there was no overlap in data collection between teams if more than one team was participating at the hospital, and ensuring that all eligible patients were identified and enrolled.
- Local collaborators: individuals involved in screening potentially eligible patients, enrolling all eligible patients including taking consent (if required), collecting baseline data, and completing 30-day patient follow-up.

All individuals participating in the study were included as co-authors on resulting publications. This is an important recognition of their contribution, ensuring an equitable research partnership and avoiding 'parachute research'[261]. Individuals could choose to participate in any one or multiple CovidSurg studies.

2.5 CovidSurg cohort studies

2.5.1 Overview of CovidSurg cohort studies

This thesis includes three cohort studies run through the CovidSurg Collaborative: CovidSurg-1 enrolled patients with perioperative SARS-CoV-2 infection during the first COVID wave (early 2020), CovidSurg-Week enrolled surgical patients operated in in October 2020 including both patients with and without SARS-CoV-2 infection, and CovidSurg-3 enrolled patients with perioperative SARS-CoV-2 infection during the period of Omicron variant dominance (December 2021 to February 2022).

The methodology for these three cohort studies was intended to be as consistent as possible to facilitate comparison of data across the three different time points. However, there are some differences reflecting the change in practice over time in the management of perioperative SARS-CoV-2. In addition, the need to tailor methodology also arose from the need to address each study's specific research question. Finally, study protocols were iteratively improved for future studies based on experience was accrued as each study was completed.

2.5.2 Key principles

In order to produce globally generalisable results, we aimed to facilitate as many hospitals in as many countries as possible around the world to participate. We also wanted to minimise bias in the data we collected. To reduce potential selection bias, it was important that all eligible patients were enrolled in the study. To reduce potential information bias, it was important to ensure high levels of data completeness and accuracy. It was also important to complete studies as quickly as possible to provide real-time data to guide clinical practice during a period of high clinical uncertainty due to a lack of evidence to guide practice.

A key principle informing the design of collaborative studies is that minimising the burden on collaborating centres, maximises participation. This was achieved by avoiding the need for changes to normal patient pathways, avoiding the need for additional follow-up visits or non-routine invasive tests, and reducing the likelihood of onerous or time-consuming study approval processes.

CovidSurg studies had simple inclusion criteria to enable collaborators to accurately and efficiently screen patients, maximising case ascertainment (the proportion of eligible patients enrolled in the study). Data collection instruments were streamlined, prioritising collection of the key variables that were essential to address study aims. There is a trade-off between the ideal dataset and the data that it is feasible to collect, with increasing data collection complexity likely to result in diminishing data completeness.

2.5.3 Protocol dissemination

A key strength of collaborative research models is the ability to collect data across diverse patient populations in order to maximise the generalisability of the data[268]. Since almost all UK hospitals have participated in at least one collaborative study[277], it is likely that the findings of UK-based collaborative studies are broadly generalisable across UK hospitals. However, generalisability is more challenging in a global context. LMIC clinicians face multiple barriers to participating in collaborative research, this includes lack of research staff, insufficient staff research skills, a lack of prioritisation of research and unreliable internet connections[281,282]. These factors could result in a bias in what surgeons and hospitals participate in collaborative studies; for example, larger, better resourced central teaching hospitals may be more likely to participate than remote district hospitals. This would limit the generalisability of research findings in the latter setting.

The Dissemination Committee's main role was to support the dissemination of the study protocols to as wide a range of hospitals in their countries as possible. This was achieved by advertising studies through national surgical associations, presenting at surgical and anaesthetic research forums, and contacting individuals who had participated in previous collaborative studies.

A past innovation aimed at expanding participating in research collaborative studies was use of social media to advertise the opportunity for individuals to join studies and contribute data[283-285]. In one UK-based study, 285 of 1,562 (18.2%) collaborators were alerted to the study through social media[283]; social media platforms used including surgical association websites, Facebook, Twitter, and YouTube. It is unknown whether the use of social media increases or decreases study generalisability; in the UK, a 2015 study found that fewer than half of colorectal surgeons made use of social media platforms such as LinkedIn or Twitter[286]. Clinicians in tertiary LMIC hospitals may be more likely to participate in international professional social media groups than their counterparts in district and rural hospitals. Therefore, a reliance on dissemination through social media may be more likely to succeed in recruiting clinicians in larger, better resourced hospitals, meaning that the cross-section of hospitals participating in the study is not representative of all hospitals in the country. This would reduce study generalisability.

In order to facilitate participation by as many international centres as possible, key study materials (study protocols and case report forms [CRFs]) were translated to key languages, based on advice from the Dissemination Committee. Translations were completed by Dissemination Committee members.

2.5.4 Governance

It was the responsibility of each Hospital Lead to follow the appropriate study approval process at their hospital. These processes varied between countries. These processes could include national ethical approvals (e.g. Brazil), local ethical approval processes (e.g. Germany), a combination of national and local approvals (e.g. India), or alternative pathways to research ethics (e.g. United Kingdom). In some countries it was necessary to take informed patient consent, whilst in other countries this requirement was waived by research ethics committees. Dissemination Committee members supported Hospital Leads in their countries to navigate the relevant processes and coordinated national ethics submissions, if required.

In the United Kingdom the study was registered as either service evaluation or clinical audit. The reference for CovidSurg-1 approval at the lead centre (University Hospital Birmingham) was CARMS-15986. The previous GlobalSurg-1[250] and GlobalSurg-2[287] cohort studies utilised similar methodology to the CovidSurg cohort studies; the South East Scotland Research Ethics Service advised that the GlobalSurg studies were exempt from the requirement for ethical review (references NR/1404AB12 and NR/1510AB5).

When seeking study approvals, collaborators were encouraged to emphasise that in each case these were non-profit, investigator-led, observational studies that collected only routine, anonymised data with no change to clinical care pathways. In CovidSurg-Week and CovidSurg-3 collaborators who had participated in previous CovidSurg studies were encouraged to approach their ethics committee or equivalent to request approval of the new study as an amendment to the approval to the previous study.

2.5.5 Data collection

Data was collected using standardised case report forms (CRFs), with each CRF relating to a different point in the patient journey. The CRFs were:

- Baseline form: capture of basic demographic variables and information about comorbidities. This form was completed as soon as possible after the patient was enrolled in the study.
- SARS-CoV-2 form: capture of details of SARS-CoV-2 infection status and SARS-CoV-2 mitigation measures in place. This form was completed as soon as possible after the patient was enrolled in the study.
- Intraoperative form: capture of the indication for surgery and operative details. This form was completed as soon as possible after completion of surgery.
- Follow-up form: capture of 30-day outcome data. This form was completed either on postoperative day 30 or as soon after day 30 as possible.

For convenience, collaborators were given than option to initially collect data on printed CRFs, however, all data was required to be uploaded to a secure online database, Research Electronic Data Capture (REDCap)[288,289]. Only non-identifiable data were uploaded to REDCap; for this reason, age was only recorded by decile. All personal data remained at participating hospitals and were not submitted to the central team. Prior to the CovidSurg studies, the REDCap system had been successfully used without incident to collect data for previous GSU studies. The REDCap server was held at a secure location at the University of Birmingham, with safeguards in place to maintain both the security and integrity of the data. Data were processed in accordance with the requirements of the General Data Protection

Regulations (GDPR). In line with university policies, raw data will be stored for 25 years.

Collaborators were encouraged to upload data as promptly as possible to REDCap to enable real-time data quality monitoring. Several features of the REDCap system were utilised to improve data quality:

- Eligibility screening: in order to enter a patient into the REDCap database, collaborators were required to confirm the patient's eligibility for inclusion. Further data entry was not possible until eligibility was confirmed.
- In-built instructions: detailed data field definitions were provided within the database, with links to relevant sections of the study protocol, if required.
- Data field design: whenever possible either categorical or continuous data were collected in preference to free text data fields. For example, an initial list of operation codes was developed by simplifying the Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS) code list. This was included in the CovidSurg-1 database as a dropdown menu; collaborators were able to enter free text procedure information if there was no appropriate code. For subsequent studies, additional procedure codes were created based on this free text which had been entered in CovidSurg-1, and the free text option was removed.
- Data field validation: for continuous data fields REDCap is able to restrict the values that can be input, for example to a particular range. This was used to restrict variables (e.g. white cell count) to clinically plausible values.
- Missing data warnings: all data fields were set as mandatory, meaning that collaborators would receive a warning when saving a page on the REDCap database if there were incomplete data fields.

- Data quality warnings: the REDCap system was programmed to show data quality warnings if collaborators input inconsistent data. For example, if a patient was recorded as having a history of ischaemic heart disease and being ASA (American Society of Anethesiology) grade 1, a warning would show that the data was inconsistent (a history of ischaemic heart disease implies ASA grade 2 or greater) and that it should be corrected.
- Missing data reports: Collaborators had access to a missing data report for the patient records they had entered. This identified patient records that had key data items missing. Collaborators were encouraged to regularly check these reports and to complete any missing fields. In addition, in the last two weeks of each study any collaborators with missing data were emailed reminders to check and address their missing data reports.

2.5.6 Patient inclusion criteria

The aim of the CovidSurg studies was to address an urgent need for evidence to inform surgical care during the pandemic. Since there was a need for evidence across all specialties, these studies were designed to be broadly generalisable by including patients undergoing any type of surgery. This had a secondary advantage in maximising the number of patients enrolled during fixed study windows, therefore increasing the power of these studies.

For all three studies patients undergoing surgery were eligible for inclusion, regardless of the type of surgery, the indication for surgery, urgency of surgery (elective or emergency), or patient age.

It is challenging to create a precise but brief definition of surgery. Although a simple definition might be that surgery involves a skin incision, there are some surgeries

that do not involve skin incision (for example, extracorporeal shock wave lithotripsy) and some non-surgical procedures that do involve a skin incision (e.g. endovascular procedures performed by interventional radiologists). Whilst surgeries are typically performed in an operating theatre environment, not all procedures in an operating theatre are surgeries; for example, insertion of a central line or oesophago-gastro-duodenoscopy under general anaesthetic would not usually be considered surgery. Therefore, we developed a pragmatic definition of surgery as any procedure that is routinely performed in an operating theatre by a surgeon, with the exclusion of a series of minor non-surgical procedures. A special case were endoscopic procedures; those that are usually performed in an operating theatre by a surgeon were included (e.g. rigid cystoscopy), whereas those that are usually performed outside of an operating theatre (i.e. in the outpatient clinic or an endoscopy suite) or by a non-surgeon were excluded (e.g. flexible cystoscopy). In order to avoid ambiguity over this definition in CovidSurg-1, a list of excluded procedures was provided to collaborators in the CovidSurg-Week and CovidSurg-3 studies (Table 2.1).

Table 2.1: List of excluded procedures

Specialty	Excluded procedures
Abdominal surgery	Ascitic drain (drainage of peritoneal cavity)
	Endoscopic ultrasound
	Laparoscopic ultrasound
Breast surgery	Breast biopsy
Cardiac surgery	Insertion of cardiac pacemaker
	PCI: percutaneous coronary intervention
	Transluminal balloon angioplasty of coronary artery
Colorectal surgery	Colonoscopy (diagnostic or therapeutic)
	Flexible sigmoidoscopy (diagnostic or therapeutic)
	Proctoscopy (diagnostic or therapeutic)
Dental procedures	Implantation of tooth
	Insertion of dental prosthesis
	Orthodontic operations
	Restoration of tooth
	Extraction of tooth
Gynaecology	Cervical biopsy
	Colposcopy (diagnostic or therapeutic)
Obstetrics	Any vaginal delivery (normal delivery, breech delivery, forceps delivery, vacuum delivery)
	Surgical termination of pregnancy
Ophthalmology	Removal of foreign body from cornea
Orthopaedics	Bone biopsy
	Injection in to joint
	Muscle biopsy
Otolaryngology	Laryngoscopy (diagnostic or therapeutic)
	Nasendoscopy (diagnostic)
	Packing of cavity of nose
Thoracic surgery	Bronchoscopy (diagnostic)
	Insertion of chest drain
Upper gastrointestinal surgery	ERCP: endoscopic retrograde cholangiopancreatography (diagnostic or therpaeutic)
	Liver biopsy
	OGD: Oesophago-gastro-duodenoscopy (diagnostic or therapeutic)
Urology*	Bladder biopsy
	Extracorporeal shock wave lithotripsy (ESWL)
	Flexible cystoscopy (diagnostic)
	Percutaneous nephrostomy
Vascular surgery	Endovenous laser treatment (EVLT) for varicose veins
	Insertion or removal of dialysis catheter
	injection into varicose vein of leg
	Transluminal (endovascular) procedures on arteries (diagnostic or therapeutic), including with open cut down to the artery
	Transluminal (endovascular) procedures on veins (diagnostic or therapeutic)
	Insertion or removal of Hickmann line
Other	Insertion of central venous catheter/ line (CVC)
	Insertion of chest drain
	Lumbar (spinal) puncture
	Percutaneous tracheostomy
	Skin biopsy (including shave biopsy of skin)
	Therapeutic epidural injection
	Vacuum dressing

Each patient could only be included once within each study. If a patient underwent more than one operation during the patient inclusion windows, the operation closest to the date of the SARS-CoV-2 diagnosis was taken as the index operation.

CovidSurg-Week included all patients regardless of their SARS-CoV-2 status, whereas CovidSurg-1 and CovidSurg-3 only included patients with perioperative SARS-CoV-2. Since only a small proportion (typically under 5%) of patients develop peri-operative SARS-CoV-2, there is a very significant difference in the data collection and administration burden when collecting all patients regardless of SARS-CoV-2 status versus patients with perioperative SARS-CoV-2 only. With the resources available to the study team, it was only possible to attempt to collect data on all patients in one study.

The following definitions were used:

- Perioperative SARS-CoV-2: SARS-CoV-2 infection diagnosed within 7 days before or 30 days following surgery (the day of surgery was taken as day zero). This definition was created for the CovidSurg-1 study at a time when there was no accepted definition for perioperative SARS-CoV-2. The preoperative bound of this definition was based on early data indicating that patients remained infectious for around 7 days after diagnosis. The postoperative bound was based on postoperative day 30 being the traditional cut-off for short-term perioperative outcome measurement.
- Confirmed SARS-CoV-2: SARS-CoV-2 infection confirmed by positive RT-PCR.
- Suspected SARS-Cov-2: SARS-CoV-2 infection diagnosed clinically, based on CT chest imaging, or based on laboratory tests other than RT-PCR.

Patients initially included as having suspected SARS-CoV-2 infection were re-classified as non-SARS-CoV-2 if they received a negative RT-PCR result.

During the first wave, SARS-CoV-2 swab testing was not routinely available at all hospitals, particularly in LMICs[15,56]. Therefore, to enable all hospitals to participate, in CovidSurg-1 patients were eligible for inclusion based on a positive laboratory SARS-CoV-2 PCR swab test, positive radiological findings, or clinical diagnosis by a senior physician of SARS-CoV-2 infection. Patients who were initially eligible for inclusion based on a clinical or radiological diagnosis who subsequently had a negative SARS-CoV-2 test result were excluded.

By the time that CovidSurg-3 was undertaken in late 2021, SARS-CoV-2 testing, either with PCR swab test or rapid antigen test, was broadly available in most settings. Therefore, patients were only eligible for inclusion in CovidSurg-3 if they had either a positive PCR swab test or rapid antigen test result within the inclusion window (7 days before to 30 days after surgery).

2.5.7 Outcome measures

The outcome measures were broadly consistent across all studies. Outcomes were assessed up to and including day 30 (taking day of surgery of surgery as day zero). Collaborators were encouraged to complete follow-up on day 30 or as soon afterwards as possible. In line with study approvals, follow-up was limited to review of routinely available information; no study-specific follow-up was undertaken. Collaborators were asked to review inpatient records, radiological imaging results, electronic patient records to check for re-admissions, and clinic notes from routine outpatient or telephone follow-up (if performed as part of routine clinical care).

The primary outcome measure for all three studies was 30-day mortality. The key secondary outcome measures were:

- 30-day postoperative pulmonary complications. This was a composite outcome measure of the most frequent COVID-19-related pulmonary complications recorded in medical patients in the early COVID-19 literature. The concept of a composite outcome for postoperative pulmonary complications was adapted from the Prevention of Respiratory Insufficiency after Surgical Management (PRISM) randomised controlled trial[290]. Pulmonary complications were defined as pneumonia, acute respiratory distress syndrome (ARDS), and/or unexpected postoperative ventilation (see Table 2.2).
- 30-day pneumonia was defined based on the US Centers for Disease Control (CDC) definition[291] (see Table 2.2).
- 30-day ARDS was defined based on the Berlin consensus criteria[292] (see Table 2.3).
- 30-day unexpected postoperative ventilation was defined as any episode of non-invasive ventilation, invasive ventilation, or extracorporeal membrane oxygenation after initial extubation following surgery, or unexpected failure to extubate following surgery.
- 30-day postoperative intensive care unit (ICU) admission. ICU was defined as a service providing close observation and invasive treatment for patients with potential or established organ failure. ICU admission was categorised as planned (planned prior to surgery due to expectation the patient would either require close monitoring in ICU or organ support) or unplanned (postoperative ICU admission that was not planned preoperatively, with the

patient either admitted directly from theatre or from the postoperative ward due to deterioration).

Table 2.2: US Centers for Disease Control definition of pneumonia

Patients should have at least one of the following:

- Fever (>38°C) with no other recognised cause.
- Leucopaenia (white cell count <4x109) or leucocytosis (white cell count >12x109).
- For adults >70 years old, altered mental status with no other recognised cause.

and at least **two** of the following:

- New onset of purulent sputum or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements.
- New onset or worsening cough, or dyspnoea, or tachypnoea.
- Rales, crackles or bronchial breath sounds.
- Worsening gas exchange (hypoxaemia, increased oxygen requirement).

Wherever possible, the diagnosis should be confirmed with a chest radiograph.

Source: US Centers for Disease Control[291]

Table 2.3: Berlin consensus criteria for ARDS

Acute Respiratory Distress Syndrome criteria	
Timing	Within 1 week of known clinical insult or worsening respiratory symptoms
Chest imaging	Bilateral opacities (not fully explained by effusions / collapse / nodules).
Origin	Respiratory failure (not fully explained by cardiac failure / fluid overload).
Oxygenation	200mmHg < PaO2/FIO2 ≤ 300mmHg with PEEP or CPAP ≥5cm H2O FIO2: fraction of inspired oxygen; PaO2: partial pressure of arterial oxygen; PEEP: positive end-expiratory pressure.

All four criteria should be met to fulfil criteria to diagnose ARDS[292]

2.5.8 Data validation

Data validation is the process of independently verifying the quality of a dataset. A pragmatic decision was taken not to attempt validation of the CovidSurg datasets, since any such process would delay database lock by at least one to two months. Given the urgency to provide evidence to inform clinical care, a significant delay to releasing data was felt to be unjustified.

However, several previous collaborative cohort studies utilising very similar methodology to the CovidSurg studies have published the outcomes of data validation processes. These processes typically focussed on validating case ascertainment and data accuracy. Validation was undertaken by an individual from within the hospital where data were collected, but who had not been involved in the initial data collection. Although it would be preferable to utilise a truly independent, external data validator, this has not been possible within the resource constraints of previous collaborative studies.

Five previous studies have reported case ascertainment[293-297]. As these studies all studied patients who had undergone specific surgical procedures, validation was based on independent review of theatre logbooks and ward lists, to identify any patients who had been missed by the original data collection team. Rates of case ascertainment in individual studies ranges from 90.7% to 98.1%. Seven studies reported data accuracy. Two studies validated all data items within patient records selected for review, whereas five studies pre-selected between 3 and 12 key data items for validation within each selected patient records. These data items were independently reviewed against source material (e.g. operation notes, electronic medical records) to identify any discrepancies. Rates of data accuracy in individual studies ranges from 96.6% to 99.8%. Based on the four studies that reported a denominator for data accuracy calculation, the pooled rate of data accuracy was 98.3% (49581/50460).

2.6 Statistical analysis

Analyses were carried out using Stata 15 (StataCorp LP, USA). In order to ensure consistency of denominators, missing data were included in flowcharts and

descriptive analyses. Imputation for missing data was not planned as a < 2% rate of missing data was anticipated, based on previous studies[276,287].

Normally distributed continuous data were presented as means with 95% confidence intervals (CI). The unpaired t-test was used to test differences between groups. For categorical variables, counts and proportions were presented. The chi-squared and Fisher´s exact tests were used to test differences between groups.

The first three studies were prospective observational cohort studies. Adjusted analyses were conducted to adjust for factors that could possibly confound the relationships being explored. I will illustrate this taking, Chapter 4 as an example. The aim of this study was to establish the optimal timing of surgery after a positive SARS-CoV-2 test result. In the primary analysis, the dependent variable was 30-day mortality (coded as 0 for no [alive] and 1 for yes [dead]) and the independent variable was timing of surgery after a SARS-CoV-2 positive test (coded as a categorical variable, with the group with “no SARS-CoV-2 diagnosis” being the reference group).

Univariate binary logistic regression would allow the calculation of the odds of mortality for each timing category relative to the “no SARS-CoV-2 diagnosis” group. However, there would be likely to be significant confounding by variables that influence both the dependent variable (30-day mortality) and independent variable (timing of surgery). For example, it is likely that the delay to surgery after a positive SARS-CoV-2 test result for emergency surgery patients would be shorter than for elective patients; in addition, emergency surgery patients have higher baseline mortality than elective surgery patients. Therefore, even if there is truly no relationship between the timing of surgery and mortality, confounding by urgency of surgery may result in a univariate analysis finding that shorter delays to surgery

following a positive SARS-CoV-2 test result are associated with higher odds of mortality.

Confounding can be addressed by performing multivariable logistic regression, whereby the relationship is established between the dependent variable and multiple independent variables. This statistical technique allows analyses to be adjusted for possible confounding variables, reducing the likelihood of confounding.

There are several techniques for selecting which variables should be included in multivariable logistic regression models, including both backwards and forwards stepwise variable selection which seek to identify the optimal combination of variables that maximise model performance. However, I chose to select variables *a priori* for each study. This ensures transparency (avoids 'p-hacking'), as variables are selected before their effect on the results of the analysis are known.

The specific details of the adjusted models used in each study, along with associated subgroup and sensitivity analyses, are described in the methodology sections in chapters 3-5.

2.7 Summary

This chapter has described the methodology underpinning the conduct of the three CovidSurg cohort studies reported in chapters 3-5. In chapter 3 I describe the results of the first CovidSurg cohort study.

3 MORTALITY AND PULMONARY COMPLICATIONS IN PATIENTS UNDERGOING SURGERY WITH PERIOPERATIVE SARS-COV-2 INFECTION

3.1 Contribution

This chapter presents data published in *The Lancet*[298]. I have abbreviated methods section to avoid duplicating material in chapter 2. I have extensively updated the introduction and discussion in light of subsequent literature published after the *Lancet* paper. I have removed a small amount of material from the results that was not relevant to the primary and secondary aims of the study.

I was co-first author on this paper. I was the co-lead investigator with Mr Aneel Bhangu; participating in conceiving the study and methodology, and leading the administration of the study. I led the data analysis, supported by Mr Omar Omar (senior statistician) and Mr Aneel Bhangu. I drafted the first version of the manuscript, revised this based on comments from co-authors, and led the responses to *The Lancet's* peer reviewers.

3.2 Synopsis

The aim of this study was to determine whether perioperative SARS-CoV-2 infection was associated with increased mortality risk in the first COVID-19 wave. This international, multicentre, cohort study included patients with perioperative SARS-CoV-2 infection who underwent surgery between 1 January 2020 and 31 March 2020. The primary outcome measure was 30-day postoperative mortality and the secondary outcome measure was 30-day postoperative pulmonary complications. Of the 1,128 included patients, most (835, 74.0%) had undergone emergency surgery. Most SARS-CoV-2 infections were registered postoperatively in 806 (71·5%) patients. Overall, the 30-day mortality rate was 23.8% (268/1128) and the postoperative pulmonary complication rate 51.2% (577/1128). In adjusted analyses, 30-day mortality was associated with male sex, age ≥70 years versus <70 years,

ASA grades 3-5 versus grades 1-2, cancer versus non-cancer indication for surgery, emergency versus elective surgery, and major versus minor surgery.

3.3 Introduction

By 15 March 2020, 168,000 SARS-CoV-2 cases had been confirmed worldwide, with over 10,000 new cases being registered each day[16]. In chapter 1 I have described several large studies that were published early in the pandemic reporting the outcomes of COVID-19 both in patients admitted to hospital[78] and in the general population[79]. In contrast, early reports of the safety of surgery in patients with SARS-CoV-2 were limited to case reports[206,207] and small case series (see section 1.2.2.1). As a result, recommendations in initial guidelines for surgical care during the pandemic were based on expert opinion[235,236].

Surgical patients experience high rates of postoperative pulmonary complications. This may reflect pro-inflammatory cytokine and immunosuppressive responses to surgery and mechanical ventilation[299]. RECON was a prospective international multicentre cohort study conducted in 2019 which captured postoperative pulmonary complication rates[300]. It reported a 7.1% postoperative pulmonary complication rate, based on data for 3,031 elective abdominal cancer surgery patients[301]. POPULAR, a prospective observational cohort study which captured data for 22,803 patients undergoing non-cardiac surgery across 211 hospitals in 28 European countries, reported a 7.6% postoperative pulmonary complication rate[302].

Given the high rates of pneumonia and ARDS reported in medical COVID-19 patients[75,76], it is possible that surgical patients who develop perioperative SARS-CoV-2 infection would be particularly susceptible to severe COVID-19 disease. An international Delphi consensus exercise identified the need to establish the safety of

surgery in patients with perioperative SARS-CoV-2 as one of the highest surgical research priorities during the pandemic (Table 1.10)[246].

The aim of this international multicentre study was to determine whether perioperative SARS-CoV-2 infection was associated with increased mortality in the first COVID-19 wave.

3.4 Methods

The data collection process is described in detail in chapter 2. In summary, this was an international, multicentre, observational cohort study. In the UK, the study was registered as clinical audit or service evaluation. At the lead centre (University Hospital Birmingham) the study approval reference was CARMS-15986. In other countries, local principal investigators followed local and national regulations to secure relevant study approvals.

3.4.1 Patient inclusion criteria

Patients were eligible for inclusion if they underwent any type of surgery and developed perioperative SARS-CoV-2, defined as SARS-CoV-2 infection diagnosed within 7 days before or 30 days following surgery. All consecutive eligible patients operated from 1 January 2020 to 31 March 2020 were included.

3.4.2 Outcome measures

The primary outcome measure was 30-day mortality and the secondary outcome measures at 30-days were postoperative pulmonary complications, pneumonia, ARDS, unexpected postoperative ventilation, and intensive care unit admission.

3.4.3 Statistical analysis

3.4.3.1 Unadjusted and adjusted models

Multilevel logistic regression was used to perform both unadjusted and adjusted analyses. These analyses produced odds ratios (OR) and 95% CI. In both unadjusted and adjusted models, country was included as a random effect with hospital nested within country.

Only factors that occurred before the outcome of interest were included in the models. Factors were selected *a priori* based on their clinical relevance.

Adjusted models were used to adjust for possible confounding factors. The same factors as in the unadjusted models were included in the adjusted models.

The primary adjusted model, based on all available data, had 30-day mortality as the outcome. The purpose of this model was to identify predictors of 30-day mortality in patients with perioperative SARS-CoV-2.

An additional adjusted model, had 30-day postoperative pulmonary complications as the outcome. This model was intended to identify predictors of 30-day postoperative pulmonary complications.

3.4.3.2 Sensitivity analyses

In order to determine the robustness of the findings, a number of sensitivity analyses were performed. The first sensitivity analysis only included patients with confirmed perioperative SARS-CoV-2 infection. The second sensitivity analysis only included patients with preoperatively diagnosed SARS-CoV-2 infection.

3.5 Results

This analysis included 1128 patients from across 235 hospitals in 24 countries (Table 3.1). Overall, 53.6% (605/1128) of patients were male, 19.0% (214/1128) were aged <50 years, 31.3% (353/1128) were aged 50-69 years, and 49.5% (558/1128) were aged ≥70 years, with age missing for three patients (Table 3.2).

Table 3.1: Countries contributing data

Country	Number of hospitals	Number of patients
Algeria	1	1
Azerbaijan	1	1
Belgium	2	8
Croatia	1	3
Denmark	1	1
Egypt	6	12
France	8	20
Germany	4	6
Greece	3	8
Ireland	4	18
Israel	1	1
Italy	44	181
Jordan	1	1
Libya	3	4
Mexico	1	1
Netherlands	4	6
Pakistan	1	1
Portugal	4	16
Spain	29	170
Sudan	1	1
Switzerland	2	7
Turkey	4	11
United Kingdom	82	484
United States	27	167

Table 3.2: Baseline and demographic characteristics

	30-day mortality			Pulmonary complications		
	No (n=845)	**Yes (n=268)**	**p-value**	**No (n=526)**	**Yes (n=577)**	**p-value**
Age, n (%)			<0.001			<0.001
<29 years	56 (100)	0 (0.0)		39 (70.9)	16 (29.1)	
30-49 years	146 (94.2)	9 (5.8)		86 (55.8)	68 (44.2)	
50-69 years	277 (79.8)	70 (20.2)		159 (46.0)	187 (54.0)	
≥70 years	364 (65.9)	188 (34.1)		240 (44.0)	305 (56.0)	
Missing	2	1		2	1	
Sex, n (%)			<0.001			0.003
Male	424 (71.1)	172 (28.9)		252 (42.8)	337 (57.2)	
Female	417 (81.6)	94 (18.4)		270 (53.1)	238 (46.9)	
Ambiguous	1 (50.0)	1 (50.0)		1 (50.0)	1 (50.0)	
Missing	3	1		3	1	
ASA grade, n (%)			<0.001			<0.001
1-2	344 (88.4)	45 (11.6)		235 (60.6)	153 (39.4)	
3-5	475 (68.7)	216 (31.3)		278 (40.6)	407 (59.4)	
Missing	26	7		13	17	
Comorbidities, n (%)			<0.001			<0.001
None	107 (93.0)	8 (7.0)		73 (63.5)	42 (36.5)	
1	192 (82.8)	40 (17.2)		115 (50.7)	112 (49.3)	
≥2	527 (70.8)	217 (29.2)		322 (43.5)	418 (56.5)	
Missing	19	3		16	5	
Comorbidities, n (%)						
Current smoker	80 (75.5)	26 (24.5)	0.909	42 (40.0)	63 (60.0)	0.097
Asthma	57 (73.1)	21 (26.9)	0.542	36 (48.0)	39 (52.0)	0.955
Cancer	146 (77.2)	43 (22.8)	0.639	92 (48.9)	96 (51.1)	0.707
Chronic kidney disease	109 (66.5)	55 (33.5)	0.002	64 (39.3)	99 (60.7)	0.020
Chronic obstructive pulmonary disease	75 (64.7)	41 (35.3)	0.003	44 (37.9)	72 (62.1)	0.026
Congestive heart failure	55 (64.7)	30 (35.3)	0.012	29 (34.5)	55 (65.5)	0.012
Dementia	48 (55.2)	39 (44.8)	<0.001	30 (35.3)	55 (64.7)	0.017
Diabetes Mellitus	207 (73.9)	73 (26.1)	0.367	124 (44.1)	157 (55.9)	0.166
Hypertension	399 (71.0)	163 (29.0)	<0.001	253 (45.3)	305 (54.7)	0.114
Myocardial infarction	70 (63.1)	41 (36.9)	0.001	39 (35.4)	71 (64.6)	0.007
Peripheral vascular disease	67 (62.0)	41 (38.0)	<0.001	48 (44.4)	60 (55.6)	0.477
Stoke/ transient ischaemic attack	55 (61.1)	35 (38.9)	0.001	45 (50.0)	45 (50.0)	0.647
Symptoms at admission, n (%)*						
No symptoms reported	111 (77.6)	32 (22.4)	0.281	78 (56.5)	60 (43.5)	0.020
Symptoms reported	499 (73.3)	182 (26.7)		309 (45.6)	368 (54.4)	
Abdominal pain	193 (77.5)	56 (22.5)	0.134	122 (49.4)	125 (50.6)	0.472
Dyspnoea	83 (61.9)	51 (38.1)	<0.001	32 (23.9)	102 (76.1)	<0.001
Cough	108 (73.0)	40 (27.0)	0.746	55 (37.2)	93 (62.8)	0.005
Diarrhoea	18 (69.2)	8 (30.8)	0.571	12 (46.2)	14 (53.8)	0.890
Fatigue	42 (70.0)	18 (30.0)	0.460	18 (30.0)	42 (70.0)	0.005
Fever >38 °C	177 (76.6)	54 (23.4)	0.289	94 (40.9)	136 (59.1)	0.018
Haemoptysis	2 (66.7)	1 (33.3)	0.771	1 (33.3)	2 (66.7)	0.623
Myalgia	27 (79.4)	7 (20.6)	0.465	9 (26.5)	25 (73.5)	0.012
Nausea/ vomiting	100 (79.4)	26 (20.6)	0.138	62 (49.6)	63 (50.4)	0.607
Sputum	7 (41.2)	10 (58.8)	0.002	6 (35.3)	11 (64.7)	0.309
Other	209 (70.6)	87 (29.4)	0.094	139 (47.3)	155 (52.7)	0.930
Preoperative respiratory support, n (%)						
None/ oxygen only	805 (76.4)	249 (23.6)	0.134	520 (49.7)	526 (50.3)	<0.001
Non-invasive ventilation	12 (80.0)	3 (20.0)	0.710	1 (6.7)	14 (93.3)	0.001
Invasive ventilation	31 (66.0)	16 (34.0)	0.103	2 (4.3)	45 (95.7)	<0.001

ASA: American Society of Anesthesiologists classification

Data only presented for patients with 30-day mortality outcome available (n=1113) and pulmonary complications outcome available (n=1103). Percentages are presented in rows.

** Data only presented for emergency patients*

3.5.1 Diagnosis

SARS-CoV-2 infection was diagnosed preoperatively in 26.1% (294/1128) of patients and postoperatively in 71.5% (806/1128), with timing of diagnosis missing for 28 patients. SARS-CoV-2 diagnosis was confirmed by laboratory testing in 85.9% (969/1128) of patients, radiological findings in 7.1% (80/1128), and clinical findings in 6.0% (68/1128), with method of diagnosis missing for 11 patients. Overall, 31.6% (357/1128) underwent preoperative CT thorax and the most common radiological finding was ground glass opacity (Table 3.3).

Table 3.3: Preoperative assessment

	30-day mortality			Pulmonary complications		
	No (n=845)	Yes (n=268)	p-value	No (n=526)	Yes (n=577)	p-value
Lab values						
Haemoglobin (g/L)*	118.6 (24.7)	116.1 (24.1)	0.150	118.5 (23.5)	117.6 (25.4)	0.537
Missing	18	4		15	7	
WCC (x10^9/L)*	10.5 (7.6)	10.6 (6.8)	0.859	10.1 (5.1)	10.8 (8.9)	0.169
Missing	19	4		15	8	
SARS-CoV-2 diagnosis, n (%)			0.719			0.085
Confirmed (RT-PCR positive)	727 (76.0)	230 (24.0)		454 (47.9)	493 (52.1)	
Suspected: radiological (CT chest)	58 (72.5)	22 (27.5)		29 (36.3)	51 (63.7)	
Suspected: clinical	53 (77.9)	15 (22.1)		36 (52.9)	32 (47.1)	
Missing	7	1		7	1	
Timing of SARS-CoV-2 diagnosis, n (%)			0.128			0.155
Preoperative	231 (78.8)	62 (21.2)		148 (51.0)	142 (49.0)	
Postoperative	595 (74.4)	205 (25.6)		367 (46.2)	428 (53.8)	
Missing	19	1		11	7	

*CT: computed tomography; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; WCC: white cell count. Data only presented for patients with 30-day mortality outcome available (n=1113) and pulmonary complications outcome available (n=1103). Percentages are presented in rows. *Last available blood test results from before surgery, presented as mean with standard deviation*

3.5.2 Procedures

Emergency surgery was performed in 74.1% (835/1128) of patients and elective surgery in 24.8% (280/1128, Table 3.4), with urgency missing for 13 patients. Indications for surgery were benign disease in 54.5% (615/1128), cancer in 24.7%

(278/1128), and trauma in 20.1% (227/1128), with indication missing for 8 patients. A total of 22.3% (251/1128) of procedures were categorised as minor and 74.6% (841/1128) as major, with grade of surgery missing for 36 patients. Procedures included gastrointestinal and general (33.1%, 373/1128), orthopaedic (26.8%, 302/1128), cardiothoracic (7.6%, 86/1128), hepatobiliary (5.5%, 62/1128), obstetric (4.5%, 51/1128), vascular (4.0%, 45/1128), head and neck (3.6%, 40/1228), neurosurgery (3.5%, 39/1128), urological (3.3%, 37/1128), and other (5.1%, 58/1128) surgeries. Procedure was missing for 36 patients. A full breakdown of procedures is provided in Table 3.5.

Table 3.4: Operative details

	30-day mortality			Pulmonary complications		
	No (n=845)	Yes (n=268)	p-value	No (n=526)	Yes (n=577)	p-value
Urgency of surgery, n (%)			0.020			0.873
Elective	225 (80.9)	53 (19.1)		130 (46.9)	147 (53.1)	
Emergency	610 (74.0)	214 (26.0)		387 (47.5)	428 (52.5)	
Missing	10	1		9	2	
Anaesthesia, n (%)			0.383			0.488
Local	34 (69.4)	15 (30.6)		24 (49.0)	25 (51.0)	
Regional	119 (78.8)	32 (21.2)		78 (51.7)	73 (48.3)	
General	658 (75.2)	217 (24.8)		403 (46.5)	464 (53.5)	
Missing	34	4		21	15	
Surgical diagnosis, n (%)			0.030			0.502
Benign or obstetric case	480 (78.3)	133 (21.7)		281 (46.3)	326 (53.7)	
Cancer	183 (72.9)	68 (27.1)		114 (45.6)	136 (54.4)	
Trauma	157 (70.1)	67 (29.9)		112 (50.5)	110 (49.6)	
Missing	25	0		19	5	
Grade of surgery, n (%)			0.001			0.022
Minor	209 (83.6)	41 (16.4)		132 (53.2)	116 (46.8)	
Major	607 (72.9)	226 (27.1)		372 (45.0)	455 (55.0)	
Missing	29	1		22	6	
Specialty, n (%)			<0.001			<0.001
Breast	3 (100.0)	0 (0)		2 (66.6)	1 (33.3)	
Cardiac	33 (66.0)	17 (34.0)		3 (5.9)	48 (94.1)	
Gastrointestinal and general	286 (76.9)	86 (23.1)		172 (46.4)	199 (53.6)	
Gynaecology	20 (95.2)	1 (4.8)		16 (76.2)	5 (23.8)	
Head and neck	32 (80.0)	8 (20.0)		10 (25.6)	29 (74.4)	
Hepatobiliary	50 (84.8)	9 (15.2)		29 (50.9)	28 (49.1)	
Neurosurgery	31 (81.6)	7 (18.4)		19 (50.0)	19 (50.0)	
Obstetrics	50 (98.0)	1 (2.0)		26 (51.0)	25 (49.0)	
Ophthalmology	4 (100.0)	0 (0)		3 (75.0)	1 (25.0)	
Orthopaedics	213 (71.2)	86 (28.8)		165 (55.7)	131 (44.3)	
Other	19 (73.1)	7 (26.9)		11 (42.3)	15 (57.7)	
Plastic	3 (100.0)	0 (0)		1 (33.3)	2 (66.7)	
Thoracic	20 (57.1)	15 (42.9)		12 (34.3)	23 (65.7)	
Urology	25 (67.6)	12 (32.4)		15 (42.3)	20 (57.1)	
Vascular	27 (60.0)	18 (40.0)		20 (44.4)	25 (55.6)	
Missing	29 (96.7)	1 (3.3)		22 (78.6)	6 (21.4)	

Data only presented for patients with 30-day mortality outcome available (n=1113) and pulmonary complications outcome available (n=1103). Percentages are presented in rows.

Table 3.5: Procedures included by the study stratified by urgency of surgery

	Elective		Emergency		Total
	Minor	Major	Minor	Major	
Breast surgery	1	2	0	0	3
Breast biopsy	1				1
Mastectomy		4			2
Cardiac Surgery	0	15	3	33	51
Aortic valve surgery		5		8	13
Coronary artery bypass graft		5		7	12
Mitral valve surgery		3		15	18
Other procedure		2		2	4
Other valvular surgery			3	1	4
Gastrointestinal and general surgery	7	76	122	165	373
Adhesiolysis (laparoscopic)			2		3*
Adhesiolysis (laparotomy)				24	24
Appendicectomy	1		42		43
Colostomy - formation		2		5	7
Colostomy - refashioning or resiting		1			1
Colostomy - reversal		3			3
Diagnostic laparoscopy			4		4
Diagnostic laparotomy			14		14
Drainage of superficial haematoma			1		1
Feeding gastrostomy				1	1
Feeding jejunostomy		1		1	2
Formation of ileostomy		2			2
Hernia repair - femoral			3		3
Hernia repair - incisional	2		3		5
Hernia repair - inguinal	2		6		8
Hernia repair - other			6		6
Hernia repair - umbilical	2		2		4
Ileostomy - reversal				1	1
Left hemicolectomy		5		9	14
Miscellaneous proctology			5		5
Neck wound exploration			2		2
Other colorectal procedure		1		3	4
Other gastric procedure		1		1	2
Other oesophageal procedure				1	1
Other small bowel procedure				5	5
Pyloroplasty				1	1
Repair of perforated duodenal ulcer				3	3
Repair of perforated peptic ulcer				8	8
Resection - abdominoperineal resection		5		1	6
Resection - anterior resection		19		6	25
Resection - ileocaecal resection		2		6	8
Resection - oesophagectomy		4		1	5
Resection - right hemicolectomy		13		30	43
Resection - sigmoid hemicolectomy		4		26	30
Resection - small bowel resection				19	20*
Resection - subtotal colectomy		2		3	6*
Resection - total colectomy				6	6
Resection - total or partial gastrectomy		6		2	8
Sleeve gastrectomy		3		1	4
Splenectomy		1		2	3
Superficial abscess drainage (not perianal)			16		16
Transanal endoscopic microsurgery		1			1
Wound exploration & washout			15		15
Gynaecology	2	7	4	7	21
Hysterectomy - abdominal		6		3	10*
Hysterectomy - vaginal		1			1
Other procedure	2		4		6
Repair of uterus				1	1
Salpingectomy				3	3
Head & Neck surgery	7	14	13	6	40
Excision of salivary gland	1				1
Neck dissection		2			2
Other procedures on mandible		6		3	9
Pharynx procedures other than excision	1				1
Procures on the mouth	1				1
Procures on the tongue	4				4
Reduction and/or fixation of mandible		1		2	3

Tracheostomy			13		13
Thyroidectomy		5		1	6
Hepatobiliary surgery	0	34	0	28	62
Cholecystectomy		4		18	22
Hepatectomy		10			10
Liver transplant		1		3	4
Other biliary tract procedure		1		1	2
Other hepatic procedure		1		2	3
Other pancreatic procedure				2	2
Pancreatectomy		5		1	6
Pancreaticoduodenectomy		12		1	13
Neurosurgery	1	12	3	23	39
Excision of pituitary gland		1			1
Biopsy of lesion of brain tissue	1		1		2
Craniotomy		2		2	4
Drainage of extradural space				1	1
Drainage of lesion of tissue of brain			2		2
Drainage of subdural space		1		6	7
Excision of tissue of brain		4		1	5
Other procedure		2		5	7
Procedures on the meninges		1		4	5
Procedures on the ventricles				1	1
Repair of cranium		1		2	3
Repair of dura				1	1
Obstetrics	1	7	1	42	51
Caesarean section		7		42	49
Evacuation of contents of uterus	1		1		2
Opthalmology	4	0	0	0	4
Other ophthalmic procedurs	1				1
Phacoemulsification	3				3
Orthopaedics	2	18	19	262	302
Amputation of foot				3	3
Amputation of leg		1		21	22
Amputation of toe			10		10
Arthroscopy (diagnostic)			2		2
Bursa procedures	1		1		2
Closed reduction and external fixation of fracture				2	2
Closed reduction and internal fixation of fracture				15	15
Closed reduction of dislocation of joint			1		1
Debridement and irrigation of joint				13	13
Decompression or excision of intervebral disc		5		3	8
Dynamic hip screw		1		48	49
Hemiarthroplasty		1		65	66
Knee arthroscopy - therapeutic				4	4
Knee replacement		3		2	5
Open reduction and extramedullary fixation of fracture				12	12
Open reduction and intramedullary fixation of fracture		1		36	37
Open reduction, no fixation of fracture			2		2
Other procedures on limbs		2		5	7
Other spinal procedure		1		9	10
Other upper limb procedures				1	1
Removal of implant	1		4		5
Revision of total hip replacement		2		11	13
Shoulder replacement				1	1
Spinal cord procedures		1		1	2
Tendon procedures				3	4*
Total hip replacement				6	6
Other procedures	11	6	9	0	26
Biopsy of skin	1				1
Block dissection of lymph nodes		4			4
Central venous catheter insertion	1		2		3
Dental extraction			1		1
Lymph node biopsy	4		1		5
Miscellaneous	4	1	3		8
Multiorgan resection		1			1
Suture of skin of head or neck	1				1
Vacuum dressing application			2		2
Plastic surgery	0	1	1	1	3
Free flap				1	1
Local flap			1		1

Split skin graft		1			1
Thoracic surgery	2	17	12	4	35
Bronchoscopy, therapeutic	2				2
Chest tube insertion			6		6
Lobectomy		16			16
Lung transplant				1	1
Procedures on bronchus				1	1
Resection of chest wall tumour		1			1
Thoracoscopy			6		6
Thoracotomy				2	2
Urology	3	14	13	7	37
Cystectomy		2		1	3
Diagnostic cystoscopy			3		3
Diagnostic uretoscopy	2				2
Kidney transplant		2		3	5
Nephrectomy		6		2	8
Orchiopexy			1		1
Other bladder procedure			1		1
Other procedures for kidney stones		1			1
Procedures on penis		1			1
Prostatectomy		2			2
Replantation of ureter				1	1
Scrotal procedures			1		1
Transurethral resection of bladder tumour	1		2		3
Ureteric stent insertion			5		5
Vascular surgery	1	3	8	33	45
Bypass of femoral artery				5	5
Embolectomy / thombectomy				10	10
Femoral artery endarterectomy		1		2	3
Formation of arterio-venous fistula		1		2	3
Other procedure	1		8	10	19
Repair of abdominal aorta aneurysm		1		2	3
Repair of femoral artery aneurysm				2	2
Missing procedure/ surgical grade details					36

**Urgency of surgery data missing for one patient who underwent small bowel resection, one who underwent laparoscopic adhesiolysis, one patient who underwent subtotal colectomy, one who underwent abdominal hysterectomy and one who underwent tendon repair*

3.5.3 Mortality

Overall 30-day mortality was 23.8% (268/1128, Table 3.6). Men had higher 30-day mortality than women (28.4% [172/605] versus 18.2% [94/517], p<0.001). Patients aged ≥70 years had higher mortality than patients aged <70 years (33.7% [188/558] versus 13.9% [79/567], p<0.001). Mortality was higher after emergency than elective surgery (25.6% [214/835] versus 18.9% [53/280], p=0.023, Figure 3.1). The subgroup with the highest mortality rates were men aged ≥70 years (Figure 3.2).

In adjusted analyses (Table 3.7), predictors of 30-day mortality were male sex (OR 1.75, 95% CI 1.28-2.40, p<0.001), age ≥70 years versus age <70 years (OR 2.30,

95% CI 1.65-3.22, p<0.001), ASA grades 3-5 versus grades 1-2 (OR 2.35, 95% CI 1.57-3.53, p<0.001), cancer versus benign/ obstetric diagnosis (OR 1.55, 95% CI 1.01-2.39, p=0.046), emergency versus elective surgery (OR 1.67, 95% CI 1.06-2.63, p=0.026), and major versus minor surgery (OR 1.52, 95% CI 1.01-2.31, p=0.047).

Table 3.6: Postoperative outcomes

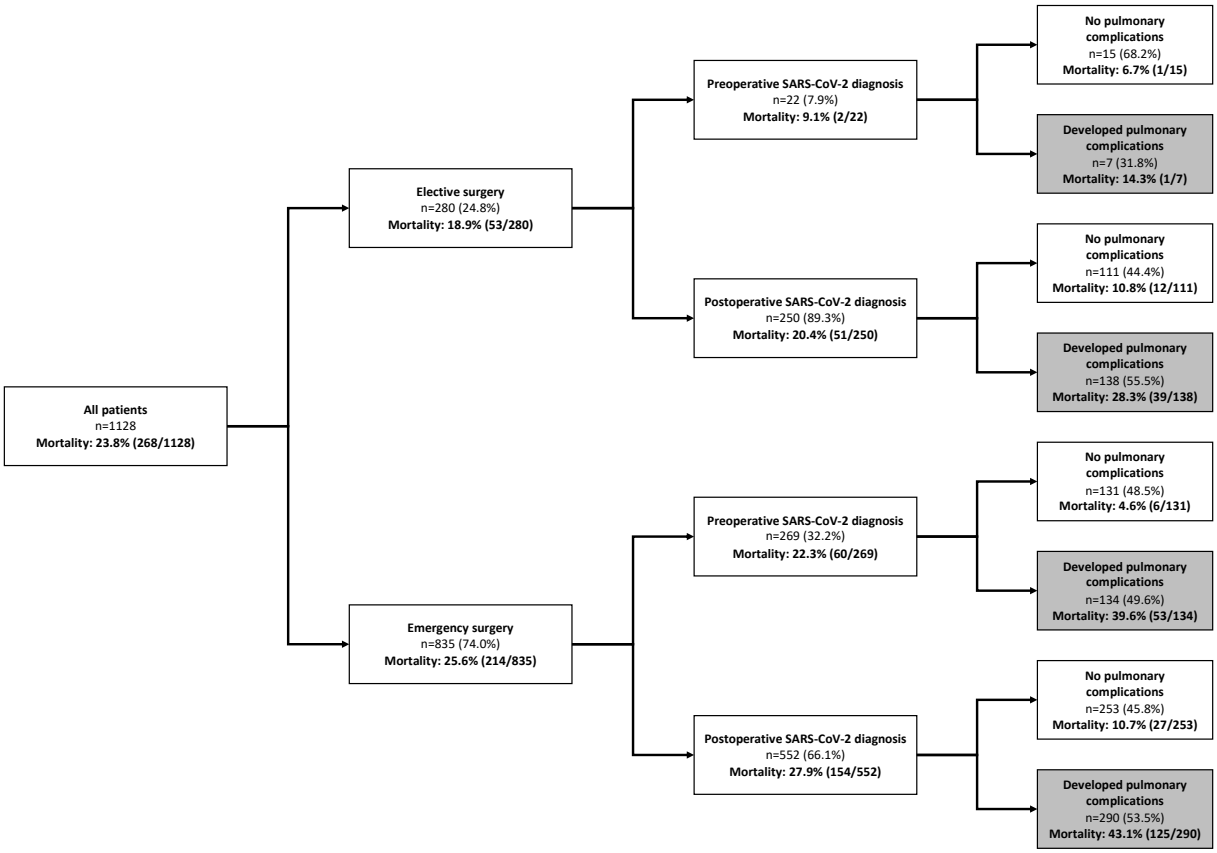
	Urgency			Grade of surgery		
	Elective (n=280)	**Emergency (n=835)**	**p-value**	**Minor (n=251)**	**Major (n=841)**	**p-value**
Mortality						
7-day mortality	7 (2.5)	52 (6.2)	0.015	8 (3.2)	51 (6.1)	0.074
30-day mortality	53 (18.9)	214 (25.6)	0.020	41 (16.3)	226 (26.9)	0.001
Mortality missing	2 (0.7)	11 (1.3)		1 (0.4)	8 (1.0)	
Pulmonary complications						
Composite of pulmonary complications	147 (52.5)	428 (51.3)	0.873	116 (46.2)	455 (54.1)	0.022
Pneumonia	118 (42.1)	334 (40.0)	0.527	94 (37.5)	355 (42.2)	0.178
ARDS	41 (14.6)	119 (14.3)	0.872	33 (13.2)	127 (15.1)	0.442
Unexpected postoperative ventilation			0.262			0.160
Non-invasive ventilation	23	31		12	41	
Invasive ventilation	40	156		41	153	
Composite data missing	3	21		4	14	
Duration of invasive ventilation			0.049			0.023
1-23 hours	16	32		7	41	
24-47 hours	5	27		3	28	
48-71 hours	2	21		3	20	
≥72 hours	17	79		29	66	
Missing	240	676		209	686	
Postoperative ICU admission, n (%)			0.003			0.177
None	158 (56.4)	570 (68.3)		177 (70.5)	538 (64.0)	
Planned	64 (22.9)	189 (22.6)		46 (18.3)	203 (24.1)	
Unplanned from theatre	16 (5.7)	25 (3.0)		10 (4.0)	31 (3.7)	
Unplanned from ward	23 (8.2)	38 (4.6)		17 (6.8)	43 (5.1)	
Missing	19 (6.8)	13 (1.6)		1 (0.4)	26 (3.1)	

ARDS: acute respiratory distress syndrome; ICU: intensive care unit; IQR: interquartile range.

Urgency data missing for 13 patients and grade of surgery data missing for 36 patients.

Percentages shown are based on denominator of total patients in the subgroup.

Figure 3.1: 30-day mortality rates stratified by timing of surgery and development of pulmonary complications

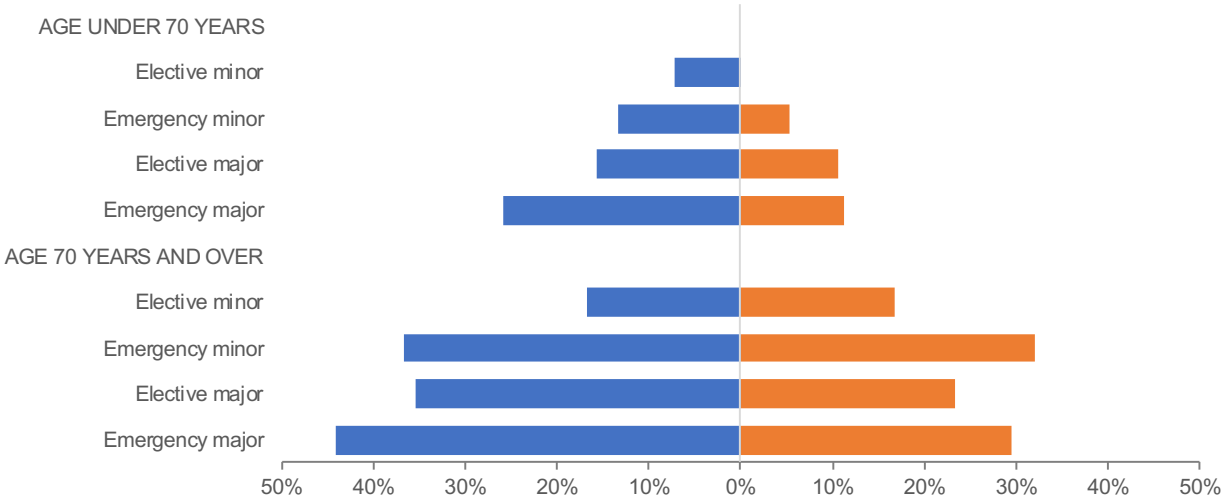


Patients with missing data are included in denominators.

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.

Pulmonary complications defined as pneumonia, acute respiratory distress syndrome, and/or unexpected postoperative ventilation.

Figure 3.2: 30-day mortality rates by patient subgroup



Charts show 30-day postoperative mortality rates, with males represented by blue bars and females by orange bars. Grade of surgery was classified based on the Bupa Schedule as either minor (minor or intermediate in Bupa Schedule) or major (major or complex major in Bupa Schedule).

Table 3.7: Unadjusted and adjusted models of predictors for 30-day mortality

Factor	Unadjusted	Adjusted	
	OR (95%CI)	OR (95%CI)	p-value
Age			
0–69 years	Reference	Reference	–
≥70 years	3.12 (2.31 to 4.22)	2.30 (1.65 to 3.22)	<0.001
Sex			
Female	Reference	Reference	–
Male	1.82 (1.35 to 2.44)	1.75 (1.28 to 2.40)	<0.001
ASA physical status			
1–2	Reference	Reference	–
3–5	3.45 (2.41 to 4.94)	2.36 (1.58 to 3.53)	<0.001
Unknown	2.73 (1.01 to 7.35)	2.42 (0.86 to 6.82)	0.094
Comorbidities			
None	Reference	Reference	–
1	2.75 (1.24 to 6.13)	1.72 (0.75 to 3.97)	0.201
≥ 2	5.36 (2.56 to 11.21)	2.12 (0.95 to 4.71)	0.066
White cell count			
WCC ($x10^9$/L)	1.00 (0.98 to 1.02)	1.00 (0.98 to 1.03)	0.811
Indication for surgery			
Benign/ Obstetric	Reference	Reference	–
Malignant	1.35 (0.95 to 1.90)	1.55 (1.01 to 2.39)	0.046
Trauma	1.57 (1.11 to 2.23)	0.97 (0.65 to 1.45)	0.890
Grade of surgery			
Minor	Reference	Reference	–
Major	1.83 (1.26 to 2.66)	1.52 (1.01 to 2.31)	0.047
Urgency of surgery			
Elective	Reference	Reference	–
Emergency	1.43 (1.01 to 2.02)	1.67 (1.06 to 2.63)	0.026
SARS-CoV-2 diagnosis			
Preoperative	Reference	Reference	–
Postoperative	1.28 (0.92 to 1.78)	0.94 (0.65 to 1.36)	0.753

The adjusted model included 1037 patients with complete data; 7 patients who died up to 30 days, and 84 patients who did not die were excluded due to missing data.

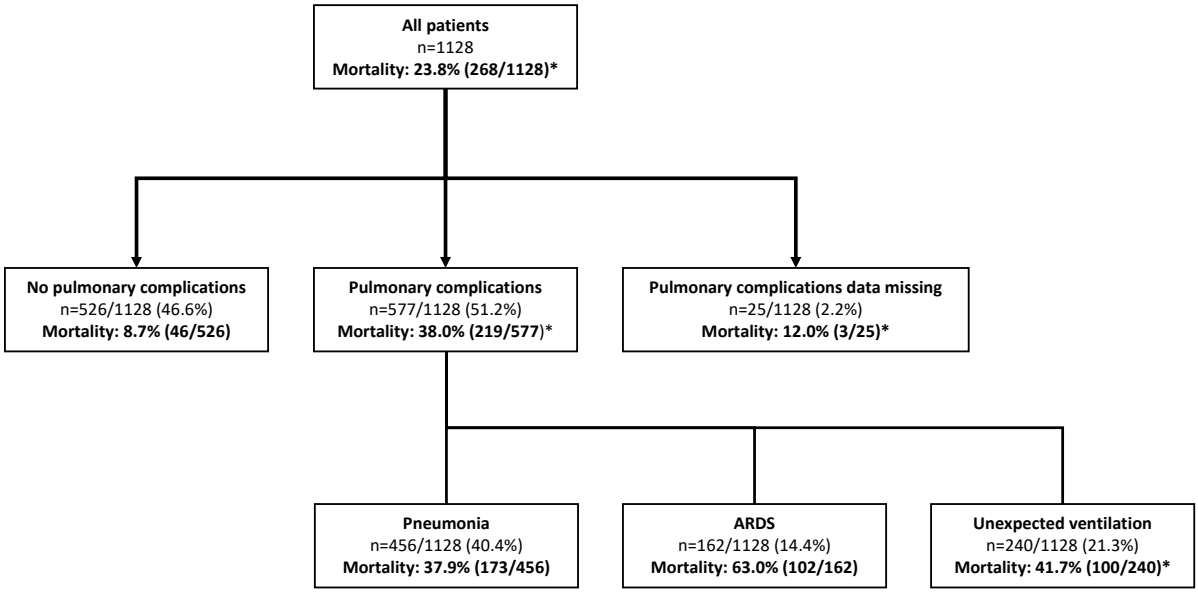
ASA: American Society of Anesthesiologists grade; CI: confidence interval; OR: odds ratio; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; WCC: white cell count

3.5.4 Pulmonary complications

In total, 51.2% (577/1128) of patients suffered at least one pulmonary complication (Figure 3.3), with rates of 40.4% (456/1128) for pneumonia, 21.3% (240/1128) for unexpected ventilation, and 14.4% (162/1128) for ARDS. Patients who developed pulmonary complications had a higher 30-day mortality than those who did not (38.0% [219/577] versus 8.7% [46/526], p<0.001, Table 3.6). Pulmonary complications were present in 82.6% (219/265) of all deaths. Amongst patients who developed pulmonary complications, 30-day mortality was highest in those who developed ARDS (63.0%, 102/162). Pulmonary complications were associated with

high 30-day mortality rates across elective patients with a postoperative SARS-CoV-2 diagnosis (28.3%, 39/138), emergency patients with a preoperative SARS-CoV-2 diagnosis (39.6%, 53/134), and emergency patients with a postoperative SARS-CoV-2 diagnosis (43.1%, 125/290). Pulmonary complication rates were similar in patients with laboratory confirmed and clinically diagnosed SARS-CoV-2 infection (50.9% [493/969] versus 47.1% [32/68], p=0.543).

Figure 3.3: 30-day mortality rates associated with components of pulmonary complications



Mortality data was missing for 15 patients. Pulmonary complications data were also missing for 14 of these patients, and 1 patient was recorded as having had a pulmonary complication (unexpected ventilation).

ARDS: acute respiratory distress syndrome.

In adjusted analyses (Table 3.8) pulmonary complications were independently associated with age ≥70 years versus <70 years (OR 1.45, 95% CI 1.07-1.96, p=0.016) and ASA grades 3-5 versus grades 1-2 (OR 2.74, 95% CI 1.89-3.99, p<0.001).

Table 3.8: Unadjusted and adjusted models of predictors of pulmonary complications

Factor	Unadjusted	Adjusted	
	OR (95%CI)	OR (95%CI)	p-value
Age			
0–69 years	Reference	Reference	–
≥70 years	1.52 (1.13 to 2.04)	1.09 (0.78 to 1.52)	0.627
Sex			
Female	Reference	Reference	–
Male	1.63 (1.22 to 2.16)	1.45 (1.07 to 1.96)	0.016
ASA physical status			
1–2	Reference	Reference	–
3–5	3.12 (2.25 to 4.34)	2.74 (1.89 to 3.99)	<0.001
Unknown	3.87 (1.30 to 11.49)	3.73 (1.25 to 11.19)	0.019
Comorbidities			
None	Reference	Reference	–
1	2.18 (1.24 to 3.84)	1.75 (0.97 to 3.16)	0.065
≥ 2	3.08 (1.84 to 5.13)	1.62 (0.91 to 2.87)	0.101
White cell count			
WCC ($x10^9$/L)	1.01 (0.99 to 1.03)	1.01 (0.99 to 1.03)	0.445
Indication for surgery			
Benign/ Obstetric	Reference	Reference	–
Malignant	1.12 (0.78 to 1.60)	1.13 (0.72 to 1.76)	0.596
Trauma	1.07 (0.71 to 1.61)	0.92 (0.58 to 1.43)	0.698
Grade of surgery			
Minor	Reference	Reference	–
Major	1.33 (0.94 to 1.87)	1.22 (0.83 to 1.78)	0.318
Urgency of surgery			
Elective	Reference	Reference	–
Emergency	1.02 (0.72 to 1.43)	1.16 (0.75 to 1.82)	0.504
SARS-CoV-2 diagnosis			
Preoperative	Reference	Reference	–
Postoperative	1.51 (1.08 to 2.11)	1.41 (0.97 to 2.05)	0.076

The adjusted model included 1029 patients with complete data; 19 patients who developed pulmonary complications and 80 patients who did not develop pulmonary complications were excluded due to missing data.

ASA: American Society of Anesthesiologists grade; CI: confidence interval; OR: odds ratio; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; WCC: white cell count

The rate of pulmonary embolism at 30-days was 2.0% (22/1128). The 30-day mortality rate in patients with pulmonary embolism was equivalent to that in patients who did not have pulmonary embolism (22.7% [5/22] versus 23.8% [263/1106], p=0.909).

3.5.5 Sensitivity analyses

In a sensitivity analysis including only patients with laboratory confirmed SARS-CoV-2, the overall 30-day mortality rate was 23.7% (230/969) and pulmonary complications occurred in 50.9% (493/969) of patients. In adjusted analyses (Table

3.9), predictors of 30-day mortality were consistent with the main analysis: male sex, age ≥70 years, ASA grades 3-5, cancer surgery, and emergency surgery. The only independent predictor for 30-day pulmonary complications was ASA grades 3-5.

Table 3.9: Sensitivity analysis with adjusted models of predictors for 30-day mortality and pulmonary complications, in laboratory proven SARS-CoV-2 infected patients

Factor	30-day mortality		Pulmonary complications	
	Adjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
Age				
0–69 years	Reference	–	Reference	–
≥70 years	2.38 (1.65 to 3.43)	<0.001	0.94 (0.65 to 1.35)	0.734
Sex				
Female	Reference	–	Reference	–
Male	1.86 (1.32 to 2.61)	<0.001	1.38 (1.00 to 1.91)	0.052
ASA physical status				
1–2	Reference	–	Reference	–
3–5	2.14 (1.38 to 3.32)	0.001	2.70 (1.80 to 4.05)	<0.001
Unknown	2.14 (0.69 to 6.65)	0.188	3.47 (1.05 to 11.48)	0.041
Comorbidities				
None	Reference	–	Reference	–
1	1.77 (0.68 to 4.61)	0.240	1.76 (0.90 to 3.43)	0.100
≥ 2	2.20 (0.89 to 5.47)	0.089	1.81 (0.95 to 3.45)	0.072
White cell count				
WCC ($x10^9$/L)	1.00 (0.97 to 1.02)	0.839	1.01 (0.99 to 1.04)	0.327
Indication for surgery				
Benign/ Obstetric	Reference	–	Reference	–
Malignant	1.68 (1.05 to 2.69)	0.032	1.04 (0.64 to 1.69)	0.862
Trauma	1.07 (0.70 to 1.62)	0.759	0.95 (0.59 to 1.51)	0.823
Grade of surgery				
Minor	Reference	–	Reference	–
Major	1.35 (0.86 to 2.11)	0.188	1.28 (0.85 to 1.93)	0.240
Urgency of surgery				
Elective	Reference	–	Reference	–
Emergency	1.84 (1.13 to 3.00)	0.015	1.19 (0.74 to 1.93)	0.470
SARS-CoV-2 diagnosis				
Preoperative	Reference	–	Reference	–
Postoperative	0.94 (0.63 to 1.42)	0.779	1.21 (0.80 to 1.83)	0.368

The adjusted models included 901 patients with complete data for mortality and 893 with complete data for pulmonary complications.

ASA: American Society of Anesthesiologists grade; CI: confidence interval; OR: odds ratio; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; WCC: white cell count

In a sensitivity analysis including only patients with preoperatively diagnosed SARS-CoV-2, the overall 30-day mortality rate was 21.1% (62/294) and pulmonary complications occurred in 48.3% (142/294) of patients. In adjusted analyses (Table

3.10), predictors of 30-day mortality were male sex and ASA grades 3-5. The only independent predictor for 30-day pulmonary complications was ASA grades 3-5.

Table 3.10: Sensitivity analysis with adjusted models of predictors for 30-day mortality and pulmonary complications, in patients diagnosed with SARS-CoV-2 pre-operatively

Factor	30-day mortality		Pulmonary complications	
	Adjusted OR (95%CI)	p-value	Adjusted OR (95%CI)	p-value
Age				
0–69 years	Reference	–	Reference	–
≥70 years	1.83 (0.86 to 3.88)	0.116	0.97 (0.39 to 2.38)	0.946
Sex				
Female	Reference	–	Reference	–
Male	2.37 (1.21 to 4.66)	0.012	2.06 (1.00 to 4.28)	0.051
ASA physical status				
1–2	Reference	–	Reference	–
3–5	4.67 (1.76 to 12.42)	0.002	9.78 (3.24 to 29.50)	<0.001
Unknown	8.19 (1.03 to 65.30)	0.047	2.92 (0.23 to 36.96)	0.408
Comorbidities				
None	Reference	–	Reference	–
1	1.55 (0.40 to 5.99)	0.526	1.81 (0.60 to 5.42)	0.289
≥ 2	2.73 (0.81 to 9.24)	0.105	0.79 (0.27 to 2.33)	0.668
White cell count				
WCC ($x10^9$/L)	1.03 (0.99 to 1.07)	0.131	1.06 (1.00 to 1.12)	0.062
Indication for surgery				
Benign/ Obstetric	Reference	–	Reference	–
Malignant	0.52 (0.17 to 1.59)	0.251	1.60 (0.45 to 5.69)	0.467
Trauma	1.03 (0.40 to 2.63)	0.950	2.13 (0.61 to 7.38)	0.235
Grade of surgery				
Minor	Reference	–	Reference	–
Major	1.99 (0.91 to 4.35)	0.084	1.66 (0.69 to 3.99)	0.260
Urgency of surgery				
Elective	Reference	–	Reference	–
Emergency	1.54 (0.28 to 8.40)	0.620	2.09 (0.47 to 9.24)	0.333

The adjusted models included 279 patients with complete data for mortality and 276 with complete data for pulmonary complications.

ASA: American Society of Anesthesiologists grade; CI: confidence interval; OR: odds ratio; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; WCC: white cell count

3.6 Discussion

3.6.1 Main findings

This study found that perioperative SARS-CoV-2 infection is associated with high rates of postoperative mortality; the overall 30-day mortality was 23.8%. Mortality risk was high across all patient subgroups, including elective surgery (18.9%), emergency surgery (25.6%), minor surgery (16.3%), and major surgery (26.9%).

These mortality rates are substantially higher than published pre-pandemic baseline mortality rates. For example, overall 30-day postoperative mortality pre-pandemic was 0.5% in New Zealand[303] and 0.8% in England[304]. We found that patients with perioperative SARS-CoV-2 infection had greater mortality than even the highest risk emergency surgery patients pre-pandemic. The 2019 UK National Emergency Laparotomy Audit (NELA) reported 30-day mortality rates of 16.9% in patients with a high preoperative risk of death, 16.8% in patients with an unexpected critical care admission, and 23.4% in frail patients aged over 70 years[305]. A global study of emergency surgery outcomes across 58 countries reported 30-day mortality of 14.9% in high-risk patients (emergency midline laparotomy)[250].

Most deaths were in patients who had experienced postoperative pulmonary complications. Whereas pre-pandemic rates of postoperative complications were under 8%[301,302], over half of patients with perioperative SARS-CoV-2 developed postoperative complications. Rates of severe pulmonary complications were particularly high in this study; whereas one in two thousand patients in the pre-pandemic African Surgical Outcomes Study developed ARDS[220], one in seven patients in this study developed ARDS. When they occurred, postoperative pulmonary complications were associated with high mortality. A multicentre US study of high-risk patients undergoing non-cardiac surgery found a mortality of 2.3% in patients with postoperative pulmonary complications; mortality associated with pulmonary complications in this study was 38%.

These findings were supported by subsequent studies published in 2020 that also found perioperative SARS-CoV-2 to be associated with high rates of postoperative complications and mortality[306]. A single centre study published in June 2020 from Italy found that patients with perioperative SARS-CoV-2 operated in February to April

2020 had ten-fold higher odds of 30-day mortality compared to matched non-SARS-CoV-2 patients[307]. A study across nine London hospitals in the UK found that amongst patients undergoing hip fracture surgery, 30-day mortality risk was higher in patients with perioperative SARS-CoV-2 infected versus uninfected patients (30.5% versus 10.3%)[308]. A multicentre study across 27 Dutch hospitals published in September 2020 found that patients with perioperative SARS-COV-2 had a 30-day mortality of 16% compared to mortality of 4% in comparator non-SARS-CoV-2 patients[306]. Following propensity score matching and adjustment, SARS-CoV-2 infection was associated with three-fold increased odds of mortality. A study published in October 2020 from two hospitals in New York, United States identified a 17% 30-day mortality rate in patients with perioperative SARS-CoV-2 infection operated in March to April 2020, compared to 1.4% in contemporaneous SARS-CoV-2 negative patients[309]. In adjusted analyses, SARS-CoV-2 infection remained significantly associated with mortality, with a risk ratio of 9.

These studies had several weaknesses. Firstly, they were completed in high-income hospitals, so their generalisability to LMIC settings is unclear. Secondly, most studies published in 2020 were only able to enrol a small number of patients with perioperative SARS-CoV-2 (the largest study included 161 SARS-CoV-2 patients[306]) limiting their statistical power. This was overcome by studies using countrywide routine datasets. For example, an analysis of Hospital Episodes Statistics data for 2.7 million public surgeries completed during the first year of the pandemic in England found that the odds of 30-days mortality were six-fold higher overall and 26-fold higher in elective patients compared to non-SARS-CoV-2 patients[310]. However, this study relied on routine clinical coding to identify patients with SARS-CoV-2 and new SARS-CoV-2 codes may have been inconsistently applied across participating

hospitals, particularly in the early months of the pandemic. Ascertainment bias may have occurred if patients with severe COVID-19 were more likely to be coded as having SARS-CoV-2 infection.

Some studies published in 2021 suggested that in some low-risk procedures perioperative SARS-CoV-2 may not increase risk. For example, a multicentre study of 1,093 patients undergoing hand surgery in England found zero mortality[311].

The analysis in this chapter was based on the 1,128 patients operated and enrolled in CovidSurg up to 31 March 2020. Patient enrolment continued until 31 July 2020, with 10,029 patients included in the final dataset. This larger sample size enabled more granular specialty-level analyses to be completed. Sub-analyses of patient data for cardiac surgery[312], emergency general surgery[313], orthopaediac surgery[314], and vascular surgery[315] confirmed that perioperative SARS-CoV-2 was associated with adverse outcomes in these groups. CovidSurg-Cancer was a parallel study to CovidSurg that focussed on the outcomes of cancer surgery during the pandemic. Both in the overall cancer surgery cohort[280], and in colorectal cancer surgery[316], gynaecological cancer surgery[317], head and neck cancer surgery[318], and hepatobiliary cancer surgery[319] sub-groups, perioperative SARS-CoV-2 was found to be associated with adverse outcomes. However, a paediatric sub-group analysis found low mortality in children (1.1%)[320], reflecting the overall low rates of severe COVID-19 in children[321].

3.6.2 Strengths and weaknesses

This observational study was not able to standardise either laboratory protocols or clinical pathways. Consequently, there was heterogeneity in how patients were tested for SARS-CoV-2 across participating centres. For example, hospital labs may

have used different assays and different cycle threshold values for determining RT-PCR positivity[322]. During the initial months of the pandemic routine testing was not universally available, particularly in LMICs. Therefore, to accommodate hospitals across a diverse range of settings, this study adopted a pragmatic approach, capturing both confirmed and suspected perioperative SARS-CoV-2 cases. Nonetheless, some eligible patients were missed, either due to a lack of testing or difficulties identifying all eligible patients in large hospitals. Although some patients entered as having suspected SARS-CoV-2 may have been misclassified (i.e. they did not truly have SARS-CoV-2 infection), this is likely to apply to a small number of patients only, since 94% of patients had laboratory confirmed SARS-CoV-2. Patients with confirmed and suspected perioperative SARS-CoV-2 were found to have similar clinical outcomes, and the study's main findings were consistent in a sensitivity analysis that only included patients with perioperative SARS-CoV-2.

A large number of collaborating investigators were involved in screening and enrolling patient and entering baseline and follow-up data. In order to reduce the risk of heterogeneity in outcome assessment, the study protocol included detailed definitions, including for outcome measures. In order to ensure that all sites were familiar with and followed the protocol, a training package was designed for local principal investigators including written and audio-visual materials.

Given the urgency to release high-quality surgical data during the early pandemic, a decision was made not to attempt to undertake a formal data validation exercise, to avoid delay to data release. As a pragmatic measure, local principal investigators were asked to verify final case ascertainment and data completeness and to rectify any errors prior to database lock.

Participating hospitals were under significant stress during the early pandemic, so a decision was made to rationalise data collection by focussing on patients with perioperative SARS-CoV-2. A lack of comparator data for non-SARS-CoV-2 patients meant that this study's interpretation was based on benchmarking against pulmonary complication and mortality rates from high-quality pre-pandemic studies. Nonetheless, this study's findings were strongly supported by subsequent studies that compared perioperative SARS-CoV-2 outcomes against contemporaneous comparators.

3.6.3 Implications for clinical practice

This analysis was published on 29 May 2020[298]. It was first international multicentre study assessing the safety of surgery during the COVID-19 pandemic. The study had direct implications for global clinical practice; it was the first study to demonstrate significant increased risk of complications and death in patients with perioperative SARS-CoV-2 infection. This indicated that the threshold for surgery during the pandemic should be raised compared to pre-pandemic practice and consideration given for postponing non-critical procedures, in order to avoid exposing patients to unnecessary increased risks.

This study provided robust data to inform shared decision making by patients and surgeons. For individual patients, the increased risks associated perioperative SARS-CoV-2 infection should be balanced against the risks of delaying surgical treatment. Individual risk assessment could be based on the risk factors for adverse outcomes identified in this study: males, elderly patients, comorbid patients, patients undergoing cancer surgery, and patients needing emergency or major surgery were found to be at increased risk of postoperative mortality.

3.6.4 Implications for future research

The key recommendation from this study was that that non-urgent surgery should be delayed in patients who have acute SARS-CoV-2 infection. However, as this study only included patients with perioperative SARS-CoV-2 it was not possible to assess how long patients should be delayed and when surgery might be safe. A new study was designed to address this question, which is reported in chapter 4.

Hospital acquired SARS-CoV-2 has been a key concern throughout the pandemic, with up to 15% of hospitalised COVID-19 patients being infected in hospital[323,324]. Therefore, all surgical patients are potentially at risk of SARS-CoV-2 infection and consequent adverse outcomes in the postoperative period. A key research priority is to establish and robustly evaluate strategies to mitigate hospital acquired SARS-CoV-2 in surgical patients. Subsequent studies evaluated measures such as preoperative isolation of surgical patients[325], preoperative SARS-CoV-2 screening[326], and the design of COVID-free surgical pathways[280].

This analysis identified risk factors for mortality which could inform shared decision making by patients and surgeons. However, a robust, validated risk prediction model might be more helpful to produce reproducible risk estimates. The full CovidSurg dataset was subsequently used to derive and validate a risk prediction model[327].

This study was intended to provide rapid guidance in early 2020 regarding the short-term safety of surgery in SARS-CoV-2 patients. Consequently, this study was not able to assess longer-term and patient-centred outcomes, which should be explored in future studies.

4 TIMING OF SURGERY FOLLOWING SARS-COV-2 INFECTION

4.1 Contribution

This chapter presents data published in *Anaesthesia*[328]. I have abbreviated methods section to avoid duplicating material in chapter 2. I have extensively updated the introduction and discussion in light of subsequent literature published after the *Anaesthesia* paper. I have removed a small amount of material from the results that was not relevant to the primary and secondary aims of the study.

I was co-first author on this paper. I was the co-lead investigator with Mr Aneel Bhangu; participating in conceiving the study and methodology, and leading the administration of the study. I performed data analysis, with input from Mr Omar Omar (senior statistician). I drafted the first version of the manuscript, revised this based on comments from co-authors, and led the responses to journal reviewers.

4.2 Synopsis

Peri-operative SARS-CoV-2 infection increases postoperative mortality. The aim of this study was to determine the optimal duration of delay between SARS-CoV-2 infection and surgery. This international, multicentre, prospective cohort study included patients operated in October 2020. The primary outcome measure was 30-day postoperative mortality. The study included 140,231 patients (116 countries), of whom 3127 patients (2.2%) had a SARS-CoV-2 diagnosis prior to undergoing surgery. Patients operated 0–2 weeks, 3–4 weeks and 5–6 weeks after a SARS-CoV-2 diagnosis were at increased risk of mortality and postoperative pulmonary complications compared to patients who had not previously had a SARS-CoV-2 infection. However, there was no increased risk in patients who surgery was performed ≥ 7 weeks after SARS-CoV-2 diagnosis. This suggests that as risks of postoperative morbidity and mortality were greatest in patients are operated within 6

weeks of diagnosis of SARS-CoV-2 infection, surgery should be delayed for at least 7 weeks following SARS-CoV-2 infection.

4.3 Introduction

In chapter 3 I described the results of an international multicentre cohort study which assessed the safety of surgery in patients with perioperative SARS-CoV-2 infection during the first COVID-19 wave. This study found that patients who were diagnosed with SARS-CoV-2 infection in the 7 days before or 30 days after surgery were experienced high rates of both postoperative complications and mortality. The overall postoperative pulmonary complication rate was 51.2% and the overall mortality rate was 23·8%. This finding was supported by several subsequent studies that found perioperative SARS-CoV-2 to be associated with high rates of postoperative complications and mortality.

By 1 October 2020, 34 million SARS-CoV-2 cases had been recorded worldwide[16]. As the cumulative number of SARS-CoV-2 cases increased, it would become increasingly common for patients needing surgery to have previously had SARS-CoV-2 infection. Whilst the data in chapter 3 indicated that surgery for patients with ongoing SARS-CoV-2 infection should be delayed whenever possible, there was little data to inform the optimal duration of delay.

Pre-pandemic studies indicated that surgery should be delayed for 4 weeks following respiratory infection. A prospective cohort study including 122 patients having cancer surgery, found that surgery ≥4 weeks after a positive SARS-CoV-2 swab result was associated with a lower risk of postoperative mortality than earlier surgery[329]. A Brazilian study included 49 patients with asymptomatic SARS-CoV-2 infection whose elective surgery was delayed, until they received clearance with a negative SARS-

CoV-2 RT-PCR test result. In these patients postoperative complication rates were comparable to non-SARS-CoV-2 patients. However, the study did not assess the optimal duration of delay following SARS-CoV-2 diagnosis. Early clinical guidelines presented conflicting recommendations, with recommended duration of delay ranging from 1 to 12 weeks.

The aim of this study was to determine the optimal timing of surgery following SARS-CoV-2 infection.

4.4 Methods

Data collection procedures are described in detail in chapter 2. In summary, this was an international, multicentre, observational cohort study. In the UK it study was registered as clinical audit or service evaluation and in other countries, local principal followed local and national regulations to secure approvals.

4.4.1 Patient inclusion criteria

Patients were eligible for inclusion if they underwent any type of surgery under either local or general anaesthesia. Hospitals pre-defined which surgical specialties would be participating as well as the patient inclusion windows they would be collecting data in. Data could be collected in up to four data inclusion windows (each of 7 consecutive days) in the period 5th October 2020 to 1 November 2020.

4.4.2 Exposure: SARS-CoV-2 status

Patients were categorised into the following groups according to the time from diagnosis of SARS-CoV-2 infection to the day of surgery: no SARS-CoV-2 diagnosis, 0–2 weeks between SARS-CoV-2 diagnosis and surgery, 3–4 weeks between SARS-CoV-2 diagnosis and surgery, 5–6 weeks between SARS-CoV-2 diagnosis and surgery, and ≥7 weeks between SARS-CoV-2 diagnosis and surgery.

For patients who had a preoperative SARS-CoV-2 diagnosis, the nature of any COVID-19 symptoms was recorded as: asymptomatic; symptomatic but symptoms now resolved; or symptomatic with ongoing symptoms. Both respiratory (e.g. cough) and non-respiratory symptoms (e.g. fever, lethargy) were considered.

4.4.3 Outcome measures

The primary outcome measure was 30-day postoperative mortality. The secondary outcome measure was 30-day postoperative pulmonary complications.

4.4.4 Statistical analysis

4.4.4.1 Unadjusted models

Logistic regression was used to perform both unadjusted and adjusted analyses. These analyses produced OR and 95% CI.

Only factors that occurred before the outcome of interest were included in the models. Factors were selected *a priori* based on their clinical relevance. These were variables that have previously been identified as independent predictors of mortality in patients with peri-operative SARS-CoV-2 infection and included: age, sex, ASA grade, RCRI, indication for surgery, grade of surgery, urgency of surgery, presence of respiratory comorbidities, and national income

4.4.4.2 Adjusted models

Adjusted logistic regression models were fitted to adjust time from SARS-CoV-2 diagnosis to surgery for confounding factors. Average marginal effects were used to produce adjusted mortality estimates stratified by time from SARS-CoV-2 diagnosis to surgery. The main model included all patients with an outcome of 30-day postoperative mortality. To address possible bias, average marginal effects were used to produce adjusted mortality rates by time from SARS-CoV-2 diagnosis to

surgery, stratified by the following pre-selected variables: age, ASA grade, urgency of surgery, and grade of surgery.

An additional model was fitted for all patients for the secondary outcome of 30-day postoperative pulmonary complications. Another model was fitted to explore the association of preoperative COVID-19 symptoms with postoperative mortality; this model only included patients who had a preoperative SARS-CoV-2 diagnosis.

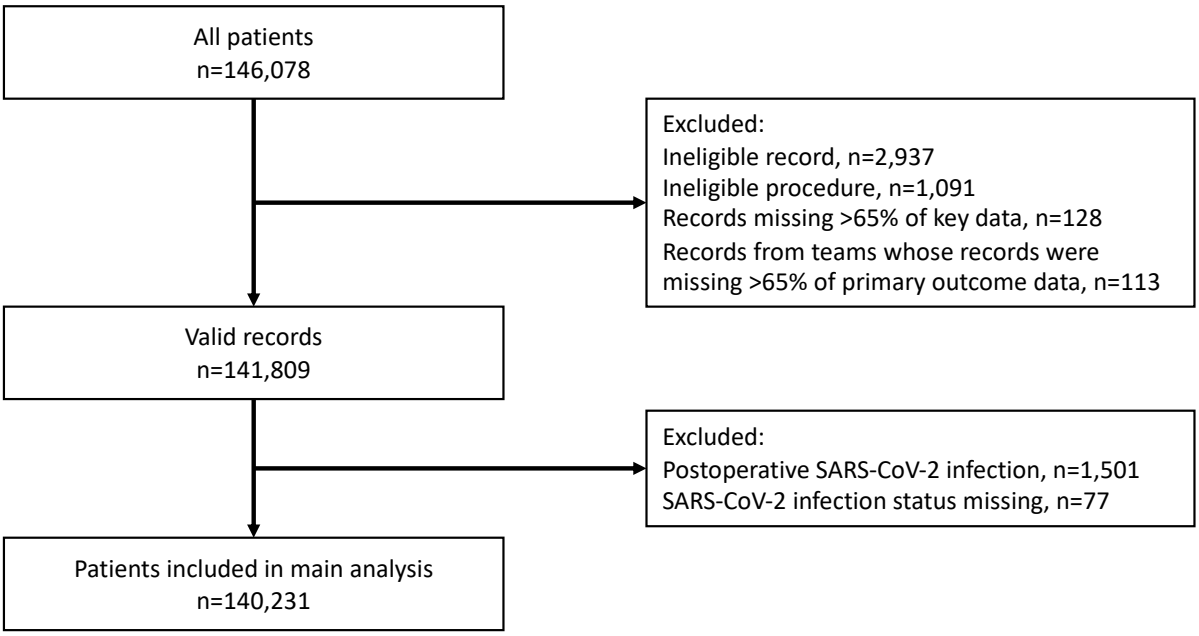
4.4.4.3 Sensitivity analyses

Surgery is more likely to be delayed for elective than emergency patients, so a sensitivity analysis was performed including only elective patients. A further sensitivity analysis was performed including only patients who either had confirmed (RT-PCR proven) SARS-CoV-2 infection or no SARS-CoV-2 diagnosis.

4.5 Results

A total of 140,231 patients were enrolled across 1,674 hospitals in 116 countries (Figure 4.1). In total, 3127 (2.2%) patients had a preoperative SARS-CoV-2 diagnosis. Of these, diagnosis was confirmed with a RT-PCR swab in 79.5% (2486/3127) of patients. In patients with suspected SARS-CoV-2 infection (no positive RT-PCR swab), diagnosis was with a rapid antigen test in 2.8% (87/3127), a CT scan in 3.8% (118/3127), antibody test in 9.0% (280/3127), and a clinical diagnosis in 5.0% (156/3127).

Figure 4.1: Study flowchart



The time from SARS-CoV-2 diagnosis to surgery was 0-2 weeks in 1,138 patients (36.4%), 3-4 weeks in 461 patients (14.7%), 5-6 weeks in 326 patients (10.4%) and ≥7 weeks in 1,202 patients (38.4%) (Table 4.1). The majority of patients were asymptomatic at the time of surgery (either having never had symptoms or symptoms had resolved).

Table 4.1: Baseline demographics and outcomes, stratified by SARS-CoV-2 status

	No pre-operative SARS-CoV-2 n=137,104	Pre-operative SARS-CoV-2, by timing of diagnosis prior to surgery				p-value
		0-2 weeks n=1,138	3-4 weeks n=461	5-6 weeks n=326	≥7 weeks n=1,202	
Age						
0–29 years	31,456 (22.9%)	331 (29.1%)	84 (18.2%)	62 (19.0%)	169 (14.1%)	<0.001
30–49 years	37,673 (27.5%)	355 (31.2%)	149 (32.3%)	101 (31.0%)	364 (30.3%)	
50–69 years	41,649 (30.4%)	265 (23.3%)	162 (35.1%)	109 (33.4%)	471 (39.2%)	
70–79 years	17,577 (12.8%)	93 (8.2%)	52 (11.3%)	41 (12.6%)	121 (10.1%)	
≥80 years	8,747 (6.4%)	94 (8.3%)	14 (3.0%)	13 (4.0%)	77 (6.4%)	
Missing	2 (0%)	-	-	-	-	
Sex						
Female	71,375 (52.1%)	610 (53.6%)	220 (47.7%)	177 (54.3%)	634 (52.7%)	0.246
Male	65,724 (47.9%)	528 (46.4%)	241 (52.3%)	149 (45.7%)	568 (47.3%)	
Missing	5 (0.0%)	-	-	-	-	
ASA grade						
1–2	103,503 (75.5%)	779 (68.5%)	316 (68.5%)	227 (69.6%)	805 (67.0%)	<0.001
3–5	33,553 (24.5%)	359 (31.5%)	145 (31.5%)	99 (30.4%)	397 (33.0%)	
Missing	48 (0.0%)	-	-	-	-	
Revised cardiac risk index						
0	61,379 (44.8%)	433 (38.0%)	176 (38.2%)	123 (37.7%)	446 (37.1%)	<0.001
1	60,722 (44.3%)	512 (45.0%)	211 (45.8%)	145 (44.5%)	564 (46.9%)	
2	11,116 (8.1%)	134 (11.8%)	50 (10.8%)	41 (12.6%)	129 (10.7%)	
≥3	3,818 (2.8%)	59 (5.2%)	24 (5.2%)	17 (5.2%)	62 (5.2%)	
Missing	69 (0.1%)	-	-	-	1 (0.1%)	
Respiratory comorbidities						
No	124,803 (91.0%)	1,024 (90.0%)	416 (90.2%)	295 (90.4%)	1,079 (89.8%)	0.302
Yes	12,190 (8.9%)	114 (10.0%)	45 (9.8%)	31 (9.5%)	123 (10.2%)	
Missing	111 (0.1%)	-	-	-	-	
Indication for surgery						
Benign	86,764 (63.3%)	629 (55.3%)	273 (59.2%)	208 (63.8%)	822 (68.4%)	<0.001
Cancer	23,612 (17.2%)	100 (8.8%)	117 (25.4%)	73 (22.4%)	234 (19.5%)	
Trauma	17,048 (12.4%)	193 (17.0%)	48 (10.4%)	27 (8.3%)	96 (8.0%)	
Obstetrics	9,673 (7.1%)	216 (19.0%)	23 (5.0%)	18 (5.5%)	50 (4.2%)	
Missing	7 (0.0%)	-	-	-	-	
Grade of surgery						
Minor	55,301 (40.3%)	400 (35.1%)	131 (28.4%)	122 (37.4%)	462 (38.4%)	<0.001
Major	81,771 (59.6%)	738 (64.9%)	330 (71.6%)	204 (62.6%)	739 (61.5%)	
Missing	32 (0.0%)	-	-	-	1 (0.1%)	
Urgency of surgery						
Elective	95,680 (69.8%)	338 (29.7%)	300 (65.1%)	232 (71.2%)	892 (74.2%)	<0.001
Emergency	41,413 (30.2%)	800 (70.3%)	161 (34.9%)	94 (28.8%)	310 (25.8%)	
Missing	11 (0.0%)	-	-	-	-	
COVID-19 symptoms						
Asymptomatic	-	731 (64.2%)	203 (44.0%)	133 (40.8%)	317 (26.4%)	<0.001
Symptomatic – resolved	-	124 (10.9%)	193 (41.9%)	163 (50.0%)	820 (68.2%)	
Symptomatic – ongoing	-	277 (24.3%)	65 (14.1%)	28 (8.6%)	56 (4.7%)	
Missing	-	6 (0.5%)	-	2 (0.6%)	9 (0.7%)	
Country income						
High	90,024 (65.7%)	461 (40.5%)	159 (34.5%)	135 (41.4%)	696 (57.9%)	<0.001
Low / Middle	47,080 (34.3%)	677 (59.5%)	302 (65.5%)	191 (58.6%)	506 (42.1%)	
30-day postoperative mortality						
No	2,065 (98.5%)	1,034 (90.9%)	429 (93.1%)	308 (94.5%)	1,176 (97.8%)	<0.001
Yes	1,973 (1.4%)	104 (9.1%)	32 (6.9%)	18 (5.5%)	24 (2.0%)	
Missing	92 (0.1%)	-	-	-	2 (0.2%)	
30-day postoperative pulmonary complications						
No	133,345 (97.3%)	989 (13.1%)	401 (87.0%)	293 (90.0%)	1,157 (96.3%)	<0.001
Yes	3,654 (2.7%)	149 (13.1%)	60 (13.0%)	33 (10.1%)	42 (3.5%)	
Missing	105 (0.1%)	-	-	-	3 (0.2%)	

ASA: American Society of Anaesthesiologists. P-values were calculated using chi-squared tests for trend comparing all five groups

Compared with patients who did not have SARS-CoV-2 infection, patients with pre-operative SARS-CoV-2 infection were more likely to be ASA physical status 3-5 (24.5% versus 32.0%, $p<0.001$), to undergo major surgery (59.6% versus 64.2%, $p<0.001$) and to undergo emergency surgery (30.2% versus 43.7%, $p<0.001$). However, there was lower proportion of patients aged ≥70 years in the cohort with SARS-CoV-2 infection (16.1% versus 19.2%, $p<0.001$).

Demographics for the sub-group of elective patients are presented in Table 4.2.

Table 4.2: Baseline demographics and outcomes in elective patients

	No preoperative SARS-CoV-2 n=95,680	Preoperative SARS-CoV-2, by timing of diagnosis prior to surgery				p-value
		0–2 weeks n=338	3–4 weeks n=300	5–6 weeks n=232	≥7 weeks n=892	
Age						
0–29 years	17,759 (18.6%)	86 (25.4%)	53 (17.7%)	37 (15.9%)	105 (11.8%)	<0.001
30–49 years	25,740 (26.9%)	115 (34%)	106 (35.3%)	78 (33.6%)	271 (30.4%)	
50–69 years	32,689 (34.2%)	97 (28.7%)	102 (34%)	85 (36.6%)	380 (42.6%)	
70–79 years	13,862 (14.5%)	28 (8.3%)	31 (10.3%)	27 (11.6%)	92 (10.3%)	
≥80 years	5,629 (5.9%)	12 (3.6%)	8 (2.7%)	5 (2.2%)	44 (4.9%)	
Missing	1 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Sex						
Female	50,618 (52.9%)	209 (61.8%)	146 (48.7%)	126 (54.3%)	475 (53.3%)	0.010
Male	45,059 (47.1%)	129 (38.2%)	154 (51.3%)	106 (45.7%)	417 (46.7%)	
Missing	3 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
ASA grade						
1–2	73,268 (76.6%)	249 (73.7%)	217 (72.3%)	170 (73.3%)	626 (70.2%)	<0.001
3–5	22,372 (23.4%)	89 (26.3%)	83 (27.7%)	62 (26.7%)	266 (29.8%)	
Missing	40 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Revised cardiac risk index						
0	44,237 (46.2%)	160 (47.3%)	127 (42.3%)	89 (38.4%)	358 (40.1%)	<0.001
1	41,223 (43.1%)	117 (34.6%)	131 (43.7%)	101 (43.5%)	401 (45%)	
2	7,745 (8.1%)	43 (12.7%)	28 (9.3%)	28 (12.1%)	90 (10.1%)	
≥3	2,425 (2.5%)	18 (5.3%)	14 (4.7%)	14 (6%)	42 (4.7%)	
Missing	50 (0.1%)	0 (0%)	0 (0%)	0 (0%)	1 (0.1%)	
Respiratory comorbidities						
No	86,695 (90.6%)	294 (87%)	271 (90.3%)	205 (88.4%)	805 (90.2%)	0.130
Yes	8,908 (9.3%)	44 (13%)	29 (9.7%)	27 (11.6%)	87 (9.8%)	
Missing	77 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Indication for surgery						
Benign	64,762 (67.7%)	161 (47.6%)	164 (54.7%)	145 (62.5%)	613 (68.7%)	<0.001
Cancer	21,809 (22.8%)	71 (21%)	108 (36%)	69 (29.7%)	223 (25%)	
Trauma	5,352 (5.6%)	37 (10.9%)	21 (7%)	13 (5.6%)	29 (3.3%)	
Obstetrics	3,754 (3.9%)	69 (20.4%)	7 (2.3%)	5 (2.2%)	27 (3%)	
Missing	3 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Grade of surgery						
Minor	38,944 (40.7%)	70 (20.7%)	79 (26.3%)	79 (34.1%)	324 (36.3%)	<0.001
Major	56,718 (59.3%)	268 (79.3%)	221 (73.7%)	153 (65.9%)	567 (63.6%)	
Missing	18 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.1%)	
COVID-19 symptoms						
Asymptomatic	–	221 (65.4%)	150 (50%)	101 (43.5%)	247 (27.7%)	<0.001
Symptomatic – resolved	–	69 (20.4%)	122 (40.7%)	118 (50.9%)	608 (68.2%)	
Symptomatic – ongoing	–	46 (13.6%)	28 (9.3%)	12 (5.2%)	31 (3.5%)	
Missing	–	2 (0.6%)	0 (0%)	1 (0.4%)	6 (0.7%)	
Country income						
High	64,769 (67.7%)	110 (32.5%)	83 (27.7%)	89 (38.4%)	512 (57.4%)	<0.001
Low / Middle	30,911 (32.3%)	228 (67.5%)	217 (72.3%)	143 (61.6%)	380 (42.6%)	
30-day postoperative mortality						
No	95,037 (99.3%)	321 (95%)	287 (95.7%)	223 (96.1%)	884 (99.1%)	<0.001
Yes	588 (0.6%)	17 (5%)	13 (4.3%)	9 (3.9%)	8 (0.9%)	
Missing	55 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
30-day postoperative pulmonary complications						
No	93,896 (98.1%)	307 (90.8%)	268 (89.3%)	213 (91.8%)	870 (97.5%)	<0.001
Yes	1,720 (1.8%)	31 (9.2%)	32 (10.7%)	19 (8.2%)	22 (2.5%)	
Missing	64 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

ASA: American Society of Anesthesiologists physical status grade

p-values from chi squares tests for trend, comparing all 5 groups

4.5.1 COVID-19 symptoms

Overall, there were 1,726 symptomatic SARS-CoV-2 infections, accounting for 55.2% (1726/3127) of all preoperative SARS-CoV-2 cases. Of these, 798 (46.2%) experienced only respiratory symptoms, 447 (25.9%) experienced only non-respiratory symptoms, and 474 (27.5%) experienced both respiratory and non-respiratory symptoms; data were missing for 7 (0.4%).

Of the 1,726 patients with COVID-19 symptoms, 969 (56.1%) had not required hospital admission for treatment of COVID-19, 497 (28.8%) had previously been admitted to hospital for COVID-19 treatment, but did not require respiratory support, and 259 (15.0%) had hospital required admission for either invasive or mechanical respiratory support; data were missing for 1 (0.1%) patient.

4.5.2 30-day mortality

The overall 30-day postoperative mortality rate was 1.5% (2151/140231). Stratified by time from SARS-CoV-2 diagnosis to surgery, mortality was: 9.1% (104/1138) at 0-2 weeks, 6.9% (32/461) at 3-4 weeks, 5.5% (18/326) at 5-6 weeks, and 2.0% (24/1202) at ≥7 weeks (Table 4.3). The 30-day postoperative mortality rate in patients who did not have a preoperative SARS-CoV-2 infection was 1.4% (1973/137104).

Table 4.3: 30-day postoperative mortality and postoperative pulmonary complication rates stratified by timing of surgery after SARS-CoV-2 diagnosis

Time from SARS-CoV-2 diagnosis to surgery	30-day postoperative mortality		30-day postoperative pulmonary complications	
	All patients n=140,231	Elective patients n=97,442	All patients n=140,231	Elective patients n=97,442
No SARS-CoV-2	1.4% (1973/137104)	0.6% (588/95680)	2.7% (3654/137104)	1.8% (1720/95680)
0–2 weeks	9.1% (104/1138)	5.0% (17/338)	13.1% (149/1138)	9.2% (31/338)
3–4 weeks	6.9% (32/461)	4.3% (13/300)	13.0% (60/461)	10.7% (32/300)
5–6 weeks	5.5% (18/326)	3.9% (9/232)	10.1% (33/326)	8.2% (19/232)
7–8 weeks	2.4% (8/330)	1.2% (3/249)	3.9% (13/330)	1.2% (3/249)
3–4 months	2.3% (10/436)	1.3% (4/313)	4.4% (19/436)	3.5% (11/313)
5–6 months	0.8% (2/246)	0% (0/187)	2.0% (5/246)	2.7% (5/187)
≥7 months	2.1% (4/190)	0.7% (1/143)	2.6% (5/190)	2.1% (3/143)

In the adjusted model, compared with patients who did not have a preoperative SARS-CoV-2 infection, there was a higher risk of 30-day mortality in patients with preoperative SARS-CoV-2 infection diagnosed 0-2 weeks, 3-4 weeks, and 5-6 weeks before surgery (Table 4.4). However, there was no significant difference in 30-day postoperative mortality in those diagnosed with SARS-CoV-2 infection ≥7 weeks before surgery.

Table 4.4. Unadjusted and adjusted model for 30-day postoperative mortality (all patients)

Factor	Unadjusted		Adjusted	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Age				
0–69 years	Reference	–	Reference	–
≥70 years	3.12 (2.86-3.40)	<0.001	1.72 (1.56-1.90)	<0.001
Sex				
Female	Reference	–	Reference	–
Male	1.41 (1.29-1.53)	<0.001	1.09 (0.99-1.19)	0.068
ASA physical status				
1–2	Reference	–	Reference	–
3–5	8.96 (8.13-9.87)	<0.001	5.32 (4.75-5.96)	<0.001
Revised cardiac risk index				
0	Reference	–	Reference	–
1	2.33 (2.07-2.61)	<0.001	1.43 (1.26-1.63)	<0.001
2	6.50 (5.69-7.42)	<0.001	1.82 (1.56-2.13)	<0.001
≥ 3	12.81 (11.02-14.89)	<0.001	2.78 (2.32-3.32)	<0.001
Respiratory comorbidities				
No	Reference	–	Reference	–
Yes	1.71 (1.51-1.94)	<0.001	1.02 (0.89-1.16)	0.767
Indication for surgery				
Benign	Reference	–	Reference	–
Cancer	1.62 (1.46-1.80)	<0.001	1.98 (1.76-2.23)	<0.001
Trauma	1.60 (1.43-1.80)	<0.001	0.91 (0.79-1.04)	0.173
Obstetrics	0.27 (0.19-0.37)	<0.001	0.23 (0.16-0.33)	<0.001
Grade of surgery				
Minor	Reference	–	Reference	–
Major	3.25 (2.90-3.63)	<0.001	2.37 (2.11-2.67)	<0.001
Urgency of surgery				
Elective	Reference	–	Reference	–
Emergency	5.60 (5.10-6.15)	<0.001	6.48 (5.83-7.21)	<0.001
Country income				
High	Reference	–	Reference	–
Low / Middle	1.76 (1.61-1.92)	<0.001	2.96 (2.69-3.26)	<0.001
Pre-operative SARS-CoV-2 by timing of diagnosis				
No diagnosis	Reference	–	Reference	–
0–2 weeks	6.88 (5.60-8.46)	<0.001	3.22 (2.55-4.07)	<0.001
3–4 weeks	5.11 (3.56-7.33)	<0.001	3.03 (2.03-4.52)	<0.001
5–6 weeks	4.00 (2.48-6.45)	<0.001	2.78 (1.64-4.71)	<0.001
≥7 weeks	1.40 (0.93-2.10)	0.107	1.02 (0.66-1.56)	0.940

ASA, American Society of Anesthesiologists physical status; CI: confidence interval; OR: odds ratio

Adjusted 30-day mortality in patients who did not have SARS-CoV-2 infection was 1.5%. Adjusted mortality was increased in patients who had surgery at 0-2 weeks (4.1%), 3-4 weeks (3.9%), and at 5-6 weeks (3.6%) after SARS-CoV-2 diagnosis (Figure 4.2). In patients who had surgery ≥7 weeks after SARS-CoV-2 diagnosis, the 30-day mortality was similar to patients who did not have SARS-CoV-2 infection (1.5%). These findings were consistent across subgroups stratified by age, ASA physical status, and grade and urgency of surgery (Figure 4.3).

Figure 4.2: Overall adjusted 30-day postoperative mortality from main and sensitivity analyses

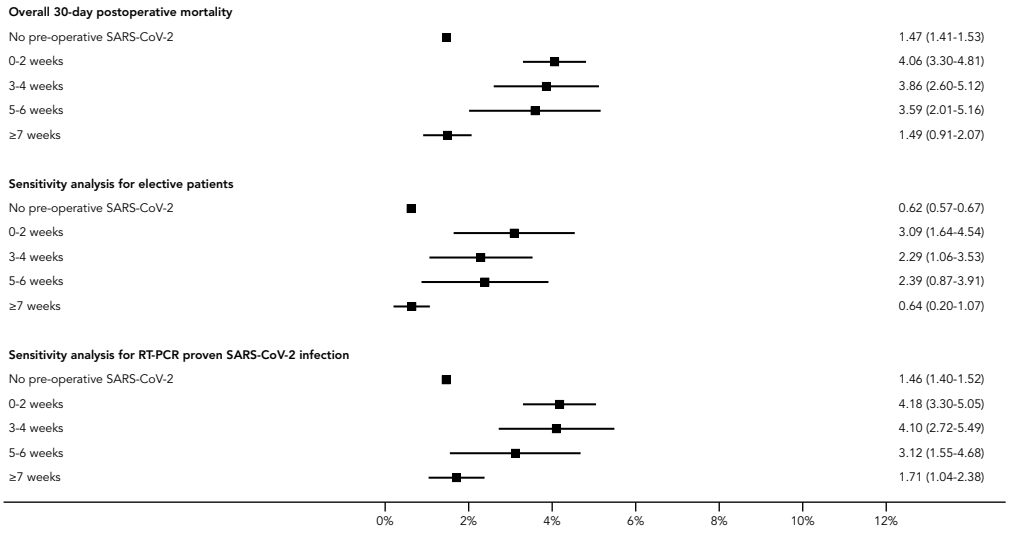
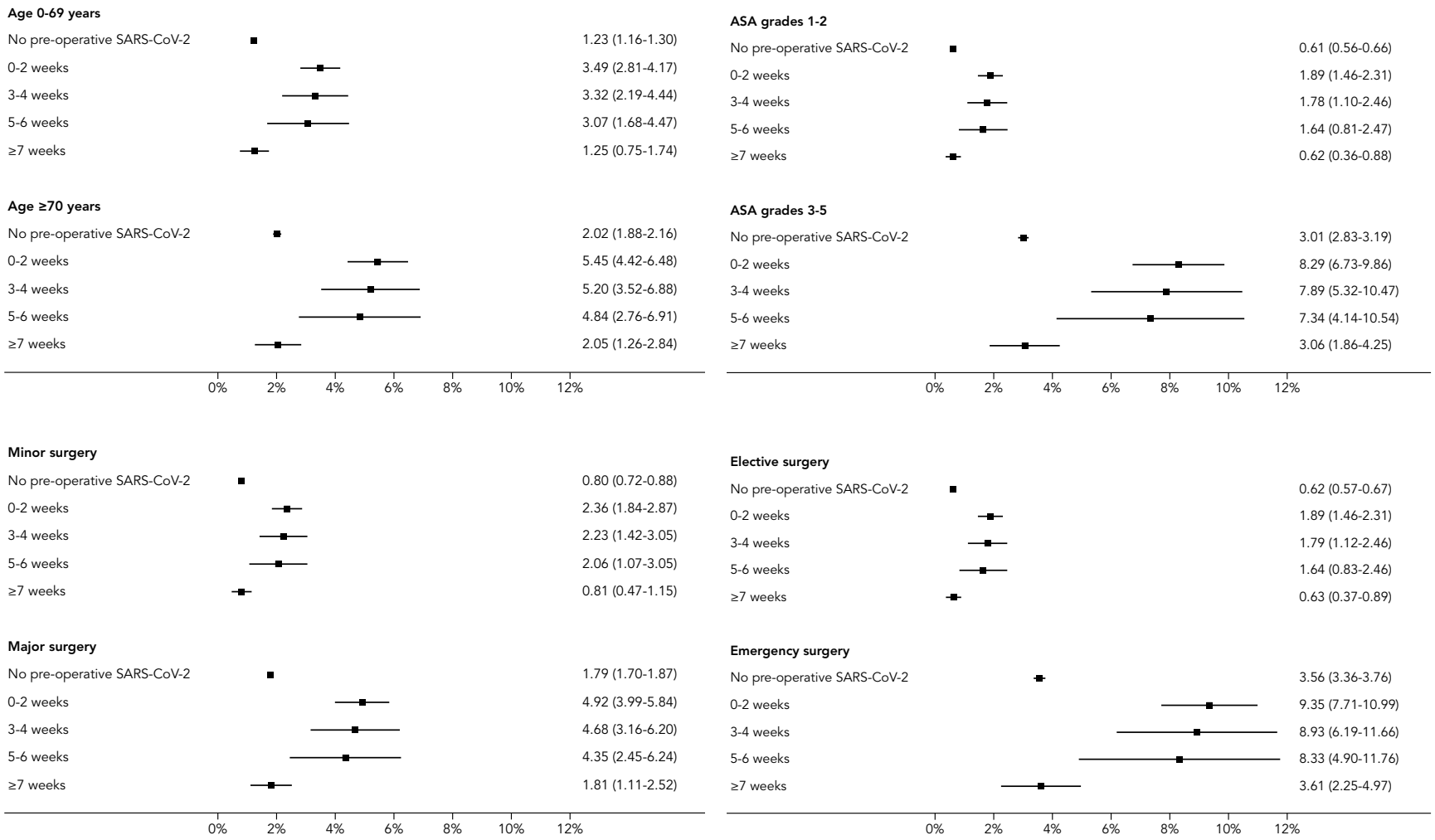


Figure 4.3: Adjusted 30-day postoperative mortality rates from main analysis, stratified by pre-defined subgroups



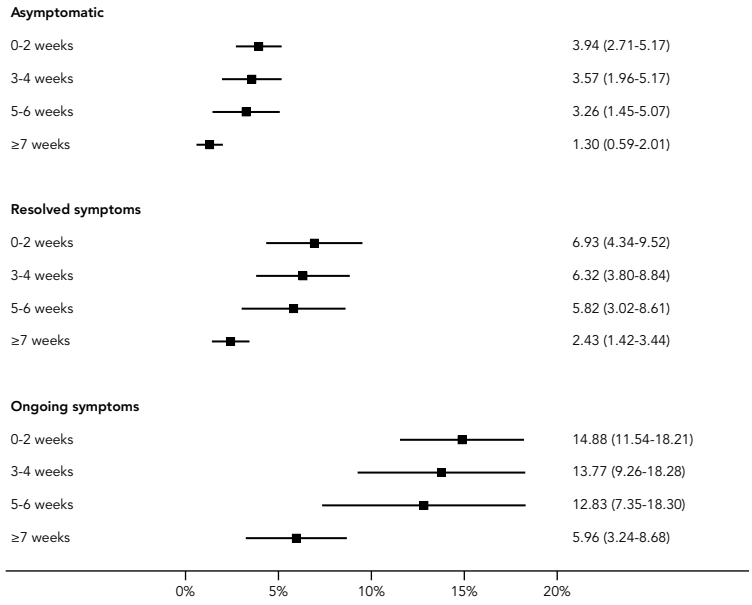
In the analysis restricted to patients who had experienced preoperative SARS-CoV-2 infection, patients with ongoing COVID-19 symptoms had higher adjusted 30-day mortality than patients whose symptoms had resolved or who had been asymptomatic (Figure 4.4, full model in Table 4.5). Following a ≥7 week delay between SARS-CoV-2 infection and surgery, patients with ongoing COVID-19 symptoms had higher mortality than patients whose symptoms had resolved or who had been asymptomatic.

Table 4.5: Unadjusted and adjusted models for 30-day postoperative mortality in patients with pre-operative SARS-CoV-2 infection

Factor	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age				
0–69 years	Reference	–	Reference	–
≥70 years	4.37 (3.19-5.99)	<0.001	2.03 (1.37-3.01)	<0.001
Sex				
Female	Reference	–	Reference	–
Male	1.56 (1.14-2.11)	0.005	1.10 (0.77-1.58)	0.599
ASA grade				
1–2	Reference	–	Reference	–
3–5	8.34 (5.82-11.97)	<0.001	4.26 (2.76-6.57)	<0.001
Revised cardiac risk index				
0	Reference	–	Reference	–
1	2.20 (1.40-3.45)	0.001	1.46 (0.87-2.46)	0.155
2	5.90 (3.59-9.70)	<0.001	1.72 (0.94-3.15)	0.079
≥3	12.97 (7.66-21.96)	<0.001	3.37 (1.72-6.61)	<0.001
Respiratory comorbidities				
No	Reference	–	Reference	–
Yes	1.91 (1.26-2.88)	0.002	0.88 (0.54-1.43)	0.608
Indication for surgery				
Benign	Reference	–	Reference	–
Cancer	1.00 (0.67-1.51)	0.992	1.88 (1.13-3.13)	0.015
Trauma	1.38 (0.91-2.11)	0.133	1.64 (0.95-2.86)	0.078
Obstetrics	0.21 (0.08-0.57)	0.002	0.46 (0.15-1.43)	0.180
Grade of surgery				
Minor	Reference	–	Reference	–
Major	1.99 (1.39-2.84)	<0.001	1.55 (1.03-2.34)	0.038
Urgency of surgery				
Elective	Reference	–	Reference	–
Emergency	3.88 (2.76-5.46)	<0.001	2.54 (1.64-3.93)	<0.001
Country income				
High	Reference	–	Reference	–
Low / Middle	1.43 (1.05-1.95)	0.025	2.25 (1.54-3.29)	<0.001
Pre-operative SARS-CoV–2, by timing of diagnosis				
0–2 weeks	Reference	–	Reference	–
3–4 weeks	0.74 (0.49-1.12)	0.155	0.89 (0.55-1.46)	0.654
5–6 weeks	0.58 (0.35-0.97)	0.039	0.81 (0.44-1.49)	0.496
≥7 weeks	0.20 (0.13-0.32)	<0.001	0.30 (0.17-0.52)	<0.001
COVID-19 symptoms				
Asymptomatic	Reference	–	Reference	–
Symptomatic – resolved	1.15 (0.74-1.77)	0.533	1.95 (1.17-3.24)	0.010
Symptomatic – ongoing	9.14 (6.21-13.45)	<0.001	5.42 (3.53-8.34)	<0.001

ASA: American Society of Anaesthesiologists; OR: odds ratio

Figure 4.4: Adjusted 30-day postoperative mortality rates in patients with preoperative SARS-CoV-2 infection, stratified by COVID-19 symptoms



4.5.3 30-day postoperative pulmonary complications

Overall, 2.8% (3938/140231) of patients developed postoperative pulmonary complications within 30 days; 1.7% (2387/140231) developed pneumonia, 0.8% (1100/140231) developed ARDS, and 0.8% (1137/140231) had an unexpected requirement for mechanical ventilation. Patients who had surgery 0-2 weeks, 3-4 weeks, and 5-6 weeks after SARS-CoV-2 diagnosis had significantly higher adjusted 30-day postoperative pulmonary complication rates than patients who did not have SARS-CoV-2 infection (Table 4.6). However, patients who had surgery ≥7 weeks after SARS-CoV-2 infection had similar rates of postoperative pulmonary complications as patient without SARS-CoV-2 infection (Figure 4.5). Amongst patients operated ≥7 weeks following SARS-CoV-2 diagnosis, those with ongoing COVID-19 symptoms were at greatest risk of 30-day postoperative pulmonary complications (Table 4.7, Figure 4.6).

Table 4.6: Unadjusted and adjusted model for 30-day postoperative pulmonary complications in all patients

Factor	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age				
0–69 years	Reference	–	Reference	–
≥70 years	2.19 (2.05-2.34)	<0.001	1.20 (1.11-1.30)	<0.001
Sex				
Female	Reference	–	Reference	–
Male	1.60 (1.50-1.71)	<0.001	1.38 (1.29-1.48)	<0.001
ASA grade				
1–2	Reference	–	Reference	–
3–5	5.26 (4.93-5.62)	<0.001	3.05 (2.82-3.30)	<0.001
Revised cardiac risk index				
0	Reference	–	Reference	–
1	2.03 (1.87-2.20)	<0.001	1.49 (1.36-1.63)	<0.001
2	5.50 (4.99-6.06)	<0.001	2.13 (1.90-2.38)	<0.001
≥3	9.08 (8.07-10.22)	<0.001	2.76 (2.40-3.17)	<0.001
Respiratory comorbidities				
No	Reference	–	Reference	–
Yes	2.36 (2.17-2.56)	<0.001	1.58 (1.44-1.73)	<0.001
Indication for surgery				
Benign	Reference	–	Reference	–
Cancer	1.52 (1.40-1.64)	<0.001	1.49 (1.37-1.62)	<0.001
Trauma	1.40 (1.28-1.53)	<0.001	1.00 (0.90-1.11)	0.978
Obstetrics	0.50 (0.42-0.60)	<0.001	0.55 (0.45-0.67)	<0.001
Grade of surgery				
Minor	Reference	–	Reference	–
Major	3.22 (2.96-3.49)	<0.001	2.61 (2.39-2.85)	<0.001
Urgency of surgery				
Elective	Reference	–	Reference	–
Emergency	2.73 (2.56-2.91)	<0.001	2.85 (2.65-3.07)	<0.001
Country income				
High	Reference	–	Reference	–
Low / Middle	1.25 (1.17-1.34)	<0.001	1.72 (1.60-1.84)	<0.001
Pre-operative SARS-CoV-2, by timing of diagnosis				
No diagnosis	Reference	–	Reference	–
0–2 weeks	5.50 (4.61-6.55)	<0.001	3.40 (2.80-4.11)	<0.001
3–4 weeks	5.46 (4.15-7.18)	<0.001	3.89 (2.89-5.23)	<0.001
5–6 weeks	4.11 (2.86-5.90)	<0.001	3.39 (2.30-4.99)	<0.001
≥7 weeks	1.32 (0.97-1.81)	0.075	1.06 (0.77-1.46)	0.738

ASA: American Society of Anaesthesiologists; OR: odds ratio

Figure 4.5: Overall adjusted 30-day postoperative pulmonary complication rate from main analysis and sensitivity analysis for patients having elective surgery

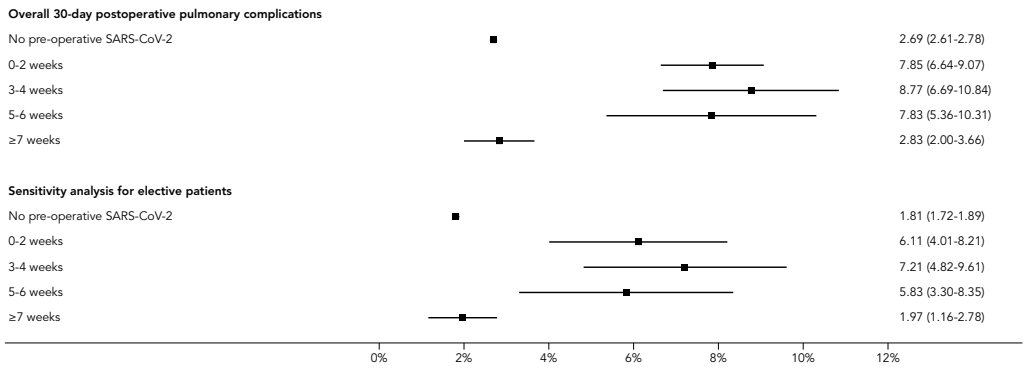
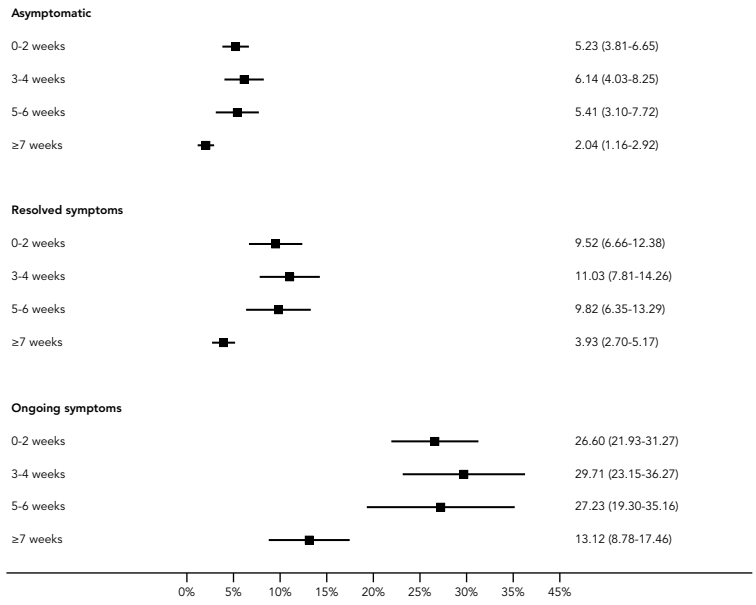


Table 4.7: Unadjusted and adjusted models for 30-day postoperative pulmonary complications in patients with preoperative SARS-CoV-2 infection

Factor	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age				
0–69 years	Reference	-	Reference	-
≥70 years	3.51 (2.70-4.57)	<0.001	2.09 (1.49-2.92)	<0.001
Sex				
Female	Reference	-	Reference	-
Male	1.68 (1.31-2.15)	<0.001	1.25 (0.93-1.68)	0.135
ASA grade				
1–2	Reference	-	Reference	-
3–5	4.64 (3.59-6.01)	<0.001	2.05 (1.46-2.87)	<0.001
Revised cardiac risk index				
0	Reference	-	Reference	-
1	2.10 (1.49-2.97)	<0.001	1.58 (1.05-2.37)	0.030
2	5.60 (3.79-8.29)	<0.001	2.11 (1.29-3.45)	0.003
≥3	10.73 (6.91-16.65)	<0.001	3.90 (2.18-6.97)	<0.001
Respiratory comorbidities				
No	Reference	-	Reference	-
Yes	3.03 (2.23-4.12)	<0.001	1.86 (1.28-2.71)	0.001
Indication for surgery				
Benign	Reference	-	Reference	-
Cancer	0.79 (0.56-1.12)	0.182	1.10 (0.72-1.68)	0.654
Trauma	1.25 (0.88-1.77)	0.212	1.90 (1.19-3.03)	0.007
Obstetrics	0.18 (0.08-0.41)	<0.001	0.38 (0.15-0.97)	0.042
Grade of surgery				
Minor	Reference	-	Reference	-
Major	1.58 (1.20-2.08)	0.001	1.40 (1.01-1.94)	0.042
Urgency of surgery				
Elective	Reference	-	Reference	-
Emergency	2.43 (1.89-3.13)	<0.001	1.41 (1.01-1.98)	0.047
Country income				
High	Reference	-	Reference	-
Low / Middle	1.64 (1.27-2.11)	<0.001	2.31 (1.68-3.17)	<0.001
Pre-operative SARS-CoV–2, by timing of diagnosis				
0–2 weeks	Reference	-	Reference	-
3–4 weeks	0.99 (0.72-1.37)	0.967	1.20 (0.81-1.79)	0.358
5–6 weeks	0.75 (0.50-1.11)	0.153	1.04 (0.64-1.70)	0.877
≥7 weeks	0.24 (0.17-0.34)	<0.001	0.36 (0.23-0.56)	<0.001
COVID-19 symptoms				
Asymptomatic	Reference	-	Reference	-
Symptomatic – resolved	1.46 (1.03-2.07)	0.033	2.04 (1.36-3.05)	0.001
Symptomatic – ongoing	12.04 (8.65-16.75)	<0.001	8.60 (5.95-12.41)	<0.001

ASA: American Society of Anaesthesiologists; OR: odds ratio

Figure 4.6: Adjusted 30-day postoperative pulmonary complication rate in patients with pre-operative SARS-CoV-2 infection stratified by COVID-19 symptoms



4.5.4 Sensitivity analyses for elective patients

Sensitivity analyses including only elective patients also showed that patients having surgery at 0-2 weeks, 3-4 weeks, and 5-6 weeks after SARS-CoV-2 diagnosis had significantly higher adjusted odds of 30-day postoperative mortality (Table 4.8) and 30-day postoperative pulmonary complications (Table 4.9) than patients who did not have SARS-CoV-2 infection. Patients operated ≥7 weeks after SARS-CoV-2 infection did not have significantly increased mortality compared with patients without SARS-CoV-2 infection.

Table 4.8: Sensitivity analysis for elective patients with unadjusted and adjusted models for 30-day postoperative mortality

Factor	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age				
0–69 years	Reference	–	Reference	–
≥70 years	2.59 (2.21-3.04)	<0.001	1.53 (1.28-1.82)	<0.001
Sex				
Female	Reference	–	Reference	–
Male	1.56 (1.34-1.83)	<0.001	1.25 (1.06-1.47)	0.008
ASA grade				
1–2	Reference	–	Reference	–
3–5	6.89 (5.83-8.15)	<0.001	4.62 (3.80-5.62)	<0.001
Revised cardiac risk index				
0	Reference	–	Reference	–
1	2.69 (2.17-3.35)	<0.001	1.79 (1.42-2.25)	<0.001
2	7.55 (5.90-9.65)	<0.001	2.40 (1.82-3.16)	<0.001
≥3	14.92 (11.29-19.72)	<0.001	3.98 (2.90-5.46)	<0.001
Respiratory comorbidities				
No	Reference	–	Reference	–
Yes	1.83 (1.47-2.26)	<0.001	1.06 (0.85-1.33)	0.583
Indication for surgery				
Benign	Reference	–	Reference	–
Cancer	3.16 (2.69-3.71)	<0.001	2.25 (1.90-2.66)	<0.001
Trauma	1.50 (1.06-2.13)	0.022	2.06 (1.43-2.97)	<0.001
Obstetrics	0.12 (0.03-0.47)	0.003	0.21 (0.05-0.85)	0.029
Grade of surgery				
Minor	Reference	–	Reference	–
Major	2.80 (2.30-3.41)	<0.001	1.75 (1.43-2.14)	<0.001
Country income				
High	Reference	–	Reference	–
Low / Middle	2.09 (1.79-2.44)	<0.001	3.16 (2.67-3.74)	<0.001
Pre-operative SARS-CoV-2, by timing of diagnosis				
No diagnosis	Reference	–	Reference	–
0–2 weeks	8.56 (5.22-14.04)	<0.001	5.50 (3.24-9.34)	<0.001
3–4 weeks	7.32 (4.17-12.84)	<0.001	3.95 (2.18-7.15)	<0.001
5–6 weeks	6.52 (3.33-12.76)	<0.001	4.14 (2.05-8.33)	<0.001
≥7 weeks	1.46 (0.73-2.95)	0.288	1.03 (0.50-2.09)	0.945

ASA: American Society of Anesthesiologists physical status

Table 4.9: Sensitivity analysis for elective patients with unadjusted and adjusted model for 30-day postoperative pulmonary complications

Factor	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age				
0–69 years	Reference	-	Reference	-
≥70 years	1.78 (1.61-1.97)	<0.001	1.08 (0.96-1.20)	0.200
Sex				
Female	Reference	-	Reference	-
Male	1.73 (1.57-1.90)	<0.001	1.61 (1.45-1.78)	<0.001
ASA physical status				
1–2	Reference	-	Reference	-
3–5	4.19 (3.82-4.60)	<0.001	2.48 (2.22-2.78)	<0.001
Revised cardiac risk index				
0	Reference	-	Reference	-
1	2.20 (1.95-2.48)	<0.001	1.59 (1.40-1.82)	<0.001
2	5.90 (5.13-6.79)	<0.001	2.43 (2.06-2.85)	<0.001
≥3	9.98 (8.39-11.86)	<0.001	3.54 (2.90-4.32)	<0.001
Respiratory comorbidities				
No	Reference	-	Reference	-
Yes	2.66 (2.37-2.99)	<0.001	1.83 (1.62-2.07)	<0.001
Indication for surgery				
Benign	Reference	-	Reference	-
Cancer	2.17 (1.97-2.39)	<0.001	1.62 (1.47-1.80)	<0.001
Trauma	1.07 (0.86-1.34)	0.538	1.40 (1.11-1.76)	0.005
Obstetrics	0.83 (0.62-1.11)	0.215	1.33 (0.97-1.81)	0.073
Grade of surgery				
Minor	Reference	-	Reference	-
Major	3.66 (3.22-4.15)	<0.001	2.70 (2.37-3.07)	<0.001
Country income				
High	Reference	-	Reference	-
Low / Middle	1.35 (1.23-1.49)	<0.001	1.70 (1.53-1.88)	<0.001
Pre-operative SARS-CoV-2, by timing of diagnosis				
No diagnosis	Reference	-	Reference	-
0–2 weeks	5.51 (3.80-8.00)	<0.001	3.77 (2.53-5.62)	<0.001
3–4 weeks	6.52 (4.50-9.43)	<0.001	4.58 (3.09-6.78)	<0.001
5–6 weeks	4.87 (3.04-7.80)	<0.001	3.57 (2.17-5.88)	<0.001
≥7 weeks	1.38 (0.90-2.11)	0.138	1.09 (0.71-1.69)	0.683

ASA: American Society of Anaesthesiologists; OR: odds ratio

These findings were also consistent across subgroups stratified by age, ASA physical status, and grade and urgency of surgery, in the elective patient population (Table 4.10).

Table 4.10: Sensitivity analysis for elective patients with unadjusted and adjusted 30-day postoperative mortality (95%CI) in key subgroups

		No pre-operative SARS-CoV-2	Pre-operative SARS-CoV-2, by timing of diagnosis prior to surgery			
			0–2 weeks	3–4 weeks	5–6 weeks	≥7 weeks
Overall						
All patients	Unadjusted	0.6% (588/95680)	5.0% (17/338)	4.3% (13/300)	3.9% (9/232)	0.9% (8/892)
	Adjusted	0.6% (0.6-0.7%)	3.1% (1.6-4.5%)	2.3% (1.1-3.5%)	2.4% (0.9-3.9%)	0.6% (0.2-1.1%)
Age						
<70 years	Unadjusted	0.5% (353/76188)	4.0% (12/298)	2.7% (7/261)	3.0% (6/200)	0.8% (6/756)
	Adjusted	0.5% (0.5-0.6%)	2.7% (1.4-4%)	2.0% (0.9-3.1%)	2.1% (0.7-3.4%)	0.6% (0.2-0.9%)
≥70 years	Unadjusted	1.2% (235/19491)	12.5% (5/40)	15.4% (6/39)	9.4% (3/32)	1.5% (2/136)
	Adjusted	0.8% (0.7-0.9%)	4.0% (2.1-5.9%)	3.0% (1.3-4.6%)	3.1% (1.1-5%)	0.8% (0.3-1.4%)
ASA physical status						
1–2	Unadjusted	0.3% (191/73268)	2.8% (7/249)	0.9% (2/217)	1.2% (2/170)	0.6% (4/626)
	Adjusted	0.3% (0.3-0.3%)	1.6% (0.8-2.4%)	1.1% (0.5-1.8%)	1.2% (0.4-2%)	0.3% (0.1-0.5%)
3–5	Unadjusted	1.8% (397/22372)	11.2% (10/89)	13.3% (11/83)	11.3% (7/62)	1.5% (4/266)
	Adjusted	1.3% (1.2-1.5%)	6.6% (3.5-9.6%)	4.9% (2.3-7.5%)	5.1% (1.9-8.3%)	1.4% (0.4-2.3%)
Grade of surgery						
Minor	Unadjusted	0.3% (111/38944)	4.1% (3/73)	8.4% (7/83)	3.8% (3/79)	0.3% (1/338)
	Adjusted	0.4% (0.3-0.5%)	2.1% (1-3.2%)	1.6% (0.7-2.5%)	1.6% (0.5-2.7%)	0.4% (0.1-0.7%)
Major	Unadjusted	0.8% (477/56718)	5.3% (14/265)	2.8% (6/217)	3.9% (6/153)	1.3% (7/553)
	Adjusted	0.7% (0.6-0.8%)	3.5% (1.9-5.2%)	2.6% (1.2-4%)	2.7% (1-4.5%)	0.7% (0.2-1.2%)

ASA: American Society of Anesthesiologists physical status

Rates adjusted for age, sex, ASA, Revised Cardiac Risk Index, respiratory comorbidity, grade of surgery, country income, timing of surgery following SARS-CoV-2 diagnosis

4.5.5 Sensitivity analyses for confirmed SARS-CoV-2

Sensitivity analyses including only patients with RT-PCR confirmed SARS-CoV-2 infection (Table 4.11) showed that patients having surgery at 0-2 weeks, 3-4 weeks, and 5-6 weeks after SARS-CoV-2 diagnosis had significantly higher adjusted 30-day postoperative mortality than patients who did not have SARS-CoV-2 infection. Patients operated ≥7 weeks after SARS-CoV-2 infection did not have significantly increased mortality compared with patients without SARS-CoV-2 infection.

Table 4.11: Sensitivity analysis for confirmed SARS-CoV-2 infection, with unadjusted and adjusted models for 30-day postoperative mortality

Factor	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age				
0–69 years	Reference	–	Reference	–
≥70 years	3.14 (2.88-3.43)	<0.001	1.75 (1.58-1.93)	<0.001
Sex				
Female	Reference	–	Reference	–
Male	1.40 (1.29-1.53)	<0.001	1.09 (0.99-1.19)	0.077
ASA grade				
1–2	Reference	–	Reference	–
3–5	8.95 (8.12-9.87)	<0.001	5.29 (4.72-5.93)	<0.001
Revised cardiac risk index				
0	Reference	–	Reference	–
1	2.32 (2.06-2.60)	<0.001	1.42 (1.25-1.62)	<0.001
2	6.49 (5.67-7.42)	<0.001	1.82 (1.56-2.13)	<0.001
≥3	12.69 (10.90-14.76)	<0.001	2.73 (2.28-3.26)	<0.001
Respiratory comorbidities				
No	Reference	–	Reference	–
Yes	1.72 (1.52-1.94)	<0.001	1.02 (0.89-1.17)	0.763
Indication for surgery				
Benign	Reference	–	Reference	–
Cancer	1.64 (1.48-1.82)	<0.001	1.98 (1.76-2.23)	<0.001
Trauma	1.60 (1.42-1.80)	<0.001	0.90 (0.78-1.03)	0.122
Obstetrics	0.27 (0.19-0.37)	<0.001	0.23 (0.16-0.32)	<0.001
Grade of surgery				
Minor	Reference	–	Reference	–
Major	3.29 (2.94-3.68)	<0.001	2.39 (2.12-2.69)	<0.001
Urgency of surgery				
Elective	Reference	–	Reference	–
Emergency	5.57 (5.07-6.12)	<0.001	6.53 (5.87-7.27)	<0.001
Country income				
High	Reference	–	Reference	–
Low / Middle	1.73 (1.59-1.88)	<0.001	2.96 (2.69-3.26)	<0.001
Pre-operative SARS-CoV-2, by timing of diagnosis				
No diagnosis	Reference	–	Reference	–
0–2 weeks	7.03 (5.57-8.87)	<0.001	3.35 (2.58-4.36)	<0.001
3–4 weeks	5.55 (3.82-8.07)	<0.001	3.28 (2.17-4.98)	<0.001
5–6 weeks	3.59 (2.09-6.15)	<0.001	2.36 (1.30-4.27)	0.005
≥7 weeks	1.73 (1.14-2.62)	0.010	1.19 (0.76-1.84)	0.445

4.6 Discussion

4.6.1 Main findings

This study found that patients operated within 6 weeks of SARS-CoV-2 diagnosis were at an increased risk of both 30-day postoperative mortality and 30-day postoperative pulmonary complications. Complication and mortality rates decreased to baseline at ≥ 7 weeks after SARS-CoV-2 diagnosis. These findings were consistent in sensitivity analyses for elective patients. The same pattern was observed across both low-risk (younger patients, fit patients, minor surgery) and high-risk (older patients, comorbid patients, major surgery) subgroups. However, patients who are still symptomatic ≥7 weeks after SARS-CoV-2 infection have an increased mortality rate.

This study's finding that preoperative SARS-CoV-2 infection increases the risk of postoperative complications and mortality is consistent with previous studies. It is the first study to robustly evaluate the optimal timing for surgery following SARS-CoV-2 infection.

4.6.2 Strengths and weaknesses

An important limitation of this study is that categorisation of SARS-CoV-2 status was based on available preoperative test data. In the early pandemic access to SARS-CoV-2 testing was limited in many settings, particularly in LMICs[330-332]. This may have resulted in some patients who had experienced SARS-CoV-2 infection being misclassified as never having been infected. Although this could be particularly likely for patients with asymptomatic infection, it is reassuring that a high proportion of patients in the cohort were recorded as having had asymptomatic infection, suggesting that many such cases were detected.

The main analysis included patients with suspected preoperative SARS-CoV-2 and some of these cases may have been misdiagnoses. This was addressed by sensitivity analyses including only data for patients with confirmed SARS-CoV-2 infection. The results of these sensitivity analyses were consistent with the main analyses.

This study was based on time from SARS-CoV-2 diagnosis to surgery. It is possible that for some patients diagnosis was delayed, underestimating the true delay from time of infection to surgery. In addition, data were only collected for the first diagnosis of SARS-CoV-2, so it is unknown if some patients had SARS-CoV-2 reinfection between the time of their first SARS-CoV-2 diagnosis and time of surgery.

Cut-offs for delay from SARS-CoV-2 diagnosis to surgery beyond 7 weeks were not formally tested due to low numbers. However, delay beyond 7 weeks is unlikely to offer a significant advantage, as adjusted mortality rates for delay intervals ≥7 weeks were broadly stable, and overall mortality following a delay of ≥7 weeks was similar to that in non-SARS-CoV-2 patients.

4.6.3 Implications for clinical practice

The results of this study suggested that surgery should be delayed for at least 7 weeks following SARS-CoV-2 infection to reduce the risk of postoperative mortality and pulmonary complications. However, the data indicated that patients who remain symptomatic at ≥7 weeks after SARS-CoV-2 infection may benefit from a further delay until their symptoms resolve. The decision to delay surgery should be on an individual patient basis, as the risks and benefits of delay will differ depending on the patients underlying pathology and patient-specific factors. Therefore, the data from this study was important for informing shared making by surgeons and patients.

This findings of this study supported the safe restarting of surgery in the context of a rapidly increasing number of people who have survived SARS-CoV-2. Decisions should be tailored for each patient, since the possible advantages of delaying surgery for at least 7 weeks following SARS-CoV-2 diagnosis must be balanced against the potential risks of delay. For some urgent surgeries, such as resection of advanced tumours[333,334], surgeons and patients may decide that the risks of delay are not justified.

4.6.4 Implications for future research

This study captured data on patients operated in October to November 2020. This was a period when the original SARS-CoV-2 virus remained dominant in most communities, and before SARS-CoV-2 vaccine rollouts started. It is therefore unknown how generalisable this study's findings are to current practice; in most high and upper-middle income settings a majority of the population are now vaccinated, and the Omicron variant has become dominant. In chapter 5 I report a study conducted in December 2021 to March 2022 which sought to characterise current outcomes in patients with perioperative SARS-CoV-2 infection.

An important issue that this study did not address was the impact of long-COVID on surgical outcomes. Firstly, this study was designed in June 2020, before the significance of long-COVID was fully understood. As a result, it did not capture detailed data to support an analysis of long-COVID outcomes. Recent work towards the development of core outcome sets[335] and patient reported outcome measures[336] for long-COVID could inform the development of high-quality surgical studies in the future. Secondly, this study enrolled over 140,000 patients, of whom fewer than a hundred had had ongoing COVID-19 symptoms for greater than 12 weeks, making meaningful analysis of the available data difficult. However, current prevalence of

long-COVID is likely to be significantly higher than in October 2020, with an estimated 2 million people experiencing self-reported long-COVID just in the UK alone[337].

5 DOES VACCINATION REDUCE THE MORBIDITY OF PERIOPERATIVE SARS-COV-2 INFECTION?

5.1 Contribution

This chapter has not been submitted for peer reviewed publication yet. I will be the first author for the resulting manuscript. I was the lead investigator, led the conception of the study and methodology, and led the administration of the study. I performed the data analysis. I drafted the first version of the manuscript, presented below. This has been revised based on critical comments from co-authors. I have abbreviated methods section to avoid duplicating material in chapter 2.

5.2 Synopsis

During the first COVID wave perioperative SARS-CoV-2 infection was associated with high postoperative mortality rates. In the general population the currently dominant Omicron variant of concern has been found to be associated with fewer adverse outcomes than previous variants, particularly in people who have had SARS-CoV-2 vaccination. This international prospective cohort study reports the risks of perioperative SARS-CoV-2 infection in patients operated between 13 December 2021 and 28 February 2022. The primary outcome was 30-day mortality and the key secondary outcomes were postoperative pulmonary complications. Patients were classified as vaccinated if they had received a first SARS-CoV-2 vaccination dose, at least two weeks before surgery. A total of 19684 patients were included across 942 hospitals in 89 countries. Overall mortality was 5.8% (1135/19684). Mortality was lowest in patients aged under 70 years with ASA grades 1-2 (1.5%, 165/11127). Postoperative pulmonary complications occurred in 14.3% (2812/19684). In adjusted analyses, vaccination was associated with reduced odds of mortality and postoperative pulmonary complications.

5.3 Introduction

In chapter 3 I described the results of an international multicentre cohort study which demonstrated that during the first COVID-19 wave, SARS-CoV-2 infection was associated with significantly increased complications and mortality. A follow-up study in chapter 4 established that in order to mitigate these risks, whenever possible, surgery should be delayed for at least six weeks following a SARS-CoV-2 diagnosis. However, these recommendations were based on data collected in 2020, prior to the emergence of new SARS-CoV-2 variants and the initiation of the global SARS-CoV-2 vaccine rollout.

The Omicron SARS-CoV-2 variant of concern was first reported on 25 November 2021 and rapidly spread worldwide. There is a high-level of evidence indicating Omicron has increased transmissibility and potential to evade immunity. However, there is little robust evidence regarding disease severity associated with Omicron in both vaccinated and unvaccinated surgical patients, nor is there data to guide patient risk stratification during Omicron COVID-19 waves. Therefore, there was a need for renewed rapid data collection to guide global practice in 2022 onwards.

The aim of this study was to characterise the safety of surgery during the period of Omicron variant dominance.

5.4 Methods

This study followed the methodology described in chapter 2. In summary, it was a prospective international multicentre cohort study. It enrolled patients operated between 13 December 2021 and 28 February 2022. In the few countries that have comprehensive SARS-CoV-2 variant surveillance programmes there is a lag time in variant data becoming available. Therefore, in view of reports that Omicron was

rapidly spreading globally, a pragmatic decision was taken to commence patient enrolment from 13 December 2021 onwards, although at the time it was unknown whether Omicron had yet become dominant. Retrospective data suggests Omicron had achieved dominance in most countries by mid-December (see section 1.2.2.1). The study was registered at clinicaltrials.gov (NCT05161299).

As there were no changes to clinical care pathways in this observational study, in the UK it was registered as clinical audit or service evaluation. At the lead centre (University Hospital Birmingham) the study approval reference was CARMS-15986. In other countries, local principal followed local and national regulations to secure relevant study approvals. In other countries, local principal investigators were responsible for securing appropriate study approvals.

5.4.1 Patient inclusion criteria

Participating hospitals collected data on consecutive eligible patients over a minimum four-week period within the overall study window of 13 December 2021 – 28 February 2022. Patients who underwent any type of surgery were eligible if they had a positive SARS-CoV-2 PCR or rapid antigen test result in the seven days before or 30 days after surgery.

5.4.2 Exposure: SARS-CoV-2 vaccination

Patients were recorded as vaccinated if they had received a first COVID-19 dose, at least two weeks before surgery. Patients were recorded as partially vaccinated if they had received a first dose of a two-dose vaccination schedule, fully vaccinated if they had received a second dose of a two-dose vaccination schedule or a single-dose vaccine, or as having been administered a booster if they had been administered a third vaccine dose.

5.4.3 Outcome measures

The primary outcome was the 30-day mortality rate. The secondary outcome was the 30-day postoperative pulmonary complication rate.

5.4.4 Statistical analysis

5.4.4.1 Unadjusted and adjusted models

Multilevel logistic regression was used to perform both unadjusted and adjusted analyses. These analyses produced odds ratios (OR) and 95% CI. In both unadjusted and adjusted models, country was included as a random effect with hospital nested within country.

Only factors that occurred before the outcome of interest were included in the models. Factors were selected *a priori* based on their clinical relevance. In the main analyses, vaccination status was dichotomized as vaccinated versus unvaccinated.

The main adjusted model identified predictors of 30-day mortality. Secondary adjusted models had an outcome of 30-day postoperative pulmonary complications.

5.4.5 Subgroup analyses

Adjusted models for 30-day mortality were performed for urgency of surgery (elective, emergency) and country income (LMIC, HIC) subgroups.

5.4.6 Sensitivity analysis

In a sensitivity analysis, vaccination status was expanded to partially vaccinated, fully vaccinated ≤4 months before surgery, fully vaccinated 5-6 months before surgery, fully vaccinated ≥7 months before surgery, administered a booster (third) dose.

5.5 Results

The study included a total of 19,684 patients from 942 hospitals in 89 countries. Overall, 21.5% (4,232) were aged <30 years, 28.4% (5,591) were aged 30-49 years, 26.7% (5,255) were aged 50-69 years, and 23.4% (4,605) were aged ≥70 years, with age missing for one patient (Table 5.1). 63.2% (12442) were ASA grades 1-2, 36.7% were ASA grades 3-5 (7231), and ASA was missing for 11 patients. SARS-CoV-2 was diagnosed preoperatively in 53.6% (10541), postoperatively in 46.2% (9,095), and timing was missing for 48 patients. 87.2% (17,161) of diagnoses were made with a PCR test, 12.4% (2,433) with a rapid antigen test, and means of diagnosis was missing for 90 patients.

Table 5.1: Patient demographics, by 30-day mortality

Factor	Unvaccinated patients		Vaccinated patients	
	Alive	Died	Alive	Died
Age				
<70 years	5037 (94.4%)	297 (5.6%)	8566 (97.2%)	245 (2.8%)
≥70 years	646 (78.5%)	177 (21.5%)	3169 (90%)	354 (10%)
Sex				
Female	3219 (94.6%)	184 (5.4%)	6264 (96.2%)	245 (3.8%)
Male	2464 (89.5%)	290 (10.5%)	5469 (93.9%)	354 (6.1%)
ASA grade				
1-2	4032 (96.8%)	134 (3.2%)	7419 (98.6%)	104 (1.4%)
3-5	1647 (82.9%)	340 (17.1%)	4310 (89.7%)	495 (10.3%)
RCRI score				
0	2765 (96.8%)	92 (3.2%)	4365 (98%)	91 (2%)
1	2152 (92.8%)	167 (7.2%)	4981 (96.4%)	188 (3.6%)
2	512 (81%)	120 (19%)	1638 (90.6%)	169 (9.4%)
≥3	254 (72.8%)	95 (27.2%)	749 (83.2%)	151 (16.8%)
Indication				
Benign/ obstetric	4028 (93%)	302 (7%)	7357 (96%)	310 (4%)
Cancer	599 (85.1%)	105 (14.9%)	1946 (93.6%)	134 (6.4%)
Trauma	1056 (94%)	67 (6%)	2429 (94%)	155 (6%)
Urgency of surgery				
Elective	2012 (94.8%)	110 (5.2%)	5434 (97.6%)	136 (2.4%)
Emergency	3669 (91%)	364 (9%)	6301 (93.2%)	463 (6.8%)
Grade of surgery				
Minor	1987 (95.5%)	94 (4.5%)	4169 (97%)	129 (3%)
Major	3695 (90.7%)	380 (9.3%)	7565 (94.2%)	470 (5.8%)
General anaesthesia				
No	1688 (96.1%)	69 (3.9%)	3429 (97.2%)	100 (2.8%)
Yes	3990 (90.8%)	405 (9.2%)	8289 (94.3%)	499 (5.7%)
Timing of SARS diagnosis				
Preoperative	3629 (92.9%)	278 (7.1%)	5558 (93.9%)	359 (6.1%)
Postoperative	2039 (91.2%)	196 (8.8%)	6100 (96.2%)	240 (3.8%)
Country income				
High income	3784 (94.7%)	211 (5.3%)	8623 (95.5%)	409 (4.5%)
Low- and middle-income	1899 (87.8%)	263 (12.2%)	3112 (94.2%)	190 (5.8%)

5.5.1 Procedures

Emergency surgery was performed in 58.9% (11,598) of patients and elective surgery in 41.1% (8,081), with data missing for 5 patients. Indications for surgery were trauma in 20.3% (4,005), cancer in 14.8% (4,005), benign in 64.8% (12,763), and missing in 6 patients. Procedures were categorised as minor for 34.3% (6,757) of patients, major for 65.6% (12,922), with data missing for 5 patients. The greatest contribution to the study was from orthopaedic surgery (21.3%, 4,188), general surgery (12.3%, 2,428), obstetrics (12.2%, 2,399), colorectal surgery (9.5%, 1,862), and urology (5.4%, 1,055).

5.5.2 SARS-CoV-2 vaccination

Overall, 63.9% (12,586) of patients were vaccinated, 32.7% (6,446) were unvaccinated, and vaccination data were missing for 652. The overall vaccination rate was higher in HICs than LMICs (65.9% versus 59.3%, p<0.001). Stratifying by number of doses, 5.4% (1,067) of patients were partially vaccinated, 36.3% (7,138) were fully vaccinated, 21.2% (4,177) were boosted, and data regarding number of doses were missing for 204 patients who had been vaccinated. Pfizer-BioNTech was the most frequently administered vaccine. In addition, 14.8% (1,911) of patients reported having had a previous SARS-CoV-2 infection.

5.5.3 Mortality

Overall 30-day mortality was 5.8% (Figures 5.1-5.2). Mortality rates were higher in patients aged ≥70 years versus <70 years (12.1% versus 3.8%, p<0.001), patients with ASA grades 3-5 versus grades 1-2 (12.2% versus 2.1%, p<0.001), emergency versus elective patients (7.6% versus 3.2%, p<0.001), and in LMICs versus HICs (8.2% versus 4.8%, p<0.001). Mortality was lower in vaccinated than unvaccinated

patients (4.9% versus 7.6%, p<0.001). Mortality was under 5% in age <70 years and ASA grades 1-2 vaccinated patients undergoing elective surgery, and 15% or higher in age ≥70 years and ASA grades 3-5 unvaccinated patients undergoing emergency surgery. In the subgroup of patients having elective surgery, mortality was lower in patients with asymptomatic SARS-CoV-2 infection compared to patients with SARS-CoV-2 symptoms (3.8% [283/7428] versus 13.5% [379/2800], p<0.001).

Figure 5.1a: Mortality rates in elective patients in high income countries

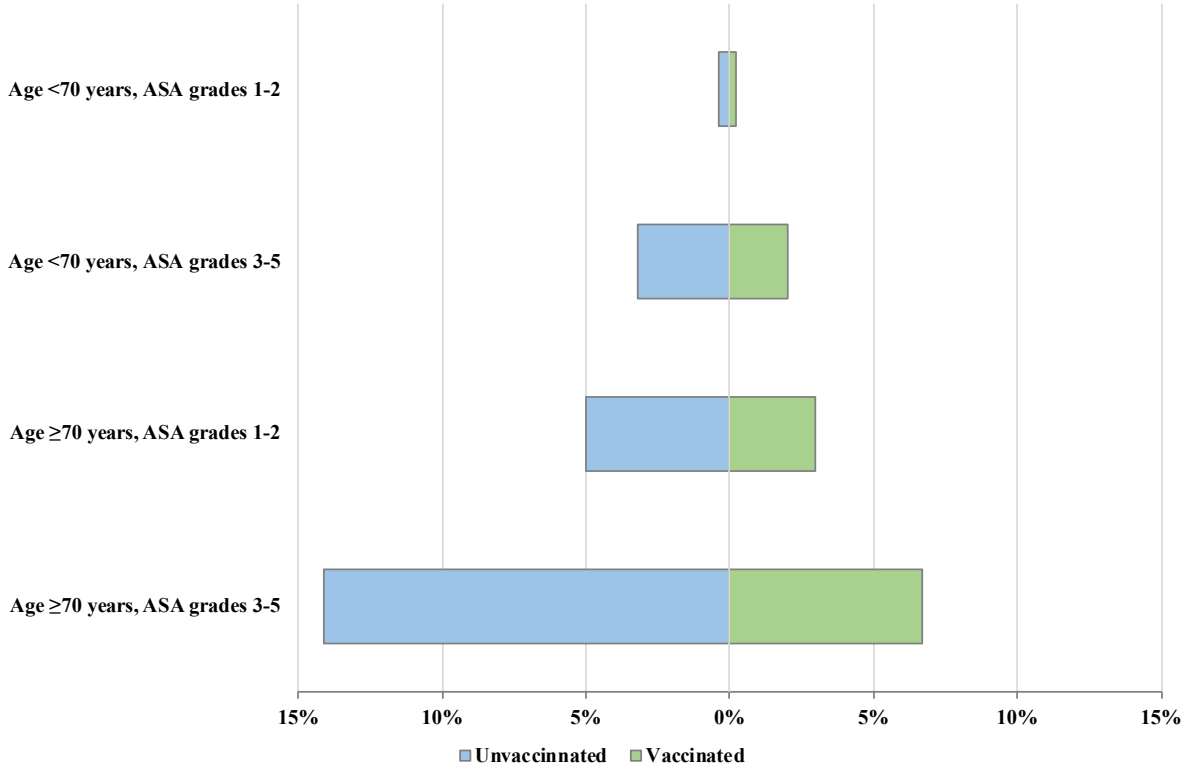


Figure 5.1b: Mortality rates in elective patients in low- and middle-income countries

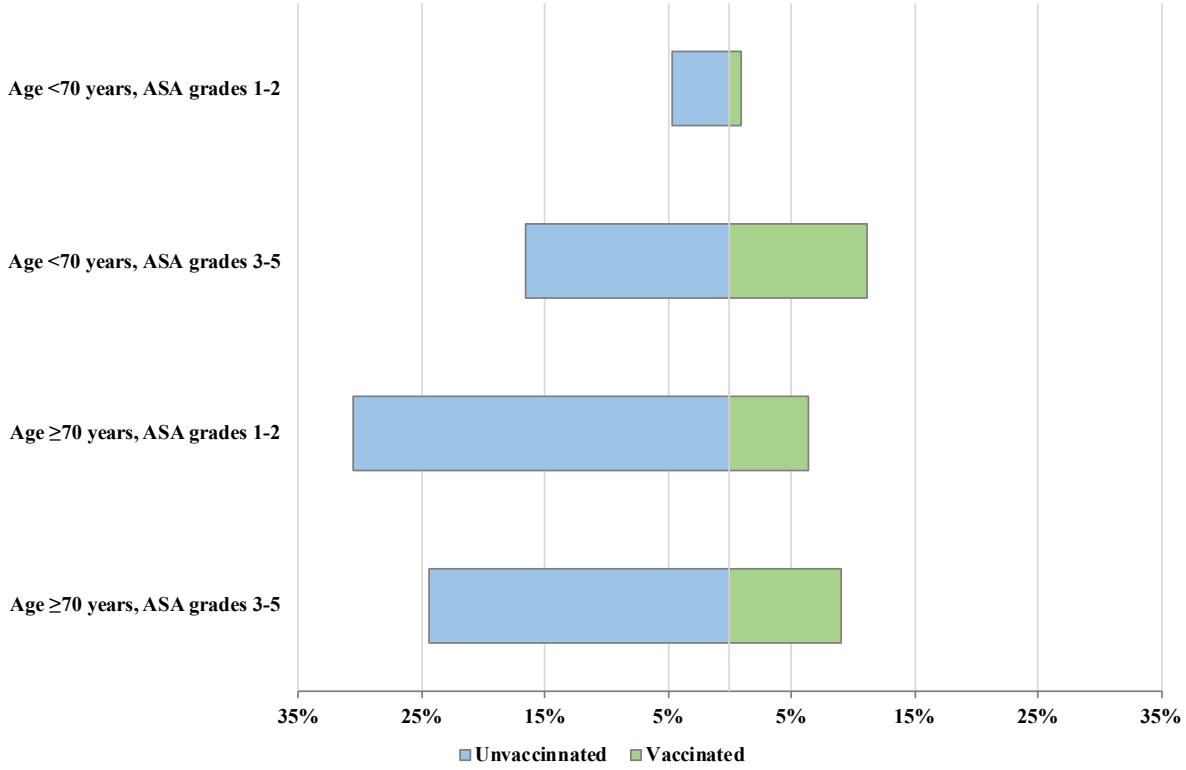
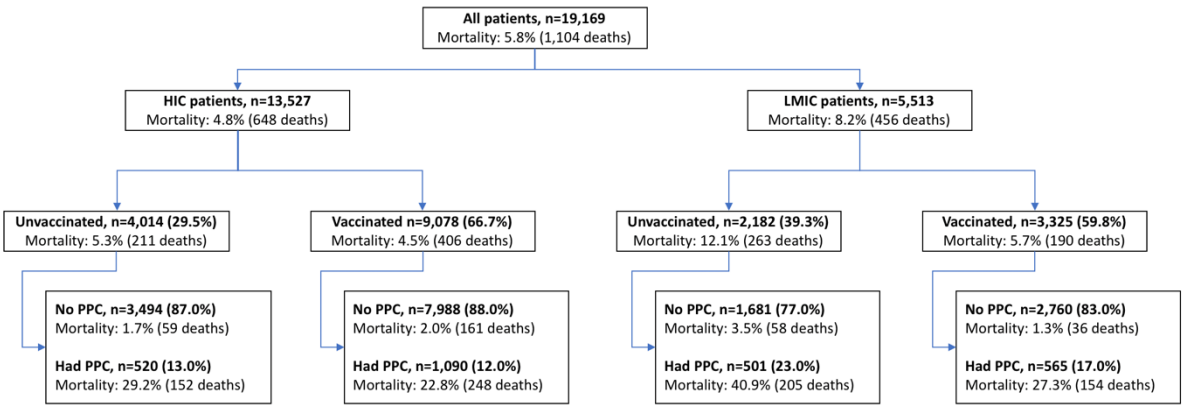


Figure 5.2: Flowchart of patient outcomes



PPC: Postoperative pulmonary complications

In adjusted analyses, predictors of 30-day mortality were age ≥70 years versus age <70 years, male sex, ASA grades 3-5 versus grades 1-2, increasing RCRI score, cancer versus benign indication, emergency versus elective surgery, major versus minor surgery, general anaesthetic use, postoperative versus preoperative SARS-CoV-2 diagnosis, and surgery in a LMIC versus HIC (Table 5.2). Vaccination was associated with reduced 30-day mortality (OR 0.53, 95% CI 0.45-0.62, p<0.001).

In subgroup analyses (Table 5.3), vaccination was associated with reduced 30-day mortality in elective patients (OR 0.39, 95% CI 0.28-0.54, p<0.001), emergency patients (OR 0.57, 95% CI 0.48-0.69, p<0.001), HICs (OR 0.61, 95% CI 0.50-0.75, p<0.001), and LMICs (OR 0.43, 95% 0.34-0.57, p<0.001). Age, sex, ASA grade, RCRI score, and surgical indication were predictors of 30-day mortality across all subgroups.

Table 5.2: Adjusted analysis in the overall cohort

Factor	Odds ratio (95% CI)	p-value
Age		
0–69 years	Reference	–
≥70 years	2.27 (1.95-2.64)	<0.001
Sex		
Female	Reference	–
Male	1.42 (1.24-1.63)	<0.001
ASA grade		
1–2	Reference	–
3–5	3.94 (3.31-4.68)	<0.001
Revised cardiac risk index		
0	Reference	–
1	1.43 (1.17-1.73)	<0.001
2	2.12 (1.70-2.64)	<0.001
≥3	2.94 (2.31-3.74)	<0.001
Indication for surgery		
Benign / Obstetric	Reference	–
Cancer	1.47 (1.22-1.77)	<0.001
Trauma	0.96 (0.80-1.15)	0.641
Grade of surgery		
Minor	Reference	–
Major	1.48 (1.25-1.74)	<0.001
Urgency of surgery		
Elective	Reference	–
Emergency	2.38 (2.01-2.83)	<0.001
General anaesthesia		
No	Reference	–
Yes	1.60 (1.34-1.93)	<0.001
Timing of SARS diagnosis		
Preoperative	Reference	–
Postoperative	0.69 (0.60-0.80)	<0.001
Country income		
High	Reference	–
Low / Middle	2.76 (2.39-3.19)	<0.001
Vaccination status		
Unvaccinated	Reference	–
Vaccinated	0.53 (0.45-0.62)	<0.001

ASA: American Society of Anaesthesiologists

Table 5.3: Sensitivity analysis with adjusted outcomes in elective patients

Factor	Odds ratio (95% CI)	p-value
Age		
0–69 years	Reference	–
≥70 years	3.26 (2.42-4.39)	<0.001
Sex		
Female	Reference	–
Male	1.49 (1.13-1.96)	0.005
ASA grade		
1–2	Reference	–
3–5	2.97 (2.17-4.06)	<0.001
Revised cardiac risk index		
0	Reference	–
1	1.74 (1.15-2.62)	0.008
2	2.84 (1.81-4.46)	<0.001
≥3	2.47 (1.46-4.19)	0.001
Indication for surgery		
Benign / Obstetric	Reference	–
Cancer	1.23 (0.91-1.66)	0.177
Trauma	1.91 (1.15-3.16)	0.012
Grade of surgery		
Minor	Reference	–
Major	1.08 (0.78-1.51)	0.634
General anaesthesia		
No	Reference	–
Yes	0.95 (0.67-1.35)	0.782
Timing of SARS diagnosis		
Preoperative	Reference	–
Postoperative	0.89 (0.66-1.19)	0.417
Country income		
High	Reference	–
Low / Middle	3.72 (2.80-4.94)	<0.001
Vaccination status		
Unvaccinated	Reference	–
Vaccinated	0.37 (0.28-0.48)	<0.001

ASA: American Society of Anaesthesiologists

5.5.4 Secondary outcomes

30-day postoperative pulmonary complications occurred in 14.3% (2812/), with pneumonia in 10.0% (1969), ARDS in 5.5% (1080), and unexpected ventilation in 3.6% (704). Pulmonary complications were less frequent in vaccinated patients and, when they occurred, were associated with lower mortality than in unvaccinated patients.

In adjusted analyses, age, ASA grade, RCRI score, surgical indication, urgency of surgery, grade of surgery, general anaesthetic use, and country income independently predicted both 30-day postoperative pulmonary complications. In

addition, sex and timing of SARS-CoV-2 diagnosis predicted postoperative pulmonary complications. Vaccination was associated with reduced odds of both 30-day postoperative complications (OR 0.64, 95% CI 0.57-0.71, p<0.001). Country-income subgroup results are shown in Table 5.4).

Table 5.4: Adjusted sub-group analyses by country-income

Model outcome	Adjusted odds ratio (95% CI)	p-value
All settings		
Mortality	0.53 (0.45-0.62)	<0.001
PPC	0.66 (0.60-0.73)	<0.001
High-income countries		
Mortality	0.62 (0.51-0.74)	<0.001
PPC	0.67 (0.60-0.76)	<0.001
Low- and middle-income countries		
Mortality	0.42 (0.34-0.52)	<0.001
PPC	0.66 (0.56-0.76)	<0.001

Reference categories are unvaccinated patients. Thus, table shows odds for outcome in vaccinated (any number of doses of vaccine at any time) compared to unvaccinated patients.

5.5.5 Sensitivity analysis

The sensitivity analysis explored the association of timing of SARS-CoV-2 vaccination with 30-day postoperative mortality. In the adjusted analysis, partially vaccinated patients (OR 0.58, 95% 0.42-0.81, p=0.01), patients fully vaccinated ≤4 months before surgery (OR 0.44, 95% CI 0.34-0.57, p<0.001), patients fully vaccinated 5-6 months before surgery (OR 0.49, 95% CI 0.37-0.65, p<0.001), patients fully vaccinated ≥7 months before surgery (OR 0.56, 95% CI 0.44-0.73, p<0.001), and patients administered a booster dose (OR 0.57, 95% CI 0.46-0.71, p<0.001) were all at reduced odds of 30-day mortality compared to unvaccinated patients.

5.6 Discussion

5.6.1 Main findings

This study identified that 30-day postoperative mortality rates have significantly reduced during the period of Omicron variant dominance compared to the data presented in chapter 3 from the first COVID wave (5.8% versus 23.8%). SARS-CoV-2 vaccination was associated with reduced mortality, partly explained by a reduction in postoperative pulmonary complication rates and severity in vaccinated patients. However, some patients experienced high mortality even if vaccinated; age ≥70 years, male sex, ASA grades 3-5, increasing RCRI score, cancer surgery, and emergency surgery were consistently associated with increased mortality and complication rates.

SARS-CoV-2 vaccination was found to be associated with decreased risk across all subgroups, including both low-risk and high-risk patients.

5.6.2 Strengths and weaknesses

Only patients who tested positive for SARS-CoV-2 infection were included in the study. It is possible that some patients with asymptomatic infection were not tested and therefore not included in the study. Since asymptomatic peri-operative SARS-CoV-2 infection was associated with reduced mortality, this could lead our over-estimating the risks of peri-operative SARS-CoV-2; this is reassuring in the context of a recommendation to relax some restrictions.

As the study did not collect data on SARS-COV-2 negative patients, it is not possible to precisely determine the excess risk associated with SARS-CoV-2 infection. However, comparison to first wave data indicates a reduction in risk across all subgroups.

5.6.3 Implications for clinical practice

These findings have important implications for health services as they seek to tackle COVID-19-related surgical backlogs. The low mortality rates associated with perioperative SARS-CoV-2 infection suggest that the benefits of COVID-19-free surgical pathways, preoperative SARS-CoV-2 screening, and surgical delay in patients who test positive for SARS-CoV-2 are likely to be marginal in low-risk patients. Therefore, health services should consider adapting surgical pathways to relax restrictions for low-risk patients, and prioritise measures to increase surgical volume. However, ongoing precautions are still required for high-risk patients and models of care should be developed to ensure that, if required, these patients are able to access critical care areas segregated from patients who have tested positive for SARS-CoV-2.

Therefore, vaccination should be offered to all surgical patients, though high-risk patients should be prioritised if there is limited vaccine availability. Counselling of pregnant women regarding SARS-CoV-2 vaccination during pregnancy should include consideration of the risks of peri-operative SARS-CoV-2 in the event of their requiring a Caesarean section.

This study did not seek to compare different vaccines against each other, but it is possible that some vaccines may perform better than others. It is unlikely to be feasible to conduct head-to-head comparisons of different vaccines in the surgical setting, so vaccine-specific effectiveness data should continue to be inferred from the general population.

5.6.4 Implications for future research

The data presented in this study suggests that health services can reduce some COVID-19 mitigation measures and plan to return to higher surgical volume. Most health systems have experienced prolonged disruption to their elective services during the pandemic and as a result they have developed backlogs of patients requiring surgery. I order to plan how to use the findings of this study to safely scale-up surgical provision, more granular information is needed to understand the scale and nature of these backlogs. In chapter 6 I have modelled the backlog in England to inform future elective recovery planning.

This study did not definitively address the need for SARS-CoV-2 vaccination boosters in surgical patients. Although patients six months post-completion of their initial SARS-CoV-2 vaccine course had good protection, it is unclear whether this will wane over a longer time period and therefore whether booster vaccine doses are beneficial in surgical patients.

In the medium-term further SARS-CoV-2 variants are likely and ongoing surveillance will be needed to identify any increase in postoperative complications or mortality resulting from the emergence of more severe variants. Such a development might require some COVID-19 mitigation measures to be reintroduced for all patients.

6 FORECASTING WAITING LISTS FOR ELECTIVE PROCEDURES IN ENGLAND

6.1 Contribution

This chapter has been posted on the medRxiv pre-print platform[338]. I was the first and corresponding author on this pre-print. I conceived the study and methodology, and performed data analysis. I drafted the first version of the manuscript, presented in this chapter with revisions made based on critical comments from co-authors.

6.2 Synopsis

During the COVID-19 pandemic there was wide-scale disruption to the delivery of elective surgical care in England. This has produced a backlog of patients requiring surgical treatment. In order to inform planning of the elective recovery, the aim of this study was to forecast the total need for elective procedures in England by 2030. I used publicly available activity data from NHS Digital to estimate procedure-level shortfalls in elective procedures performed during the pandemic compared to what would be expected based on pre-pandemic trends. I also estimated the procedure-level composition of the NHS waiting list preceding the pandemic. The total need for elective procedures in March 2022 was calculated by summing the pandemic shortfall with the pre-pandemic NHS waiting list. I then projected the need for elective procedures through to January 2030 for four scenarios: current capacity (surgical volume remains at the same level as in February-March 2022), pessimistic scenario (elective procedure volume increases to pre-pandemic levels by July 2023 followed and remains at this level until 2030), central scenario (elective procedure volume returns to pre-pandemic levels by December 2022 followed by a 2% increase per year), optimistic scenario (elective procedure volume returns to pre-pandemic levels by December 2022 followed by a 4% increase per year). I estimated that the total need for elective procedures in England in March 2022 was 4,347,469. At current capacity, the total number of elective procedures needed would increase to

14,608,195 by 2030. In the pessimistic scenario, elective procedure volume total elective procedures needed would increase to 8,507,087, in the central scenario it would increase to 5,420,999, and in the optimistic scenario it would decrease to 2,584,664 procedures. This suggests that even in the optimistic scenario there will be a substantially larger waiting list for elective procedures in 2030 than pre-pandemic.

6.3 Introduction

In chapters 3-5 I have studied the evolving safety of surgery during the pandemic. During the first COVID-19 wave, the NHS stopped most routine elective surgery, in part in response to concerns about patient safety presented by the data in chapter 3. During subsequent waves, the NHS was unable to return to baseline pre-pandemic elective procedure volume due to a combination of safety concerns and staffing pressures. The data in chapter 5 indicates that it is now safe to reduce COVID-19 mitigation measures in order to increase elective surgery volume.

According to NHS waiting list data, 6.3 million patients were waiting for elective treatment in England in March 2022. However, the waiting list does not fully reflect population need for elective procedures, since fewer new patients were seen in clinic by hospital consultants during the pandemic, as a result of reduced referrals and reduced clinic capacity due to redeployment of resources to support the acute COVID-19 response. This has resulted in a hidden waiting list comprising people who have symptoms or disease requiring elective procedures, but who have not been placed on the elective waiting list.

In February 2022, the UK Government has committed £1.5 billion to financing elective surgery hubs to tackle the elective procedure backlog in England. Whilst

there is an ambition to increase surgical capacity above pre-pandemic levels, the full extent, including the hidden waiting list, of current and future need for elective procedures is not known. The aim of this study was to project the total number of patients who will need elective procedures in England by January 2030 based on a series of scenarios.

6.4 Methods

In order to project future need for elective procedures, we first needed to determine baseline need. We estimated the number of patients who needed elective procedures in England in March 2022; this was taken as baseline need because March 2022 was the most recent month for which hospital activity data were available at the time of analysis. We then projected monthly figures for the number of patients who will need elective procedures in England through to 2030.

6.4.1 Definitions

6.4.1.1 Elective procedure

This term is used as a collective term for surgical operations and endoscopic, interventional cardiology, or interventional radiology procedures. An elective surgical operation was defined as an operation performed by a surgeon in an operating theatre on a planned admission to hospital. This definition is consistent with previous studies6,10. Obstetric operations were excluded as they do not contribute to the main waiting list. Both diagnostic and therapeutic endoscopy, interventional cardiology, and interventional radiology were included if performed in an operating theatre, endoscopy suite, or interventional radiology suite, on a planned admission to hospital. Both day-case procedures and procedures with an overnight admission were included. Minor procedures that are normally performed outside a theatre,

endoscopy suite, or interventional radiology suite (e.g. paracentesis, lumbar puncture, joint injection), non-procedural therapeutics (e.g. drug infusion), and non-interventional imaging were excluded. A breakdown of the 1,139 OPCS Classification of Interventions and Procedures codes fulfilling inclusion criteria is provided in Appendix 1. Calculations were performed at the level of individual OPCS codes, but to aid interpretation, the 1,139 OPCS codes were combined in to 130 procedure categories, which in turn were further summed to 16 sub-specialties and 10 specialties (Appendix 1).

6.4.1.2 Day-case elective procedure

Day-case procedures are completed without an overnight stay in hospital. For this analysis, we classified procedures as day-case or as requiring overnight admission. Using AHES-APC (see below), we reviewed length of hospital stay for each OPCS code in 2018-19 and classified them as day-case if they had an average length of hospital stay under 1 day, or 50% or more of cases were performed as day-cases.

6.4.1.3 Incident need for elective procedures

The number of new patients each year who develop symptoms or disease that require an elective procedure. The incident need rate is the incident need per 1,000 population.

6.4.1.4 Pandemic shortfall in elective procedures

The reduction in the number of elective procedures performed during the pandemic period (January 2020 to March 2022) compared to what would be expected based on pre-pandemic trends, adjusted for population growth and ageing.

6.4.1.5 Total need for elective procedures

The total number elective procedures needed in England, at a given point in time. This count includes all patients regardless of whether or not they are on an NHS waiting list.

6.4.1.6 NHS waiting list

Patients who are on the NHS waiting list for an elective procedure.

6.4.1.7 Hidden waiting list

Patients who need elective procedures, but who have not been added to the NHS waiting list by a hospital consultant for reasons related to the COVID-19 pandemic. This might occur in the following circumstances:

- The patient did not see their general practitioner (GP) and therefore they were not referred to a consultant.
- The patient did see their GP, who decided to not make a referral to a consultant due to factors related to the pandemic.
- The GP did make a referral to a consultant, but the patient has not yet been seen by the consultant due to the pandemic significantly increasing waiting times for clinic.
- The patient did see a hospital consultant, but, due to factors related to the pandemic, have not yet been added to the NHS waiting list.
- However, if a patient was seen by a hospital consultant and was added them to the NHS waiting list, this patient would appear on the NHS waiting list rather than the hidden waiting list.

6.4.1.8 Calculation of total need

Based on these definitions, total need was calculated as the sum of the NHS waiting list and hidden waiting list:

$$N = W + H \quad \text{Equation 1}$$

Where

N = Total need for elective procedures at baseline in a given month

W = Number of patients waiting for elective procedures on the NHS waiting list in a given month

H = Hidden waiting list in a given month

6.4.2 Conceptual framework

6.4.2.1 Key assumptions

This analysis is based on the following assumptions:

- Prior to the COVID-19 pandemic, the NHS waiting list for elective care included all people who needed elective procedures; i.e. there was no hidden waiting list pre-pandemic before the pandemic.
- Age-sex specific incident need rates for elective procedures remained constant during the pandemic period. Consequently, if there was a reduction in elective procedure activity during the pandemic period (pandemic shortfall) this would result in a backlog of patients, increasing total need for elective procedures.
- There is no attrition to individuals' need for elective procedures over time. This means that all patients who need elective procedures stay on the waiting list regardless of how long they have to wait to have their procedure.

- Age and sex specific incident need rates for elective procedures will remain constant through to 2030. Our modelling takes in to account projected changes in England's population structure over time, meaning that the number of elective procedures needed each year (incident need) may increase over time, even though we have assumed that age-sex specific incident need rates do not change.

6.4.2.2 Approach to modelling

We projected the number of patients who will need elective procedures in England each month from April 2022 to December 2029. The following calculation was performed for each month:

$N_m = N_{m-1} + I_m - P_m$ Equation 2

Where

N_m = Total need for elective procedures at the end of month m

N_{m-1} = Total need for elective procedures at the end of the month preceding month m

I_m = Incident need for elective procedures in month m. This was calculated as one twelfth of annual incident need in the relevant year. Annual incident need was adjusted for projected changes in population structure over time

P_m = Number of elective procedures performed in month m

Baseline total need for elective procedures was estimated for March 2022 based on real-world NHS activity data. Total need in March 2022 was calculated as sum of the pre-pandemic waiting list and the pandemic shortfall in elective procedures:

$N_b = W_p + S$ Equation 3

Where

N_b = Total need for elective procedures at baseline in March 2022

W_p = Number of patients on the NHS waiting list for elective procedures immediately before the pandemic in December 2019

S = Pandemic shortfall in elective procedures

6.4.3 Data sources

This study used the following NHS (National Health Service) England data which are publicly available from NHS Digital:

- Monthly Hospital Episode Statistics for Admitted Patient Care (MHES-APC) activity data for April 2018 to March 2022.
- Annual Hospital Episode Statistics for Admitted Patient Care (AHES-APC) activity data for 2018-19 and 2020-21.
- NHS England waiting list data for March 2015 to March 2022.
- NHS reference costs for 2019-20 (most recent available).

In addition, the following data were accessed from the Office for National Statistics (ONS):

- Population (age and sex) structure data for mid-2018 to mid-2020.
- Population (age and sex) structure projections for 2021 to 2029.
- Health-system level population data for mid-2020 (most recent available).

6.4.3.1 Hospital Episode Statistics

Hospital Episode Statistics (HES) captures data for inpatient NHS patient episodes across all NHS and private hospitals in England. HES has monthly (MHES-APC) and annual (AHES-APC) data releases. AHES-APC data are released around September for the preceding NHS year (April to March) and MHES-APC data are released monthly on a rolling basis.

Hospital Episode Statistics (HES) provides information on finished consultant episodes and finished admission episodes. A finished consultant episode is a period of care under a particular consultant. A patient may have multiple finished consultant episodes during a finished admission episode, a continuous period of care within a particular hospital.

AHES-APC provides a breakdown of finished consultant episodes at procedure-level (OPCS classification). In contrast, MHES-APC only provides a breakdown for finished consultant episodes at specialty-level and whilst a subtotal is given for finished consultant episodes with procedures performed, this includes a wider range of treatments than our definition of elective procedures; for example, simple injections, minor procedures (e.g. paracentesis, lumbar puncture), drug infusions. Therefore, when possible, it is preferable to use AHES-APC data since this provides a more granular breakdown.

The totals for finished consultant episodes provided by both AHES-APC and MHES-APC are not broken down in to elective versus emergency episodes. Instead, both datasets provide subtotals for the number of finished admission episodes that are elective versus emergency episodes. Therefore, we used the proportion of finished admission episodes that are elective episodes as a surrogate for the proportion of

finished consultant episodes that are elective. We used the following equation to estimate the number of elective finished consultant episodes:

$$K = FCE * (1 - (E / FAE) \quad \text{Equation 4}$$

Where:

K = Number of elective finished consultant episodes

FCE = Total number of finished consultant episodes

E = Number of finished admission episodes that were emergencies

FAE = Total number of finished admission episodes

6.4.4 Pandemic shortfall in elective procedures

The methodology for estimating the shortfall in elective procedures expanded on methodology previously published in *The Lancet*[339].

For the purpose of this study, we considered the COVID-19 pandemic to have started on 1 January 2020; the first COVID-19 case was reported in Wuhan on 31 December 2019. The most recent available MHES-APC data was for March 2022. Therefore, it was possible to estimate the shortfall in elective procedures over the period January 2020 to March 2022 (27 months).

We calculated the shortfall in elective procedures in the following way for the pandemic period (January 2020 to March 2022):

$S = I_p – P_p$ Equation 5

Where:

S = Pandemic shortfall in January 2020 to March 2022

I_p = Incident need for elective procedures during the pandemic period

P_p = Number of procedures completed during the pandemic period

6.4.4.1 Calculation of incident need

Elective procedure activity in 2018-19 (last pre-pandemic year for which AHES-APC data is available) was used as the baseline to estimate incident need for elective procedures. However, as England has a growing and aging population, incident need for elective procedures in absolute terms can be expected to increase over time. To take in to account projected changes in population structure, we estimated age-sex incident need rates and applied these to ONS population structure projections for 2020-29.

Age and sex specific incident need rates were calculated based on the AHES-APC data for 2018-19. The following equation was used to calculate age and sex specific incident need rates:

$I_g = X_g / Y_g$ Equation 6

Where:

I_g = Incident need rate for elective procedures for a specific age-sex group

X_g = Number of elective procedures performed for a specific age-sex group, 2018-19

Y_g = Total population for a specific age-sex group in England in mid-2018

We calculated total incident need for each year by summing incident need for each age-sex group:

$I_q = \Sigma (Ig * Y_{qg})$ Equation 7

Where:

I_q = Total incident need for elective procedures in year q

I_g = Incident need rate for elective procedures for age-sex group

Y_{qg} = Population for age-sex group in England in year q

To estimate incident need for elective procedures during the pandemic period (January 2020 to March 2022) age and sex specific incident need rates were calculated for the following groups (age-sex categorisation 1): female <18 years, female 18-39 years, female 40-64 years, female 65-79 years, female ≥80 years, male <18 years, male 18-39 years, male 40-64 years, male 65-79 years, male ≥80 years. Calculations were performed at OPCS code level to enable estimation of procedure-level pandemic shortfalls and therefore procedure-level total need in March 2022.

The same methodology was used to estimate incident need for elective procedures in April 2022 to December 2029, with the exception that we calculated overall total need for each year, rather than procedure-level need. This allowed us to use more granular age-sex groups for the calculation of age-sex specific incident need rates (age-sex categorisation 2); we calculated age-sex specific incident need rates separately for females and for males, with the following age breakdown: 0-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, ≥90 years.

6.4.4.2 Calculation of pandemic shortfall using AHES-APC data

The AHES-APC dataset was used in preference to MHES-APC when possible, as it enables data to be extracted for elective procedures meeting the study inclusion criteria. Therefore, the following data sources were used:

- Pre-pandemic baseline number and breakdown of elective procedures was based on AHES-APC data for 2018-19 (the last full NHS year before the pandemic).
- For the pandemic period:
    - Data for April 2020 to March 2021 was based on AHES-APC data for 2020-21 (the only HES-APC dataset where the full reporting period was during the pandemic).
    - Data for January to March 2020, and April 2021 to March 2022 were based on MHES-APC data. The most recent available MHES-APC data are for March 2022.

The AHES-APC dataset includes a breakdown of finished consultant episodes by age and separately by sex. This allowed us to calculate shortfall in 2020-21 for each

OPCS code for ten age-sex groups (age-sex categorisation 1, see above) based on Equation 5.

6.4.4.3 Calculation of pandemic shortfall using MHES-APC data

We first summed monthly MHES-APC data for April 2018 to March 2019 (pre-pandemic baseline), and for January to March 2020 and April 2021 to March 2022 (15 month pandemic period for which AHES-APC data is not available) to calculate specialty-level totals.

As MHES-APC includes a wider range of treatments than the elective procedures included in this study, we had to estimate the number of elective procedures completed in January to March 2020 and April 2021 to March 2022 from the MHES-APC data. To do this, for each specialty, we calculated the number of elective procedures in 2018-19 in AHES-APC as a proportion of total patients recorded in MHES-APC in 2018-19. We applied this proportion to MHES-APC total for the 15 pandemic months to calculate a specialty-level breakdown of elective procedures performed during this period.

The specialty-level shortfall in procedures during January to March 2020 and April 2021 to March 2022 was calculated by subtracting specialty-level estimates of elective procedures performed from the calculated incident need for elective procedures during these months.

We estimated procedure-level breakdown for the shortfall during January to March 2020 and April 2021 to March 2022 based on the assumption that the pattern of this shortfall would be consistent with the shortfalls observed in 2020-21. To do this, we took the procedure-level shortfalls calculated for 2020-21 and summed them at specialty-level (for procedures where an increase rather than decrease (shortfall) in

activity was observed in 2020-21, the shortfall was set as zero). We then calculated the proportion of the shortfall accounted for by each procedure within its specialty. These proportions were then applied to specialty-level shortfalls for January to March 2020 and April 2021 to March 2022 to achieve a procedure-level breakdown for that period.

6.4.5 NHS waiting list

NHS waiting list data were accessed from NHS Digital to estimate the number of patients on the NHS waiting list who were waiting for elective procedures in December 2019 (last pre-pandemic month) and March 20227.

Monthly NHS Waiting list data are reported by specialty for three categories:

- Incomplete pathways: patients who have been referred for treatment and are on the waiting list. This includes both patients waiting for clinic review, as well as those who are waiting for hospital admission for treatment (e.g. surgery, endoscopy).
- Admitted pathways: patients whose treatment was completed that month and whose treatment included an admitted care. This includes both day-case and inpatient admissions for a wider range of treatments than our definition of elective procedures (i.e. includes surgery, endoscopy, interventional radiology and cardiology, but also simple injections, lumbar puncture, drug infusions etc).
- Non-admitted pathways: patients whose treatment was completed that month and whose treatment did not involve admitted care (e.g. discharged from outpatient clinic).

For each specialty category in the NHS waiting list data, we estimated the number of incomplete pathways for that would translate to admitted pathways when completed using the following equation:

$Path_{est} = Path_{incomplete} * (Path_{admitted} / Path_{non\text{-}admitted})$ Equation 8

Where:

$Path_{est}$ = Number of patients on NHS waiting list that month who will require admitted care

$Path_{incomplete}$ = Number of patients on NHS waiting list that month whose pathways are incomplete

$Path_{admitted}$ = Number of patients who completed their pathway that month and whose treatment included admitted care

$Path_{non\text{-}admitted}$ = Number of patients who completed their pathway that month and whose treatment did not include admitted care

We made the following changes to the specialty categories to facilitate combination of NHS waiting list and pandemic shortfall estimates:

- We combined Gastroenterology with General Surgery.
- We combined Thoracic Medicine with CT surgery.
- We excluded the following specialties from our calculations as they would not typically meet our definition for elective procedures: General Medicine, Dermatology, Neurology, Rheumatology, Geriatric Medicine, Other Medical Services, Other Mental Health Services, Other Paediatric Services, Other Services. Although some procedures that would be on the Oral Surgery waiting list are included in this study, the overwhelming majority of procedures

are simple extractions that are excluded. Therefore we excluded the Oral Surgery figures from our calculations.

- Prior to 2022, the waiting list data included an 'Other' category. In the March 2022 data this was disaggregated in to five subcategories: one surgical [Other Surgical Services] and four non-surgical. We calculated the proportion of the 'Other' waiting list cases in March 2022 that were 'Other Surgical Services' and applied this proportion to the totals for 'Other' waiting list cases in 2019 and earlier, to estimate 'Other Surgical Services' in those months. The estimates for pandemic shortfalls that we produced did not include an 'Other' category, so we distributed the 'Other' patients to the other (included) specialty categories in the waiting list data. Patients were distributed according to the proportion of the total waiting list (excluding 'Other') accounted for by each specialty.

6.4.5.1 Composition of NHS waiting list

The NHS waiting list data are only publicly available at specialty-level. Therefore, in order to estimate total need in March 2022 at procedure-level we created estimates for the procedure-level composition of the NHS waiting list in December 2019 (Equation 3).

The AHES-APC dataset provides procedure-level data for:

- The number of elective procedures performed on patients admitted from waiting lists. Some elective procedures are planned rather than waiting list cases, meaning that the patient is given a procedure date at the time of booking (e.g. may happen for follow-up procedures).
- The mean number of days on the waiting list.

We used the 2018-19 AHES-APC data to multiply the number of waiting list admissions by their mean wait, to estimate at procedure-level an aggregated total for the number of days waited by patients for that procedure that year. Using the NHS waiting list data described above, we then calculated, at specialty-level, the proportion of the total waiting time within each specialty accounted for by each procedure. We then applied these proportions to the total number of patients on the NHS waiting list in December 2019 by specialty, to estimate the number of patients on the NHS waiting list in December 2019 at a procedure-level.

6.4.6 Estimated cost to address need for elective procedures

We projected the cost to address the need for elective procedures based on the NHS reference costs for 2019-2012, the most recent available. NHS providers submit cost data to NHS England which calculates an average cost per care episode. Reference costs are provided by health resource group (HRG), a grouping similar treatment which require comparable healthcare resources. HRGs are determined by both the treatment a patient received and also their demographics (age) and comorbidities. There is no readily available cross-reference of HRGs against OPCS codes. Therefore, for each of the 130 procedures included in this study we identified the most appropriate HRG code. We aimed to produce a conservative estimate, therefore, when there was a choice of possible relevant HRG codes we selected the least expensive possibility. When applicable, we selected HRG codes for adult and those applying to patients with a comorbidity score of 1 (Appendix 1). This process was completed by two investigators and any discrepancies were resolved through discussion.

We calculated the total cost for each procedure:

$C_{TP} = N_P * C_P$ Equation 9

Where:

CTP = Total cost for procedure group

NP = Total need per procedure

CP = Procedure-specific cost per procedure group

We summed procedure-level costs to calculate total specialty-level costs.

6.4.7 ICS-level breakdown

In order to estimate a regional breakdown for need for elective procedures, NHS waiting list data for March 2022 was accessed at Integrated Care System (ICS) level7. The ICS structure will be formally introduced in July 2022. Each ICS brings together hospital providers with other health and social care bodies within a geographic region. There are 42 ICSs in England with their population ranging from half a million to three million. In addition, there is a separate waiting list for nationally commissioned services.

The ICS-level NHS waiting list data was available broken down by specialty. Specialties were included in the analysis as described above. In order to estimate the total need for surgery at ICS-level, the hidden waiting list was estimated for each specialty for each ICS plus the nationally commissioned services. This was achieved by calculating for each ICS the proportion of all patients on the national NHS waiting list for a particular specialty in that ICS (e.g. Dorset has 11,674 patients on the General Surgery NHS waiting list, accounting for 1.4% of all patients on the national General Surgery NHS waiting list). This proportion was then multiplied by the

national estimate for the hidden waiting list for that specialty and added to the NHS waiting list figure to calculate total need (e.g. since the national hidden waiting list for General Surgery is 1,793,946 for Dorset this was multiplied by 1.4% and the result added to 11,674, resulting in an estimate of 25,208 General Surgery procedures needed in Dorset). This produced specialty-level estimates of total need for each of the 42 ICSs and also for nationally commissioned services.

It was assumed that for each specialty the waiting list for nationally commissioned services in each ICS would be proportionate to the waiting list for locally commissioned services. We calculated for each ICS the proportion of all patients on the national NHS waiting list for that specialty (excluding nationally commissioned services from the denominator). This proportion was then multiplied by the total for the relevant specialty for nationally commissioned services, and this was added to the existing estimate for need based on locally commissioned services to calculate an overall total need at specialty-level for each ICS. These figures were rounded to the nearest integer to allow easier interpretation.

For each ICS, specialty-level estimates for total need were summed to calculate an overall total need for elective procedures. To facilitate comparison across ICSs, the need for elective procedures was calculated per 1,000 population:

$R_{ICS} = (N_{ICS} / Pn_{ICS}) * 1000$ Equation 10

Where:

R_{ICS} = Elective procedures needed in ICS per 1,000 population

N_{ICS} = Total elective procedures needed in ICS

Pn_{ICS} = ICS population in mid-2020

ICS-level projections for costs to address the need for elective procedures was calculated at specialty-level and summed to produce an overall figure. Using the national estimates, an average cost per procedure was calculated for each specialty. For each specialty, this figure was multiplied by the number of procedures needed in each ICS to estimate cost for that specialty in that ICS. Costs were summed across all specialties in each ICS to calculate a total cost per ICS. To aid interpretation a cost per capita was calculated:

$Ccap_{ICS} = C_{ICS} / Pn_{ICS}$ Equation 11

Where:

$Ccap_{ICS}$ = Cost per capita to address the need for elective procedures in ICS

C_{ICS} = Total cost to address the need for elective procedures in ICS

Pn_{ICS} = ICS population in mid-2020

Data was also aggregated at a regional-level based on the seven regions defined by NHS England (East of England, London, Midlands, North East & Yorkshire, North West, South East, South West)

6.4.8 Forecasting total need to 2030

We conducted an expert survey to ascertain expectations for the speed of recovery for elective services and the potential to expand beyond pre-pandemic volume. We used an anonymous online survey to collect responses from members of the CovidSurg research network. The survey instrument is included in Table 6.1. A total of 47 clinicians across 15 specialities submitted responses and the results are summarised in Table 6.2.

Table 6.1: Expert survey instrument content

Background information	
In England, although the overall number of elective procedures performed each month has been steadily increasing, in March 2022 elective procedural activity was still approximately 15% lower than it was pre-pandemic.	
Question	**Options**
When do you think your unit will return to its pre-pandemic baseline for ELECTIVE procedural activity? *Pre-pandemic baseline means the same number of procedures performed per month as before the pandemic*	• Already at or above pre-pandemic baseline • December 2022 • July 2023 • December 2023 • July 2024 • December 2024 • July 2025 • December 2025 • July 2026 • December 2026 • July 2027 • December 2027 • July 2028 • December 2028 • July 2029 • December 2029 or later • Unlikely to ever return to pre-pandemic baseline
Once your unit has returned to it's pre-pandemic Increase above pre-pandemic baseline will not be baseline for elective procedural volume, what do you possible consider a realistic target for increasing annual ELECTIVE procedural volume, as a proportion of pre-pandemic volume? *i.e. if prepandemic elective procedural volume was 1,000, a 2% increase would mean that each year the number of elective procedures would increase by 20 (2% of 1,000). So volume in year 1 would be 1,020, in year 2 volume would be 1,040, in year 3 volume would be 1,060 etc.*	• Increase above pre-pandemic baseline will not be possible • Up to 2.4% increase per year • 2.5-4.9% increase per year • 5.0-7.4% increase per year • 7.5-9.9% increase per year • 10.0-12.4% increase per year • 12.5-14.9% increase per year • 15.0-17.4% increase per year • 17.5-19.9% increase per year • 20.0% or greater increase per year

Responses collected through anonymous online survey on 5-7 June 2022.

Table 6.2: Results of expert survey

Specialty of respondent	
Anaesthetics	2
Breast surgery	1
Cardiac surgery	3
Colorectal surgery	5
General surgery	9
Gynaecology	3
Head & Neck surgery	3
Hepatobiliary surgery	3
Neurosurgery	3
Ophthalmology	1
Orthopaedics	9
Plastic surgery	1
Thoracic surgery	1
Urology	2
Vascular surgery	1
Estimate for when elective procedures will return to pre-pandemic baseline volume	
Already at or above pre-pandemic baseline	12
July 2022	5
December 2022	6
July 2023	8
December 2023	4
July 2024	3
December 2024	1
July 2025	1
December 2025	4
July 2026 - July 2029	0
December 2029 or later	1
Unlikely to ever return to pre-pandemic baseline	2
Estimates for realistic annual increase in elective procedure volume after it has returned to its pre-pandemic baseline	
Increase above pre-pandemic baseline will not be possible	22
Up to 2.4% increase per year	9
2.5-4.9% increase per year	7
5.0-7.4% increase per year	2
7.5-9.9% increase per year	2
10.0-12.4% increase per year	2
12.5-19.9% increase per year	0
20.0% or greater increase per year	3

Based on the results of the expert survey we have modelled four scenarios to estimate the number of people in England who will need elective procedures through to 2030.

These scenarios were

- Current capacity: surgical volume remains at the same level as in February-March 2022, from April 2022 up until January 2030.
- Pessimistic scenario: elective procedure volume gradually increases from current levels up to pre-pandemic levels by July 2023 followed by a plateauing of this rate through to January 2030.

- Central scenario: elective procedure volume returns to pre-pandemic levels by December 2022 followed by a 2% increase per year.
- Optimistic scenario: elective procedure volume returns to pre-pandemic levels by December 2022 followed by a 4% increase per year.

Scenarios were modelled on a monthly basis, with the total need for selective procedures calculated for each month between April 2022 and December 2029.

We also determined the monthly increase in surgical volume (assuming a constant rate of increase) required to fulfil the need for surgery and invasive diagnostics in full by January 2030.

6.5 Results

We estimated the total need for elective procedures in England in March 2022 was 4,347,469. The greatest need was for General Surgery (35.0%, 1,522,366 of 4,347,469), Orthopaedics (22.5%, 976,875 of 4,347,469), and Ophthalmology (9.0%, 391,683 of 4,347,469, Table 6.3). There was substantial geographic variation (Figure 6.1-6.2), with the highest need in the South West (93.2 elective procedures needed per 100,000) followed by the North West (89.7 per 100,000), Midlands (83.9 per 100,000), South East (77.6 per 100,000), East of England (73.8 per 100,000), North East and Yorkshire (69.6 per 100,000), and London (56.7 per 100,000)

Table 6.3: Specialty-level breakdown of estimated total need for elective procedures in England and estimated hidden waiting list in March 2022

Specialty	Total need	Hidden waiting list
General Surgery	1,522,366	1,289,440
Orthopaedics	976,875	747,749
Ophthalmology	391,683	168,361
Urology	385,971	284,279
Head & Neck surgery	332,281	263,447
Gynaecology	246,973	175,394
Plastic Surgery	231,333	182,570
Cardiology	154,453	109,479
Cardiothoracic surgery	88,865	76,286
Neurosurgery	16,669	7,508
Total	4,347,469	3,304,513

Figure 6.1: Total number of elective procedures needed in England, by region

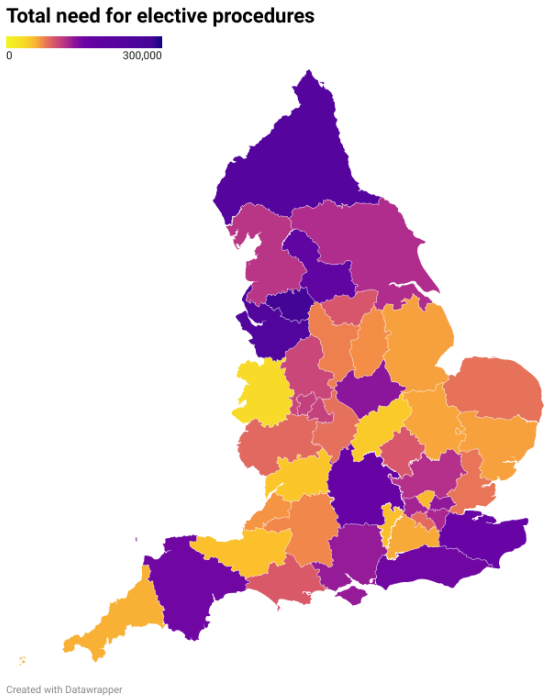
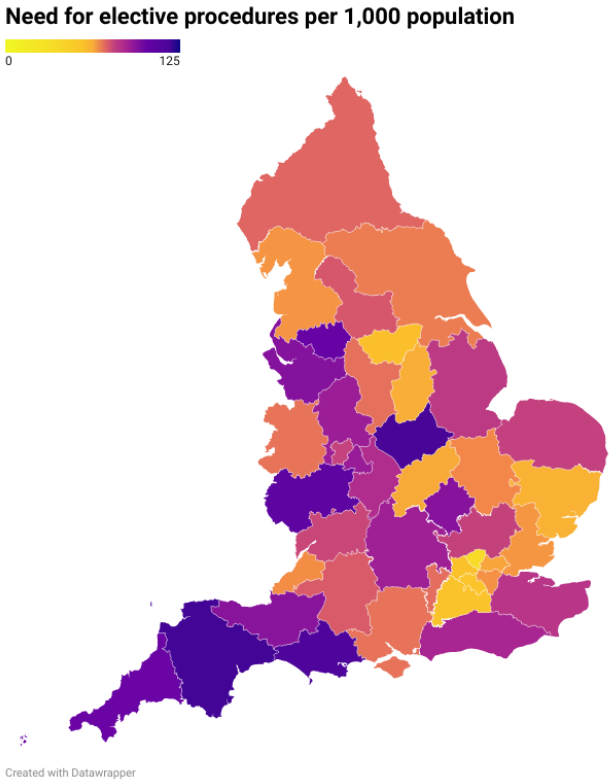


Figure 6.2: Total need for elective procedures in England per 1,000 population, by region



6.5.1 Hidden waiting list

Of the 4,347,469 required elective procedures, 1,042,956 (24.0%) of patients were on the NHS waiting list and 3,304,513 (76.0%) were on a hidden waiting list. The largest hidden waiting lists were for General Surgery (1,289,440) and Orthopaedics (747,749).

6.5.2 Day-case procedures

Overall, 84.9% (3,692,377 of 4,347,469) need was for day-case procedures. For six sub-specialties (Cardiology, Colorectal Surgery, Head & Neck Surgery, Oesophagogastric Surgery, Ophthalmology, Plastic Surgery) >95% of total need was for day-cases (Table 6.4).

Table 6.4: Sub-specialty-level breakdown of estimated total need for elective procedures in England in March 2022

Sub-specialty	Day-case	Overnight admission
Breast surgery	36,015	6,953
Cardiac surgery	1,433	27,395
Cardiology	152,762	1,691
Colorectal surgery	636,961	13,436
General surgery	144,944	29,348
Gynaecology	162,365	84,608
Head & Neck surgery	316,268	16,013
Hepatobiliary surgery	73,893	6,770
Neurosurgery	5,131	11,538
Oesophagogastric surgery	447,254	22,891
Ophthalmology	390,328	1,355
Orthopaedics	657,797	319,078
Plastic surgery	227,140	4,193
Thoracic surgery	44,652	15,385
Urology	317,910	68,061
Vascular surgery	77,524	26,377
Total	3,692,377	655,092

6.5.3 Key procedures

Overall, the greatest need was for sigmoidoscopy/ colonoscopy (568,838), gastroscopy (447,830), cataract surgery (314,790), lower limb joint replacement

(224,363), and interventional cardiology (349,300). These top five procedures accounted for 39.3% of total need (1,710,274 of 4,347,469). The top 20 procedures (Table 6.5) accounted for 68.8% (2,992,395 of 4,347,469) of total need.

Table 6.5: Top 20 elective procedures by need in England in March 2022

Procedure name	Day-case	Overnight admission	Total
Sigmoidoscopy, colonoscopy	568,886	-	568,838
Gastroscopy	446,125	1,705	447,830
Cataract surgery	314,790	-	314,790
Lower limb joint replacement	-	224,363	224,363
Interventional cardiology	152,762	1,691	154,453
Ureteroscopy, cystoscopy & related procedures	117,817	18,444	136,261
Excision of lesion of skin	128,131	-	128,131
Operations on bladder	90,486	23,263	113,749
Procedures on peripheral nerves	105,915	-	105,915
Operations on ear	86,216	1,347	87,563
Spinal nerve root procedure	78,130	-	78,130
Operations on nose	77,855	4	77,859
Groin hernia repair	76,792	-	76,792
Arthroscopic procedures	75,431	-	75,431
Surgery on ligament, tendon, muscle	72,068	1,658	73,726
Hysteroscopy & related procedures	68,744	-	68,744
Other day-case spinal surgery	68,697	-	68,697
Division or excision of bone	63,069	5,322	68,391
Tonsillectomy	61,993	-	61,993
Proctology	60,739	-	60,739

Total need for Sigmoidoscopy, colonoscopy is lower than day-case need as the need for overnight admissions for this procedure was calculated as -48

6.5.4 Projected cost to address need for elective procedures

The projected cost to fully address the need for elective procedures was £9,207,798,071. The greatest costs were for Orthopaedics (£3,751,715,700), Urology (£722,558,421), and Head & Neck Surgery (£585,055,737, Table 6.6).

Table 6.6: Projected cost to address need for elective procedures

Sub-specialty	Total cost
Breast surgery	£221,703,319
Cardiac surgery	£318,800,210
Cardiology	£372,181,343
Colorectal surgery	£540,488,976
General surgery	£465,424,135
Gynaecology	£555,252,435
Head & Neck surgery	£585,055,737
Hepatobiliary surgery	£227,444,145
Neurosurgery	£130,995,974
Oesophagogastric surgery	£335,191,264
Ophthalmology	£394,740,194
Orthopaedics	£3,751,715,700
Plastic surgery	£210,128,413
Thoracic surgery	£106,740,125
Urology	£722,558,422
Vascular surgery	£269,377,678
Total	£9,207,798,071

6.5.5 Surgical activity in February to March 2022

The pre-pandemic baseline for the number of procedures expected in a two-month period was 953,390. We estimated that 810,674 elective procedures were performed in February to March 2022. This indicates a shortfall of 142,717 procedures, equivalent to 15.0% of pre-pandemic elective volume.

6.5.6 Forecasting total need for elective procedures to 2030

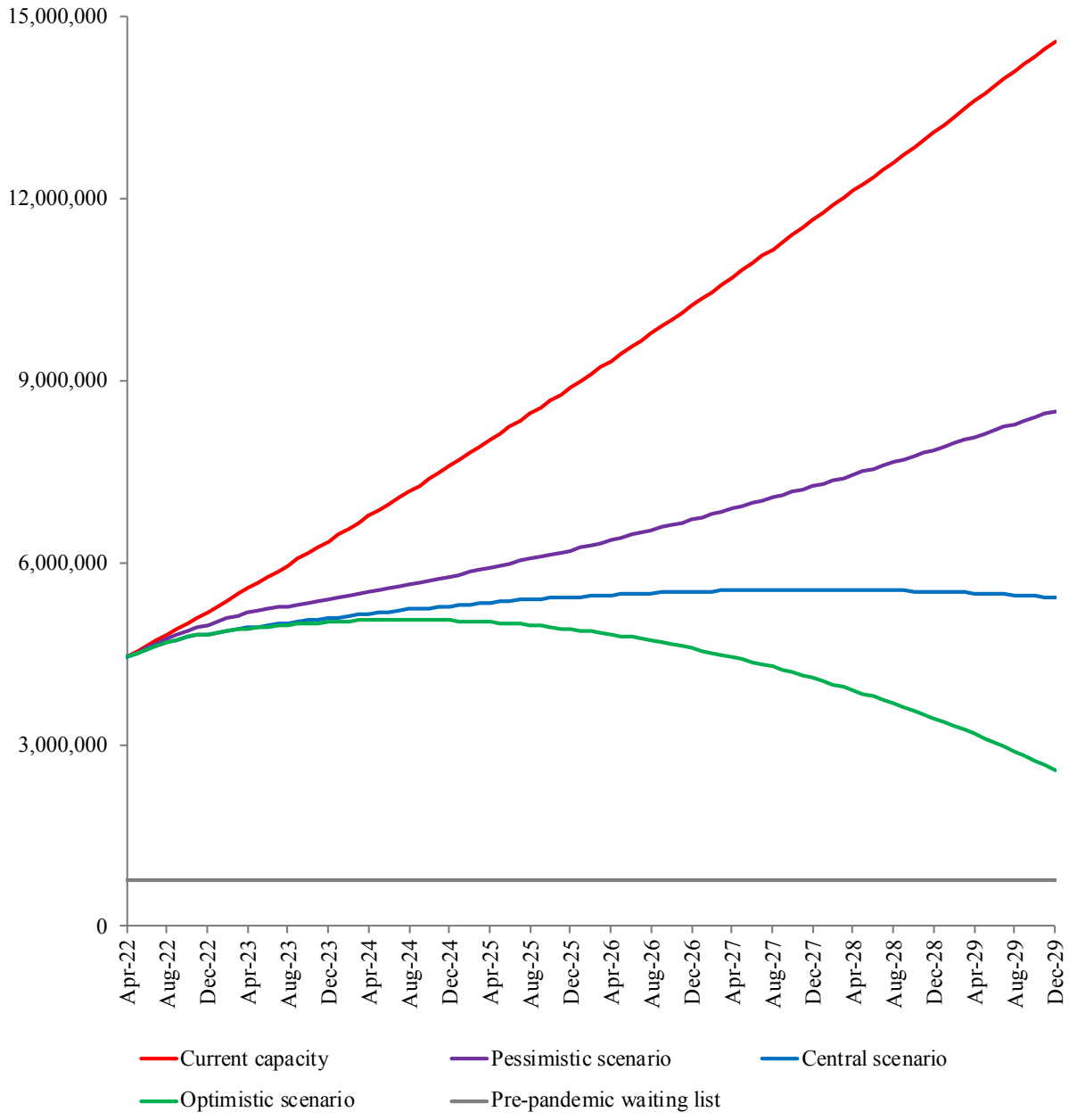
We modelled that if age-sex specific incident need rates for elective procedures remain constant, based on ONS population projections in the seven years and nine months from April 2022 to December 2029, 47,957,079 elective procedures will be needed (Table 6.7), in addition to the existing pandemic shortfall of 4,347,469. Therefore, the total number of elective procedures that will be needed through to 2030 is 52,304,550.

Table 6.7: Projections for annual incident need for elective procedures in 2022-29

Period	Annual incident need for elective procedures
April – December 2022	4,480,571
January – December 2023	6,038,213
January – December 2024	6,099,468
January – December 2025	6,157,013
January – December 2026	6,215,214
January – December 2027	6,270,663
January – December 2028	6,323,103
January – December 2029	6,372,834

We modelled that if surgical volume remains at current levels, the total number of elective procedures needed would increase to 14,608,195 by January 2030 (Figure 6.3, Table 6.8). In the pessimistic scenario, if elective procedure volume gradually increases from current levels up to pre-pandemic levels by July 2023 followed by a plateauing of this rate, the total number of elective procedures needed would increase to 8,507,087 by January 2030. In the central scenario, if elective procedure volume returns to pre-pandemic levels by December 2022 followed by a 2% increase per year, the total number of elective procedures needed in January 2030 would be 5,420,999. Finally, in the optimistic scenario, if elective procedure volume returns to pre-pandemic levels by December 2022 followed by a 4% increase per year, 2,584,664 procedures would be needed in January 2030.

Figure 6.3: Forecasts for total need for elective procedures in England in different scenarios



The pre-pandemic waiting list in December 2019 was 753,116

Table 6.8: Forecasts for total need for elective procedures in England in different scenarios

Month	Current capacity	Pessimistic scenario	Central scenario	Optimistic scenario
Mar-22	4,347,469	4,347,469	4,347,469	4,347,469
Apr-22	4,439,973	4,435,513	4,432,044	4,432,044
May-22	4,532,477	4,519,098	4,508,691	4,508,691
Jun-22	4,624,981	4,598,222	4,577,409	4,577,409
Jul-22	4,717,485	4,672,887	4,638,199	4,638,199
Aug-22	4,809,989	4,743,091	4,691,060	4,691,060
Sep-22	4,902,494	4,808,836	4,735,992	4,735,992
Oct-22	4,994,998	4,870,121	4,772,995	4,772,995
Nov-22	5,087,502	4,926,946	4,802,070	4,802,070
Dec-22	5,180,006	4,979,312	4,823,216	4,823,216
Jan-23	5,277,853	5,032,560	4,848,911	4,848,116
Feb-23	5,375,700	5,081,349	4,873,811	4,871,428
Mar-23	5,473,548	5,125,678	4,897,917	4,893,150
Apr-23	5,571,395	5,165,547	4,921,228	4,913,283
May-23	5,669,242	5,200,956	4,943,745	4,931,828
Jun-23	5,767,090	5,231,905	4,965,468	4,948,783
Jul-23	5,864,937	5,258,394	4,986,395	4,964,150
Aug-23	5,962,784	5,284,883	5,006,529	4,977,927
Sep-23	6,060,632	5,311,373	5,025,868	4,990,116
Oct-23	6,158,479	5,337,862	5,044,412	5,000,715
Nov-23	6,256,326	5,364,351	5,062,162	5,009,726
Dec-23	6,354,174	5,390,841	5,079,117	5,017,147
Jan-24	6,457,125	5,422,435	5,100,383	5,028,084
Feb-24	6,560,077	5,454,029	5,120,854	5,037,432
Mar-24	6,663,029	5,485,622	5,140,530	5,045,191
Apr-24	6,765,981	5,517,216	5,159,413	5,051,362
May-24	6,868,933	5,548,810	5,177,500	5,055,943
Jun-24	6,971,885	5,580,404	5,194,793	5,058,935
Jul-24	7,074,837	5,611,998	5,211,292	5,060,338
Aug-24	7,177,788	5,643,592	5,226,996	5,060,152
Sep-24	7,280,740	5,675,186	5,241,905	5,058,378
Oct-24	7,383,692	5,706,780	5,256,020	5,055,014
Nov-24	7,486,644	5,738,374	5,269,341	5,050,061
Dec-24	7,589,596	5,769,967	5,281,867	5,043,519
Jan-25	7,697,343	5,806,357	5,298,394	5,040,184
Feb-25	7,805,090	5,842,746	5,314,126	5,035,260
Mar-25	7,912,838	5,879,135	5,329,064	5,028,747
Apr-25	8,020,585	5,915,525	5,343,208	5,020,644
May-25	8,128,332	5,951,914	5,356,557	5,010,953
Jun-25	8,236,079	5,988,303	5,369,112	4,999,673
Jul-25	8,343,827	6,024,692	5,380,872	4,986,804
Aug-25	8,451,574	6,061,082	5,391,837	4,972,346
Sep-25	8,559,321	6,097,471	5,402,008	4,956,298
Oct-25	8,667,069	6,133,860	5,411,385	4,938,662
Nov-25	8,774,816	6,170,250	5,419,967	4,919,437
Dec-25	8,882,563	6,206,639	5,427,754	4,898,623
Jan-26	8,995,160	6,247,878	5,439,598	4,881,070
Feb-26	9,107,758	6,289,118	5,450,646	4,861,928
Mar-26	9,220,355	6,330,357	5,460,901	4,841,197
Apr-26	9,332,953	6,371,596	5,470,360	4,818,877
May-26	9,445,550	6,412,836	5,479,025	4,794,968
Jun-26	9,558,147	6,454,075	5,486,896	4,769,470
Jul-26	9,670,745	6,495,314	5,493,972	4,742,383
Aug-26	9,783,342	6,536,554	5,500,254	4,713,707
Sep-26	9,895,939	6,577,793	5,505,741	4,683,443

Oct-26	10,008,537	6,619,033	5,510,434	4,651,589
Nov-26	10,121,134	6,660,272	5,514,332	4,618,146
Dec-26	10,233,731	6,701,511	5,517,436	4,583,114
Jan-27	10,350,950	6,747,372	5,524,366	4,551,114
Feb-27	10,468,168	6,793,232	5,530,502	4,517,525
Mar-27	10,585,386	6,839,092	5,535,843	4,482,347
Apr-27	10,702,604	6,884,952	5,540,390	4,445,580
May-27	10,819,822	6,930,812	5,544,142	4,407,224
Jun-27	10,937,040	6,976,672	5,547,099	4,367,279
Jul-27	11,054,258	7,022,532	5,549,262	4,325,745
Aug-27	11,171,476	7,068,393	5,550,631	4,282,622
Sep-27	11,288,695	7,114,253	5,551,205	4,237,910
Oct-27	11,405,913	7,160,113	5,550,985	4,191,609
Nov-27	11,523,131	7,205,973	5,549,970	4,143,720
Dec-27	11,640,349	7,251,833	5,548,160	4,094,241
Jan-28	11,761,937	7,302,063	5,549,927	4,047,543
Feb-28	11,883,525	7,352,293	5,550,898	3,999,256
Mar-28	12,005,113	7,402,524	5,551,075	3,949,380
Apr-28	12,126,701	7,452,754	5,550,458	3,897,915
May-28	12,248,289	7,502,984	5,549,046	3,844,862
Jun-28	12,369,878	7,553,214	5,546,840	3,790,219
Jul-28	12,491,466	7,603,444	5,543,839	3,733,987
Aug-28	12,613,054	7,653,674	5,540,044	3,676,166
Sep-28	12,734,642	7,703,904	5,535,454	3,616,757
Oct-28	12,856,230	7,754,134	5,530,070	3,555,758
Nov-28	12,977,818	7,804,365	5,523,891	3,493,170
Dec-28	13,099,406	7,854,595	5,516,918	3,428,994
Jan-29	13,225,139	7,908,969	5,513,294	3,367,372
Feb-29	13,350,871	7,963,343	5,508,876	3,304,162
Mar-29	13,476,603	8,017,718	5,503,664	3,239,362
Apr-29	13,602,336	8,072,092	5,497,657	3,172,974
May-29	13,728,068	8,126,467	5,490,855	3,104,997
Jun-29	13,853,801	8,180,841	5,483,259	3,035,430
Jul-29	13,979,533	8,235,215	5,474,869	2,964,275
Aug-29	14,105,265	8,289,590	5,465,684	2,891,531
Sep-29	14,230,998	8,343,964	5,455,704	2,817,198
Oct-29	14,356,730	8,398,339	5,444,931	2,741,275
Nov-29	14,482,462	8,452,713	5,433,362	2,663,764
Dec-29	14,608,195	8,507,087	5,420,999	2,584,664

In order to fulfil the need for elective procedures in full by January 2030, elective procedure volume would need to increase by 8.4% (as a proportion of pre-pandemic volume) each year, reaching a maximum of 50% above the pre-pandemic baseline in January 2030.

6.6 Discussion

6.6.1 Main findings

We estimated that 4.3 million procedures were needed in England in March 2022. This is very considerably higher than the NHS waiting list; an estimated 3.3 million patients were on a hidden waiting list. Our projects suggest that the number of people needing elective procedures is likely to remain very considerably higher than the pre-pandemic waiting list peak until at least 2030. Unless elective procedure volume increases at least 2% above pre-pandemic levels each year, the number of people needing procedures will actually increase over time due to population growth and ageing. Based on our expert survey, the 8% annual increase in activity required to eliminate waiting lists even by 2030 is unlikely to be achievable.

The hidden waiting list includes people who need elective procedures and would have been referred and treated pre-pandemic. However, as a result of the pandemic these patients may have not sought medical attention. These patients will be delayed in receiving treatment and some will suffer worse health as a result. For example, patients with hip osteoarthritis needing a joint replacement are likely to experience increasing symptoms resulting in deterioration in their quality of life and their ability to complete their work and social activities. This in turn may in turn result in lifestyle changes. For patients with life threatening diseases such as cancer, delayed diagnosis and treatment could reduce chances of being successfully cured.

There is sharp variation in the overall need for elective procedures between England's regions, with the need in the South West being almost double that in London. At a sub-regional level there is variation between different integrated care systems, but we were not able to explore variation at a more granular postcode level.

It is possible that some patients living in more deprived neighbourhoods and particularly vulnerable patients such as those with mental health conditions, refugees, and intravenous drug users may find it more difficult to navigate the process to get elective treatment at a time when health services are under particularly high pressure. Moreover, a shift from NHS to private provision in more affluent neighbourhoods could relieve some pressure on NHS services in those areas, whilst services in more deprived areas remain under heavy pressure. It is important that funding is awarded to integrated care systems according to their actual needs; this analysis suggests where is wide variation in per capita funding needs. Health equity impact assessments16 should be conducted to ensure that planned initiatives to address the need for elective procedures are equitable both at national and local levels.

6.6.2 Strengths and limitations

This is the first study to focus on the need for elective procedures and to provide granular breakdowns at specialty-level and procedure-level. Previous studies have focussed on the overall NHS England waiting list, but this overlooks the large heterogeneity of treatments that patients are waiting for[340-343]. The complexity of patient pathways for surgery, endoscopy, interventional cardiology and interventional radiology is far greater than for simpler treatments like drug infusions. Surgery, endoscopy, and interventional radiology all require specific suites equipped with expensive specialist machines, and staffed by highly trained multidisciplinary teams. Any initiative to increase elective procedure volume must therefore be carefully planned.

There are several limitations to this study. An assumption was made that the pre-pandemic NHS waiting list captured all patients who needed elective procedures, but

it is likely that even pre-pandemic there were some patients who needed elective procedures who had not sought medical attention or had not been appropriately referred or listed. If this is the case, this would lead to us underestimating the current hidden waiting list and total need. NHS waiting list data is not fully cleaned. There may be some double counting of the same patient on different waiting lists, or the counting of patients who no longer require elective treatment, for example, because they have been admitted and treated as an emergency or because they have died. This would potentially result in a small over-estimation of the total need for elective procedures. However, because most of the total need is as a result of the pandemic shortfall, rather than the pre-pandemic NHS waiting list, the impact of inaccuracies in the NHS waiting list would be small overall.

We assumed that as waiting times for surgery increase there is no attrition to the need for surgery, but patients who would usually have been treated during the pandemic may no longer still need treatment; for example, if they have had successful non-operative treatment, have had spontaneous resolution of their underlying condition, or died. This would lead to an overestimation of the current need for surgery.

We assumed that age-sex specific incidence of symptoms of conditions requiring elective procedures would remain stable over time, but this may change as a result of wider social and economic circumstances, mediated through the wider determinants of health; for example, the need for cancer surgery is likely to grow if obesity rates continue to increase.

For our geographic analyses, we have assumed that the size of the hidden waiting list relative to the NHS waiting list is consistent across all NHS systems. If some systems have performed better at capturing patients in need of procedures on their

NHS waiting lists, we may be over-estimating their total need, whilst under-estimating need in other systems that have unexpectedly large hidden waiting lists. However, this would not impact the accuracy of national-level estimates.

6.6.3 Implications for clinical practice

As long waiting lists are likely to continue for the foreseeable future, difficult policy decisions are needed around the prioritisation and models of delivery for elective procedures. Consideration should be given to deprioritising procedures of lower clinical value, in order to release resources to focus on finding patients on the hidden waiting list who have serious disease requiring rapid treatment.

A key insight from this study is that most of the elective procedures needed are day-case procedures. This is likely to reflect the prioritisation of life saving surgery, such as cancer surgery, during the pandemic resulting in only small backlogs of major surgery. An important factor that could limit the ability to ramp up inpatient surgery is an ongoing pressure on general hospital beds in the NHS, particularly by high levels of emergency admissions. However, day-case procedures present greater flexibility in ramping up activity, since they are not dependent on availability of either general or intensive care beds. Initiatives such as high intensity theatre lists have been piloted to focus on high volume low complexity day-case activity17, though further research is needed to determine their optimum format. However, an important caveat to any focus on day-case activity is the need to tackle the orthopaedic backlog.

7 DISCUSSION

7.1 Synopsis of main findings

In chapter 3, I described the findings of the first international, multicentre, cohort study to characterise the outcomes of surgery in patients with perioperative SARS-CoV-2 infection. This study captured 1,128 patients who underwent surgery during the first COVID-19 wave (January to March 2022). This was the first study to robustly identify the association of perioperative SARS-CoV-2 infection with increased risk of both 30-day postoperative pulmonary complications (51.2%) and 30-day postoperative mortality (23.8%). Male patients, older patients (age ≥70 years), co-morbid patients (ASA grades 3-5 versus), cancer surgery patients, emergency surgery patients, and patients undergoing major surgery were found to have increased odds of postoperative mortality.

The key recommendation based on the data described in chapter 3 was that whenever possible surgery should be avoided in patients with acute SARS-CoV-2 infection, in order to avoid exposing them to unnecessary increased risks of postoperative morbidity and mortality. However, it was unknown for how long surgery should be deferred in these patients.

In chapter 4, I described the results of an international, multicentre, cohort study that aimed to determine the optimal timing of surgery following SARS-CoV-2 infection. This study included 140,231 patients, from across 116 countries, who were operated in October 2020. This was the first study to demonstrate that whereas patients operated 0–2 weeks, 3–4 weeks, and 5–6 weeks after a SARS-CoV-2 diagnosis were at increased risk of mortality and postoperative pulmonary complications compared to patients, patients operated ≥7 weeks after SARS-CoV-2 diagnosis were not at increased risk compared to patients who had not previously had a SARS-CoV-2 infection.

The key recommendation arising from chapter 4 was that, if possible, surgery should be delayed for at least 7 weeks following SARS-CoV-2 infection, in order to avoid the increased risk of complications and mortality during the first six weeks following infection. This data was collected in late 2020, before either the development of SARS-CoV-2 vaccines or the emergence of the Omicron SARS-CoV-2 variant. It was therefore unknown whether the findings chapters 2 and 3 still applied to current practice.

In chapter 5, I described the findings of an international prospective cohort study that captured surgical outcomes for 19,684 patients operated in December 2021 to February 2022 who had perioperative SARS-CoV-2 infection. This study showed that the rates of both 30-day mortality and 30-day postoperative pulmonary complications had substantially reduced compared to the outcomes recorded in the first COVID-19 wave (chapter 3). In low-risk patients (ASA grades 1-2, age <70 years) the risk of postoperative adverse outcomes was close to the expected baseline in non-SARS-CoV-2 patients. SARS-CoV-2 vaccination was associated with reduced odds of 30-day mortality and 30-day postoperative pulmonary complications.

The findings presented in chapter 5 indicate that surgical services should consider relaxing some of the COVID-19 mitigations implemented during the pandemic. Surgical pathways should be revised to remove measures that constrain surgical volume, particularly for low-risk patients, in order to address the elective care backlogs that most health systems have developed as a result of prolonged disruption during the pandemic.

In chapter 6, I used publicly available activity data to model total need for elective care in England and to forecast this forward to 2030. I estimated that in March 2022 4.3 million people needed elective procedures in England. I projected that even in the most optimistic scenario 2.6 million people would be on waiting lists for elective procedures in 2030. Characterisation of the current and future waiting lists for elective care allows detailed planning to safely implement the findings from Chapter 5.

7.2 Association of SARS-CoV-2 infection with postoperative mortality

The key finding in chapters 3-5 is that SARS-CoV-2 infection is associated with increased postoperative mortality and that this risk persists for around six weeks following infection. There are no studies comparing the impact of SARS-CoV-2 infection in the general population to that in surgical patients.

Comparisons of published SARS-CoV-2 case fatality rates to mortality rates observed in surgical patients are difficult. Firstly, the characteristics of patients undergoing surgery are likely to differ to the overall general population, potentially confounding comparisons. Secondly, comparisons must be made based on data collected in the same locations at the same time, to avoid confounding based on differences in dominant SARS-CoV-2 variants and both natural and vaccine-derived immunity levels. Thirdly, most case fatality data for non-surgical patients (particularly in the early pandemic) is based on patients hospitalised with COVID-19, so by definition these patients have severe COVID-19, the data in chapters 3-5 is based on surgical patients with any severity of SARS-CoV-2 infection, including those with asymptomatic infection.

The best, albeit imperfect, indication of SARS-CoV-2 infection case fatality rates in the general population in the community is from serological studies. These studies use seroprevalence surveys to estimate the proportion of the population that has had SARS-CoV-2 infection, in order to have a more accurate denominator to calculate case fatality rates. A systematic analysis of serological studies from 2020 found that SARS-CoV-2 case fatality rates increase from under 0.1% in people aged under 30 years to 20.3% in people aged 90 years and over[344]. Given that the overall mortality rate associated with perioperative SARS-CoV-2 in the first wave (Chapter 3) was 23.8%, it is likely that SARS-CoV-2 infection is associated with higher mortality in patients who under surgery than in patients who do not undergo surgery.

The reasons for why perioperative SARS-CoV-2 infection is associated with particularly high mortality are not known. However, over half of the patients with perioperative SARS-CoV-2 infection in the first COVID-19 wave who died had experienced postoperative pulmonary complications. The combination of surgery and perioperative SARS-CoV-2 infection may represent a ‘double hit’ that increases the likelihood of severe postoperative pulmonary complications that result in death.

Even prior to the pandemic patients undergoing surgery were already at considerable risk (around 7%) of postoperative pulmonary complications[301], potentially reflecting translocation of bacteria during intubation, pulmonary insult during mechanical ventilation, basal atelectasis as a result of postoperatively reduced mobility, and immunosuppression associated with the surgical stress response. In the first COVID-19 wave perioperative SARS-CoV-2 infection was associated with increased rates of postoperative pulmonary complications (to up to 50%), perhaps reflecting that surgical patients have a number of risk-factors that increase the likelihood of severe COVID-19.

Research studies are needed to robustly characterise the mechanisms which increase the risk of severe COVID-19 in surgical patients, as this may identify targets for interventions aimed at mitigating their risk.

7.3 Strengths and limitations

A key strength of this body of work is that it was able to leverage the existing GSU infrastructure to rapidly deliver large-scale cohort studies that provided timely, broadly generalisable real-world evidence to guide surgical practice during the pandemic. Over 800 hospitals participated in each of the cohort studies, significantly more than the previous record set for participation in collaborative surgical cohort studies[278]. Indeed, the scale of these collaborations is reflected in the GlobalSurg-CovidSurg Week study[328] holding the Guinness World Record for 'Most authors on a single peer-reviewed academic paper'[345]. The efficiency of study set-up, delivery, and dissemination of results is illustrated in Table 7.1.

These achievements were possible as a result of the pre-existing GSU research network that already had expertise in the delivery of global cohort studies[250,263], as well as resources to undertake the administration for such studies. The contribution of GSU to the global surgical response to COVID-19 demonstrates the importance of flexible global health infrastructure funding to supporting responsive research.

Table 7.1: Timeline of CovidSurg studies

Date	Development
1 Jan 2020 - 31 March 2020	Patient inclusion window for the CovidSurg-1 study
13 Mar 2020	Hospitals invited to express interest in participating in the CovidSurg-1 study[346]
18 Mar 2020	First patient enrolled in CovidSurg-1 on REDCap
14 May 2020	CovidSurg-1 results publicly launched through a webinar (over 6,200 live plus YouTube views)[347]
29 May 2020	CovidSurg-1 results published online at The Lancet[298]
5 Oct 2020 – 1 Nov 2020	Patient inclusion window for the CovidSurg-Week study
9 Mar 2021	CovidSurg-Week study results published online at Anaesthesia[328]
13 Dec 2021 - 28 Feb 2022	Patient inclusion window for the CovidSurg-3 study

The specific limitations relating to the methodology of each of my studies have been discussed in the discussion sections of chapter 3-6. Here I discuss the limitations of this thesis as a body of work investigating the impact of the COVID-19 pandemic on perioperative safety and surgical activity.

A key challenge for studying SARS-CoV-2 is that the regular emergence of new variants of concern means that its key characteristics, including transmissibility, immune evasion, and disease severity, frequently change. This thesis has demonstrated that the impact of perioperative SARS-CoV-2 infection is fundamentally different in early 2022 compared to early 2020, even in unvaccinated patients. This means that with the emergence of each new SARS-CoV-2 variant there will be uncertainty as to the applicability of the research described in this thesis. However, for a particular variant, its impact on postoperative outcomes appears to broadly mirror the outcomes associated with it in the general population. Consequently, trends in COVID-19 outcomes in the general population may be a guide as to the possible impact of future variants of concern in surgical patients.

In the coming years, development of next-generation vaccines and therapeutics, that prevent or reduce the severity of COVID-19, could further complicate application of the data presented in this thesis to clinical practice. Establishment of a mechanism to identify new interventions targeting COVID-19 that may have application in perioperative care would allow future research questions to be defined and prioritised. If required, collaborative studies could be designed to generate new data to evaluate such interventions in the surgical setting.

A major limitation of this body of work is that it is limited to observational studies that aimed to characterise the epidemiology of perioperative SARS-CoV-2 infection. Although I have attempted to control for selection bias and confounding in statistical

analysis, residual bias is likely. Nonetheless, for some research questions, for example regarding the impact of SARS-CoV-2 on perioperative outcomes, this is the most robust methodology possible, since randomisation would be unfeasible and unethical. However, the optimal timing of surgery following SARS-CoV-2 would be most robustly determined in an RCT with patients randomly allocated to different delays. In October 2020 the number of eligible patients at each centre for such a trial was very low, so an RCT would require many hundreds of hospitals to participate to have a sufficient sample size, and this was not practical. Similarly, the role of vaccination in reducing the risk of perioperative SARS-CoV-2 would be most effectively investigated in an RCT, however, it is likely that given the clear benefit of vaccination in the general population, surgeons would lack equipoise to randomise patients to such a trial.

7.4 Implications for the elective recovery

The data from this thesis has directly influenced clinical care during the course of the pandemic. It has received wide-ranging coverage in both social media and mainstream media (Table 7.2). The data presented in chapter 4 and published in *Anaesthesia*[328] has directly informed international guidance regarding timing of surgery following SARS-CoV-2 infection produced by multiple societies. The data presented in chapter 6 was covered by *The Sunday Times*[348].

Table 7.2: Impact of thesis outputs

Article	Altmetric score*	Mainstream media	Guidelines	Citations†
Chapter 3				
Published in *The Lancet*[298]	2,926	Canadian Broadcasting Corporation, CNN Espanol, Daily Mail (United Kingdom), iForbes (United States), La Tercera (Chile), The Hindu (India), Vanguard (Nigeria)	Cited in guidance from the World Health Organisation and the Royal College of Surgeons of England and Royal College of Anaesthetists[349,350], the Royal College of Paediatrics and Child Health[351], and the Scottish Intercollegiate Guideline Network[352]	1,500
Chapter 4				
Published in *Anaesthesia*[328]	2,761	Daily Mail (UK), Suddeutsche Zeitung (Germany), The Daily Telegraph (UK), The Independent (UK), US News & Report	American Society of Anesthesiologists[353], the Royal College of Surgeons of England, Royal College of Anaesthetists[349,350], and the Royal Australasian College of Surgeons[354]	323

**Highest achieved Altmetric score. †Google Scholar citations as of 24 November 2022*

Looking forward, the data presented in this thesis has important implications for clinical practice and policy. Key recommendations for the elective recovery are summarised in Table 7.3.

Table 7.3: Recommendations for the elective recovery

Recommendations
Clinical practice
• Whenever possible surgery should be delayed for at least 10 days following SARS-CoV-2 diagnosis, in order to reduce the risk of cross-infection of patients and staff. • For patients at low risk of COVID-19-related complications, surgical services should consider relaxing COVID-19 mitigations implemented during the pandemic. • For patients at high risk of COVID-19-related complications, protected COVID-free surgical pathways should be maintained. • Preoperative completion of a full course of SARS-CoV-2 vaccination should be recommended to all patients planned for elective surgery. In settings with limited SARS-CoV-2 access, consideration should be given to prioritizing vaccination for elective surgery patients. • Public awareness campaigns should be undertaken to encourage patients with 'hidden need' (e.g. symptoms of possible surgical disease) to seek medical attention.
Policy
• Ring-fenced funding should be provided by governments to support elective surgery recovery. • High priority patient groups waiting for elective groups should be identified and prioritized on waiting lists. • Local health systems should appraise models for scaling up safe delivery of elective care. This could include the establishment of dedicated elective surgery hubs. • Health equality impact assessments should be completed when planning the elective recovery to ensure that recovery efforts do not amplify pre-pandemic health inequalities.
Research
• Different models for scaling-up elective care should be characterized and evaluated. • Strategies for finding patients on the 'hidden waiting list' should be identified and evaluated.

7.5 Implications for future pandemic planning

The emergence of further pandemics in the future is highly likely. The risks of neglecting infectious diseases that are currently limited to low-income countries has been illustrated by recent monkeypox outbreaks in countries where the virus is not endemic[355,356]. There are a large number of infectious diseases that have the potential to emerge as major public health threats. This includes infections such Lassa fever, Rift valley fever, Nipah virus, and yellow fever[357,358]. A further threat is from the emergence of antimicrobial resistance[359], with multidrug resistant tuberculosis and resistant staphylococcus aureus increasing in prevalence.

Although in the 20 years preceding the emergence of SARS-CoV-2 there had been a number of public health emergencies of international concern, there was little robust data from them to inform surgical care during the COVID-19 pandemic. It is

important to leverage the experience of the COVID-19 pandemic to put in place structures to mitigate the impact of future pandemics on surgical care.

The impact of infectious disease on surgical care has largely been neglected in the past, but this is likely to become an increasingly prominent issue in global surgical care. Key recommendations for future pandemic planning are summarised in Table 7.4.

Table 7.4: Recommendations for future pandemic planning

Recommendations
Policy
• Hospitals and health systems should develop surgical pandemic preparedness plans to ensure surgical services are prepared and resilient to future public health emergencies. • To support rapid set-up of surgical studies in future public health emergencies, a template protocol should be created, similar to the ISARIC platform[31]. • A mechanism should be established to monitor the emergence of new public health emergencies that may have implications for surgical care. This mechanism should have capacity to rapidly produce evidence-based clinical guidance for new public health emergencies. It should also prioritise urgent research questions relating to new public health emergencies.
Research
• Strategies should be identified to mitigate the disruption to elective care associated with lockdowns.

7.6 Conclusion

In conclusion, this thesis has provided original evidence for the impact of perioperative SARS-CoV-2 infection on the safety and delivery of surgery, specifically establishing that:

1. In the first COVID-19 wave perioperative SARS-CoV-2 was associated with greatly increased risk of postoperative pulmonary complications and mortality.
2. In the first COVID-19 wave surgery within six weeks of SARS-CoV-2 diagnosis was associated with increased risk of postoperative pulmonary complications and mortality, but that this risk returned to baseline at seven weeks onwards.

3. During the period of Omicron variant dominance the risk of postoperative pulmonary complications and mortality associated with perioperative SARS-CoV-2 is significantly reduced compared with the first COVID-19 wave.
4. Pandemic-related disruption has resulted in large number of people being on waiting lists for elective procedures; large waiting lists are likely to persist through to 2030.

The data presented in this thesis will inform planning for scaling-up surgical activity safely.

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9 APPENDIX

9.1 Chapter 3 publication

COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. Lancet. 2020;396(10243):27-38.

Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study

*COVIDSurg Collaborative**

Summary

Background The impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on postoperative recovery needs to be understood to inform clinical decision making during and after the COVID-19 pandemic. This study reports 30-day mortality and pulmonary complication rates in patients with perioperative SARS-CoV-2 infection.

Methods This international, multicentre, cohort study at 235 hospitals in 24 countries included all patients undergoing surgery who had SARS-CoV-2 infection confirmed within 7 days before or 30 days after surgery. The primary outcome measure was 30-day postoperative mortality and was assessed in all enrolled patients. The main secondary outcome measure was pulmonary complications, defined as pneumonia, acute respiratory distress syndrome, or unexpected postoperative ventilation.

Findings This analysis includes 1128 patients who had surgery between Jan 1 and March 31, 2020, of whom 835 (74·0%) had emergency surgery and 280 (24·8%) had elective surgery. SARS-CoV-2 infection was confirmed preoperatively in 294 (26·1%) patients. 30-day mortality was 23·8% (268 of 1128). Pulmonary complications occurred in 577 (51·2%) of 1128 patients; 30-day mortality in these patients was 38·0% (219 of 577), accounting for 81·7% (219 of 268) of all deaths. In adjusted analyses, 30-day mortality was associated with male sex (odds ratio 1·75 [95% CI 1·28–2·40], p<0·0001), age 70 years or older versus younger than 70 years (2·30 [1·65–3·22], p<0·0001), American Society of Anesthesiologists grades 3–5 versus grades 1–2 (2·35 [1·57–3·53], p<0·0001), malignant versus benign or obstetric diagnosis (1·55 [1·01–2·39], p=0·046), emergency versus elective surgery (1·67 [1·06–2·63], p=0·026), and major versus minor surgery (1·52 [1·01–2·31], p=0·047).

Interpretation Postoperative pulmonary complications occur in half of patients with perioperative SARS-CoV-2 infection and are associated with high mortality. Thresholds for surgery during the COVID-19 pandemic should be higher than during normal practice, particularly in men aged 70 years and older. Consideration should be given for postponing non-urgent procedures and promoting non-operative treatment to delay or avoid the need for surgery.

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*Collaborating authors are listed in the appendix (pp 1–7)

Correspondence to: Mr Aneel Bhangu, National Institute for Health Research Global Health Research Unit on Global Surgery, Heritage Building, University of Birmingham, Birmingham B15 2TH, UK **a.a.bhangu@bham.ac.uk**

See Online for appendix

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has now spread to most countries, with WHO declaring a COVID-19 pandemic on March 11, 2020.[1] The pandemic has tested the resilience of health-care systems, including hospitals, which were largely unprepared for the scale of the pandemic.[2] Patients having surgery are a vulnerable group at risk of SARS-CoV-2 exposure in hospital and might be particularly susceptible to subsequent pulmonary complications, due to the pro-inflammatory cytokine and immunosuppressive responses to surgery and mechanical ventilation.[3,4] Evidence of the safety of performing surgery in SARS-CoV-2-exposed hospitals is urgently needed.

Before the SARS-CoV-2 pandemic, high-quality, multinational observational studies established overall baseline rates of postoperative pulmonary complications (up to 10%) and subsequent mortality (up to 3%) after surgery.[5–7] With initiatives such as the UK's National Emergency Laparotomy Audit (NELA), mortality was improving even in high-risk groups.[8]

Guidelines have been published for the management of surgical patients during the SARS-CoV-2 pandemic,[9–11] but they are based solely on expert opinion. The impact of SARS-CoV-2 on postoperative pulmonary complications and mortality needs to be established in order to enable surgeons and patients to make evidence-based decisions during the pandemic. This study reports the clinical

Research in context

Evidence before this study

We searched PubMed and Embase on March 15, 2020, for studies reporting on surgical patients during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. We used the search terms "COVID-19", "SARS-CoV-2", "coronavirus", and "pandemic", in combination with "surgery", and applied no language or date restrictions. We identified 13 articles (12 from China and one from Singapore), all of which provided clinical guidance, with none reporting patient-level outcomes.

Added value of this study

This international, observational, cohort study provides cross-specialty, patient-level outcomes data for patients who had surgery and acquired perioperative SARS-CoV-2 infection. 1128 patients were included across 24 countries. Overall 30-day mortality was 23·8% (268 of 1128 patients). Pulmonary complications occurred in 577 (51·2%) patients; these patients accounted for 82·6% (219 of 265) of all deaths. Independent risk factors for mortality were male sex, age 70 years or older, American Society of Anesthesiologists grades 3–5, surgery for malignant disease, emergency surgery, and major surgery.

Implications of all the available evidence

Postoperative pulmonary complications occur in half of patients with perioperative SARS-CoV-2 infection and are associated with high mortality. These pulmonary complication and mortality rates are greater than those reported for even the highest-risk patients before the pandemic. Thresholds for surgery during the SARS-CoV-2 pandemic should be higher than during normal practice; men aged 70 years and older who have emergency or major elective surgery are at particularly high risk of mortality. Consideration should be given for postponing non-critical procedures and promoting non-operative treatment to delay or avoid the need for surgery. When hospitals recommence routine surgery, this will be in hospital environments that remain exposed to SARS-CoV-2, so strategies should be developed to reduce in-hospital SARS-CoV-2 transmission and mitigate the risk of postoperative complications.

outcomes of patients who had surgery with perioperative SARS-CoV-2 infection, including the impact of pulmonary complications.

Methods

Study design

We did an international, multicentre, observational cohort study in patients with SARS-CoV-2 infection who had surgery at 235 hospitals in 24 countries (appendix p 10). Data release and ethical considerations were discussed with an independent data monitoring and ethics committee. We collected only routine, anonymised data with no change to clinical care pathways. In the UK, the study was registered at each site as either a clinical audit or service evaluation; at the lead centre (University Hospital Birmingham) it was approved as clinical audit, with registration CARMS-15986. In other countries, local principal investigators were responsible for contacting competent research ethics committees to obtain local or national approvals in line with applicable regulations, as well as seeking approvals from data protection officers. In some participating hospitals, informed patient consent was taken, whereas in other countries the requirement for patient consent was waived by local research ethics committees.

Participants

Each participating hospital included all patients undergoing surgery who had SARS-CoV-2 infection diagnosed within 7 days before or 30 days after surgery. Surgery was defined as any procedure done by a surgeon in an operating theatre under general, regional, or local anaesthesia. Patients undergoing surgery for any indication were eligible, including benign disease, cancer, trauma, and obstetrics. The study included children and adults, but individual hospitals had the option to apply local age cutoffs, if appropriate. If patients with SARS-CoV-2 infection had multiple operations, the procedure closest to the time of confirmation of SARS-CoV-2 infection was defined as the index procedure.

Participating hospitals prospectively screened patients for eligibility to ensure that all patients fulfilling eligibility criteria were captured. However, the study was initiated after the SARS-CoV-2 pandemic had peaked in some regions, so retrospective data collection was permitted if collaborators were able to identify and include all eligible patients. The importance of working across surgical specialties to identify all eligible patients was highlighted in site training, because incomplete case ascertainment could introduce bias, if patients with less severe disease were missed. Site investigators were provided with a range of written materials setting out possible strategies to capture consecutive eligible patients. In addition, investigators were invited to join social media groups and teleconferences for the purpose of troubleshooting site-specific recruitment issues and shared learning.

Procedures

Laboratory testing for SARS-CoV-2 infection was based on viral RNA detection by quantitative RT-PCR. Sampling, including nasal swabs or bronchoalveolar lavage, and analyses were done according to individual hospital protocols.

As quantitative RT-PCR testing was not available at all participating hospitals, patients were also included based on either clinical or radiological findings. Clinical

	30-day mortality			Pulmonary complications		
	No (n=845)	Yes (n=268)	p value	No (n=526)	Yes (n=577)	p value
Age	..	..	<0·0001	..	..	0·00023
<29 years	56 (100%)	0	..	39 (70·9%)	16 (29·1%)	..
30–49 years	146 (94·2%)	9 (5·8%)	..	86 (55·8%)	68 (44·2%)	..
50–69 years	277 (79·8%)	70 (20·2%)	..	159 (46·0%)	187 (54·0%)	..
≥70 years	364 (65·9%)	188 (34·1%)	..	240 (44·0%)	305 (56·0%)	..
Missing	2	1	..	2	1	..
Sex	..	..	<0·0001	..	..	0·0028
Male	424 (71·1%)	172 (28·9%)	..	252 (42·8%)	337 (57·2%)	..
Female	417 (81·6%)	94 (18·4%)	..	270 (53·1%)	238 (46·9%)	..
Ambiguous	1 (50·0%)	1 (50·0%)	..	1 (50·0%)	1 (50·0%)	..
Missing	3	1	..	3	1	..
American Society of Anesthesiologists grade	..	..	<0·0001	..	..	<0·0001
1–2	344 (88·4%)	45 (11·6%)	..	235 (60·6%)	153 (39·4%)	..
3–5	475 (68·7%)	216 (31·3%)	..	278 (40·6%)	407 (59·4%)	..
Missing	26	7	..	13	17	..
Number of comorbidities	..	..	<0·0001	..	..	0·00017
None	107 (93·0%)	8 (7·0%)	..	73 (63·5%)	42 (36·5%)	..
One	192 (82·8%)	40 (17·2%)	..	115 (50·7%)	112 (49·3%)	..
Two or more	527 (70·8%)	217 (29·2%)	..	322 (43·5%)	418 (56·5%)	..
Missing	19	3	..	16	5	..
Comorbidities						
Current smoker	80 (75·5%)	26 (24·5%)	0·909	42 (40·0%)	63 (60·0%)	0·097
Asthma	57 (73·1%)	21 (26·9%)	0·542	36 (48·0%)	39 (52·0%)	0·955
Cancer	146 (77·2%)	43 (22·8%)	0·639	92 (48·9%)	96 (51·1%)	0·707
Chronic kidney disease	109 (66·5%)	55 (33·5%)	0·0022	64 (39·3%)	99 (60·7%)	0·020
Chronic obstructive pulmonary disease	75 (64·7%)	41 (35·3%)	0·0027	44 (37·9%)	72 (62·1%)	0·026
Congestive heart failure	55 (64·7%)	30 (35·3%)	0·012	29 (34·5%)	55 (65·5%)	0·012
Dementia	48 (55·2%)	39 (44·8%)	<0·0001	30 (35·3%)	55 (64·7%)	0·017
Diabetes	207 (73·9%)	73 (26·1%)	0·367	124 (44·1%)	157 (55·9%)	0·166
Hypertension	399 (71·0%)	163 (29·0%)	0·00010	253 (45·3%)	305 (54·7%)	0·114
Myocardial infarction	70 (63·1%)	41 (36·9%)	0·00084	39 (35·4%)	71 (64·6%)	0·0068
Peripheral vascular disease	67 (62·0%)	41 (38·0%)	0·00038	48 (44·4%)	60 (55·6%)	0·477
Stoke or transient ischaemic attack	55 (61·1%)	35 (38·9%)	0·00061	45 (50·0%)	45 (50·0%)	0·647
Symptoms at admission*						
No symptoms reported	111 (77·6%)	32 (22·4%)	0·281	78 (56·5%)	60 (43·5%)	0·020
Symptoms reported	499 (73·3%)	182 (26·7%)	..	309 (45·6%)	368 (54·4%)	..
Abdominal pain	193 (77·5%)	56 (22·5%)	0·134	122 (49·4%)	125 (50·6%)	0·472
Dyspnoea	83 (61·9%)	51 (38·1%)	0·00049	32 (23·9%)	102 (76·1%)	<0·0001
Cough	108 (73·0%)	40 (27·0%)	0·746	55 (37·2%)	93 (62·8%)	0·0054
Diarrhoea	18 (69·2%)	8 (30·8%)	0·571	12 (46·2%)	14 (53·8%)	0·890
Fatigue	42 (70·0%)	18 (30·0%)	0·460	18 (30·0%)	42 (70·0%)	0·0048
Fever >38°C	177 (76·6%)	54 (23·4%)	0·289	94 (40·9%)	136 (59·1%)	0·018
Haemoptysis	2 (66·7%)	1 (33·3%)	0·771	1 (33·3%)	2 (66·7%)	0·623
Myalgia	27 (79·4%)	7 (20·6%)	0·465	9 (26·5%)	25 (73·5%)	0·012
Nausea or vomiting	100 (79·4%)	26 (20·6%)	0·138	62 (49·6%)	63 (50·4%)	0·607
Sputum	7 (41·2%)	10 (58·8%)	0·0018	6 (35·3%)	11 (64·7%)	0·309
Other	209 (70·6%)	87 (29·4%)	0·094	139 (47·3%)	155 (52·7%)	0·930

(Table 1 continues on next page)

	30-day mortality			Pulmonary complications		
	No (n=845)	Yes (n=268)	p value	No (n=526)	Yes (n=577)	p value
(Continued from previous page)						
Preoperative respiratory support						
None or oxygen only	805 (76·4%)	249 (23·6%)	0·134	520 (49·7%)	526 (50·3%)	<0·0001
Non-invasive ventilation	12 (80·0%)	3 (20·0%)	0·710	1 (6·7%)	14 (93·3%)	0·0014
Invasive ventilation	31 (66·0%)	16 (34·0%)	0·103	2 (4·3%)	45 (95·7%)	<0·0001
Last available values before surgery						
Systolic blood pressure, mm Hg†	129·0 (22·6)	131·7 (26·0)	0·118	129·9 (22·0)	129·7 (24·6)	0·896
Respiratory rate, rpm†	18·1 (5·5)	18·7 (8·8)	0·211	17·5 (5·6)	18·9 (7·1)	0·0013
Heart rate, bpm†	85·0 (18·3)	83·0 (19·0)	0·130	83·4 (16·9)	85·3 (19·6)	0·081
qSOFA score	..	..	0·011	..	..	<0·0001
0	572 (76·3%)	178 (23·7%)	..	382 (51·3%)	362 (48·7%)	..
1	155 (77·5%)	45 (22·5%)	..	73 (36·7%)	126 (63·3%)	..
≥2	37 (59·7%)	25 (40·3%)	..	9 (14·8%)	52 (82·2%)	..
Missing	81	20	..	62	37	..

Data only presented for patients with 30-day mortality outcome available (n=1113%) and pulmonary complications outcome available (n=1103%). Percentages are presented in rows. bpm=beats per min. qSOFA=quick sequential organ failure assessment. rpm=breaths per min. *Data only presented for emergency patients. †Data presented as mean with SD.

Table 1: **Baseline and demographic characteristics**

	30-day mortality			Pulmonary complications		
	No (n=845)	Yes (n=268)	p value	No (n=526)	Yes (n=577)	p value
Haemoglobin, g/L*	118·6 (24·7)	116·1 (24·1)	0·150	118·5 (23·5)	117·6 (25·4)	0·537
Missing	18	4	..	15	7	..
White blood cell count, ×10⁹ per L*	10·5 (7·6)	10·6 (6·8)	0·859	10·1 (5·1)	10·8 (8·9)	0·169
Missing	19	4	..	15	8	..
Preoperative chest x-ray	..	..	0·0041	..	..	<0·0001
Not performed	320 (79·4%)	83 (20·6%)	..	232 (58·0%)	168 (42·0%)	..
Yes: normal	321 (77·4%)	94 (22·6%)	..	205 (49·8%)	207 (50·2%)	..
Yes: abnormal	199 (68·9%)	90 (31·1%)	..	84 (29·4%)	202 (70·6%)	..
Missing	5	1	..	5	0	..
Preoperative thorax CT						
Not performed	598 (78·1%)	168 (21·9%)	0·013	376 (49·5%)	384 (50·5%)	0·077
Performed: normal	96 (75·0%)	32 (25·0%)	0·796	60 (47·6%)	66 (52·4%)	0·987
Performed: consolidation	44 (75·9%)	14 (24·14%)	0·991	23 (39·7%)	35 (60·3%)	0·208
Performed: ground glass opacity	57 (71·3%)	23 (28·7%)	0·310	31 (39·2%)	48 (60·8%)	0·119
Performed: pulmonary infiltration	27 (67·5%)	13 (32·5%)	0·205	13 (33·3%)	26 (66·7%)	0·068
Performed: other abnormality	50 (61·0%)	32 (39·0%)	0·0010	30 (37·0%)	51 (63·0%)	0·046
SARS-CoV-2 diagnosis	..	..	0·719	..	..	0·085
Laboratory confirmed	727 (76·0%)	230 (24·0%)	..	454 (47·9%)	493 (52·1%)	..
Radiological (CT thorax)	58 (72·5%)	22 (27·5%)	..	29 (36·3%)	51 (63·7%)	..
Clinical	53 (77·9%)	15 (22·1%)	..	36 (52·9%)	32 (47·1%)	..
Missing	7	1	..	7	1	..
Timing of SARS-CoV-2 diagnosis	..	..	0·128	..	..	0·155
Preoperative	231 (78·8%)	62 (21·2%)	..	148 (51·0%)	142 (49·0%)	..
Postoperative	595 (74·4%)	205 (25·6%)	..	367 (46·2%)	428 (53·8%)	..
Missing	19	1	..	11	7	..

Data only presented for patients with 30-day mortality outcome available (n=1113) and pulmonary complications outcome available (n=1103). Percentages are presented in rows. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. *Last available blood test results from before surgery, presented as mean with SD.

Table 2: **Preoperative assessment**

diagnosis consistent with SARS-CoV-2 infection was made by a senior physician and based on clinical presentation of symptoms highly indicative of SARS-CoV-2 infection, including cough, fever, and myalgia.[12] Radiological diagnosis was based on thorax CT, in keeping with locally implemented protocols. All patients included initially based on clinical or radiological criteria who subsequently had laboratory testing for SARS-CoV-2 infection and returned a negative result were excluded from the study.

Data were collected online using the Research Electronic Data Capture web application. Demographic variables recorded included age, sex, and American Society of Anesthesiologists (ASA) physical status classification. Age was collected as a categorical variable by deciles of age. ASA at the time of surgery was analysed as grades 1–2 versus grades 3–5. The timing of SARS-CoV-2 diagnosis was recorded as either preoperative or postoperative. Clinical symptoms present at the time of hospital admission were recorded for emergency admissions. Physiological variables recorded (respiratory rate, heart rate, and blood pressure) were based on readings taken immediately before surgery. The quick sequential organ failure assessment score[13] was calculated on the basis of individual variables recorded immediately before surgery. Operative variables included urgency (elective or emergency surgery), primary procedure completed, and anaesthesia used (local,

	30-day mortality			Pulmonary complications		
	No (n=845)	Yes (n=268)	p value	No (n=526)	Yes (n=577)	p value
Urgency of surgery	..	..	0·020	..	..	0·873
Elective	225 (80·9%)	53 (19·1%)	..	130 (46·9%)	147 (53·1%)	..
Emergency	610 (74·0%)	214 (26·0%)	..	387 (47·5%)	428 (52·5%)	..
Missing	10	1	..	9	2	..
Anaesthesia	..	..	0·383	..	..	0·488
Local	34 (69·4%)	15 (30·6%)	..	24 (49·0%)	25 (51·0%)	..
Regional	119 (78·8%)	32 (21·2%)	..	78 (51·7%)	73 (48·3%)	..
General	658 (75·2%)	217 (24·8%)	..	403 (46·5%)	464 (53·5%)	..
Missing	34	4	..	21	15	..
Surgical diagnosis	..	..	0·030	..	..	0·502
Benign or obstetric case	480 (78·3%)	133 (21·7%)	..	281 (46·3%)	326 (53·7%)	..
Cancer	183 (72·9%)	68 (27·1%)	..	114 (45·6%)	136 (54·4%)	..
Trauma	157 (70·1%)	67 (29·9%)	..	112 (50·5%)	110 (49·6%)	..
Missing	25	0	..	19	5	..
Grade of surgery	..	..	0·00055	..	..	0·022
Minor	209 (83·6%)	41 (16·4%)	..	132 (53·2%)	116 (46·8%)	..
Major	607 (72·9%)	226 (27·1%)	..	372 (45·0%)	455 (55·0%)	..
Missing	29	1	..	22	6	..
Specialty	..	..	<0·0001	..	..	<0·0001
Breast	3 (100·0%)	0 (0%)	..	2 (66·6%)	1 (33·3%)	..
Cardiac	33 (66·0%)	17 (34·0%)	..	3 (5·9%)	48 (94·1%)	..
Gastrointestinal and general	286 (76·9%)	86 (23·1%)	..	172 (46·4%)	199 (53·6%)	..
Gynaecology	20 (95·2%)	1 (4·8%)	..	16 (76·2%)	5 (23·8%)	..
Head and neck	32 (80·0%)	8 (20·0%)	..	10 (25·6%)	29 (74·4%)	..
Hepatobiliary	50 (84·8%)	9 (15·2%)	..	29 (50·9%)	28 (49·1%)	..
Neurosurgery	31 (81·6%)	7 (18·4%)	..	19 (50·0%)	19 (50·0%)	..
Obstetrics	50 (98·0%)	1 (2·0%)	..	26 (51·0%)	25 (49·0%)	..
Ophthalmology	4 (100·0%)	0 (0%)	..	3 (75·0%)	1 (25·0%)	..
Orthopaedics	213 (71·2%)	86 (28·8%)	..	165 (55·7%)	131 (44·3%)	..
Other	19 (73·1%)	7 (26·9%)	..	11 (42·3%)	15 (57·7%)	..
Plastic and reconstructive	3 (100·0%)	0 (0%)	..	1 (33·3%)	2 (66·7%)	..
Thoracic	20 (57·1%)	15 (42·9%)	..	12 (34·3%)	23 (65·7%)	..
Urology	25 (67·6%)	12 (32·4%)	..	15 (42·3%)	20 (57·1%)	..
Vascular	27 (60·0%)	18 (40·0%)	..	20 (44·4%)	25 (55·6%)	..
Missing	29 (96·7%)	1 (3·3%)	..	22 (78·6%)	6 (21·4%)	..

Data only presented for patients with 30-day mortality outcome available (n=1113) and pulmonary complications outcome available (n=1103). Percentages are presented in rows.

Table 3: **Operative details**

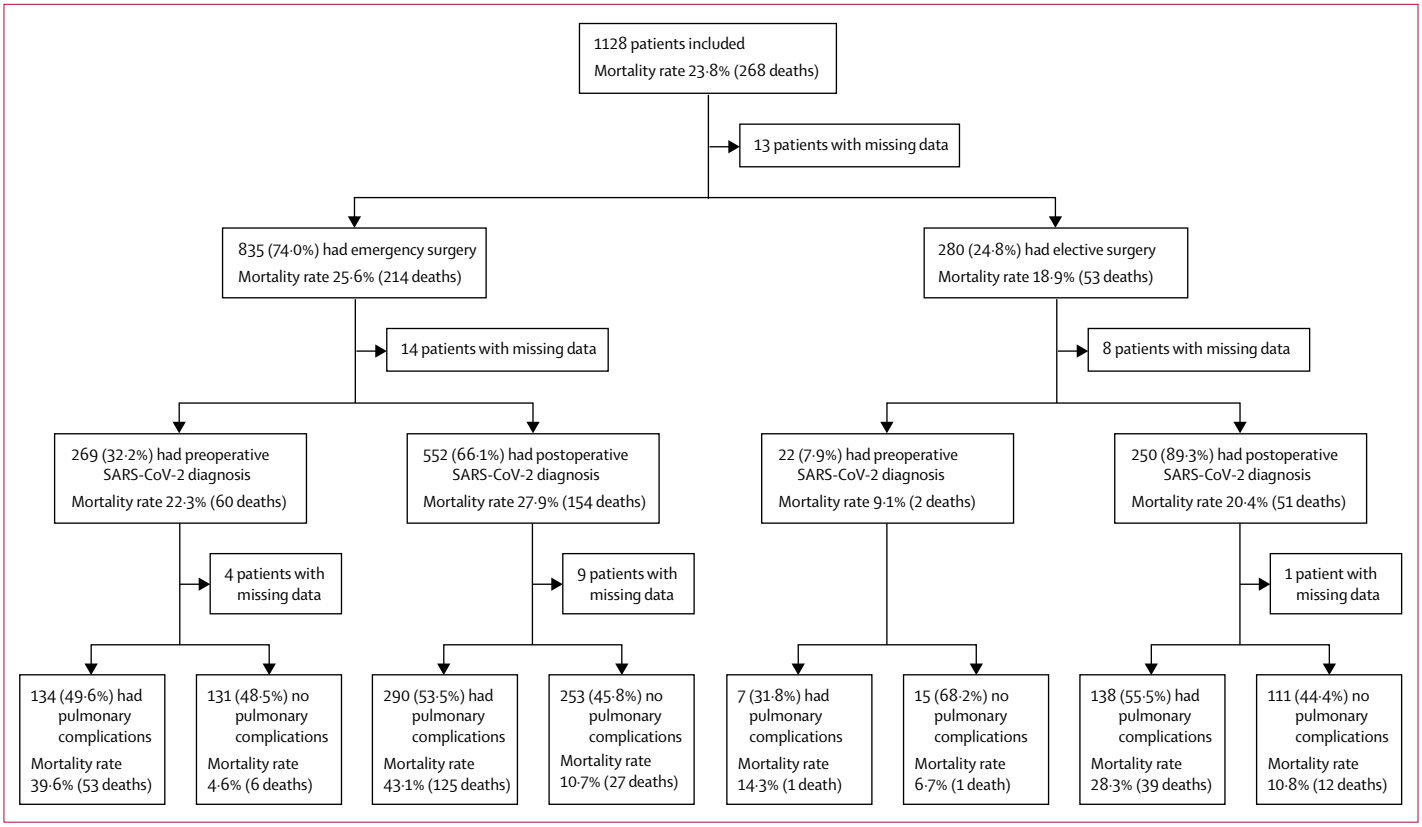

Figure 1: **30-day mortality rates by timing of surgery and development of pulmonary complications**
Patients with missing data are included in denominators (appendix p 21). Pulmonary complications are pneumonia, acute respiratory distress syndrome, or unexpected postoperative ventilation. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

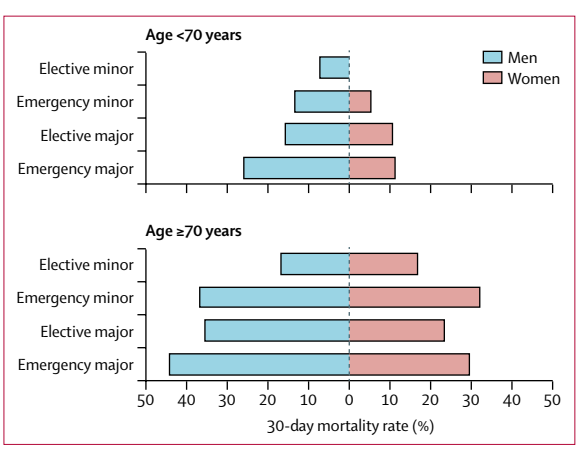

Figure 2: **30-day mortality rates by patient subgroup**
Grade of surgery was classified based on the Bupa schedule as either minor (minor or intermediate in Bupa schedule) or major (major or complex major in Bupa schedule).

regional, or general). Emergency surgery was defined as procedures classified by the National Confidential Enquiry into Patient Outcome and Death as immediate, urgent, or expedited.[14] Grade of surgery was categorised on the basis of the Bupa schedule of procedures as either minor (minor or intermediate according to the Bupa schedule) or major (major or complex major according to the Bupa schedule). Before locking of the dataset for analysis, the senior local principal investigator for each hospital was asked to confirm data completeness and that all eligible patients had been entered into the database.

For the **Bupa schedule of procedures** see https://codes.bupa.co.uk/procedures

Outcomes

The primary outcome was 30-day mortality, with the day of surgery defined as day 0. The key secondary outcome measure was the rate of pulmonary complications, a composite outcome adapted from the Prevention of Respiratory Insufficiency after Surgical Management trial.[15,16] Pulmonary complications were defined as pneumonia, acute respiratory distress syndrome (ARDS), or unexpected postoperative ventilation; these are the most frequent COVID-19-related pulmonary complications in medical patients.[12] Unexpected postoperative ventilation was defined as either any episode of non-invasive ventilation, invasive ventilation, or extracorporeal membrane oxygenation after initial extubation after surgery; or patient could not be extubated as planned after surgery. Additional secondary outcomes included pulmonary embolism, intensive care unit admission, reoperation, 7-day mortality, and length of hospital stay.

Statistical analysis

The study was done according to STROBE guidelines for observational studies.[17] Continuous data were tested for distribution, with normally distributed data presented as mean and 95% CI, and differences between groups were tested using the unpaired *t* test. The χ^2 and Fisher's exact tests were used for categorical data. Missing data were included in flowcharts and descriptive analyses, allowing denominators to remain consistent in calculations.

Multilevel logistic regression was used to calculate odds ratios (ORs) and 95% CIs. Models included factors that occurred before the outcome of interest. Country was included as a random effect with hospital nested within country, in both the unadjusted and adjusted models. The primary adjusted model included preoperative variables to identify predictors of 30-day mortality. Secondary models identified predictors of 7-day mortality and pulmonary complications. Sensitivity analyses were done, including only patients with laboratory-confirmed SARS-CoV-2 infection; and only patients with preoperatively confirmed SARS-CoV-2 infection. Analyses were done using Stata, version 15.1 for Mac.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author and analysis group had full access to all the data in the study and the corresponding author and the writing committee had final responsibility for the decision to submit for publication.

Results

At the time of analysis (May 2, 2020), 30-day follow-up had been reached for 1128 patients who had surgery between Jan 1 and March 31, 2020. 605 (53·6%) of 1128 patients were men and 523 (46·4%) were women, 214 (19·0%) were younger than 50 years, 353 (31·3%) were aged 50–69 years, and 558 (49·5%) were aged 70 years or older, with age missing for three patients (table 1).

SARS-CoV-2 infection was diagnosed preoperatively in 294 (26·1%) of 1128 patients and postoperatively in

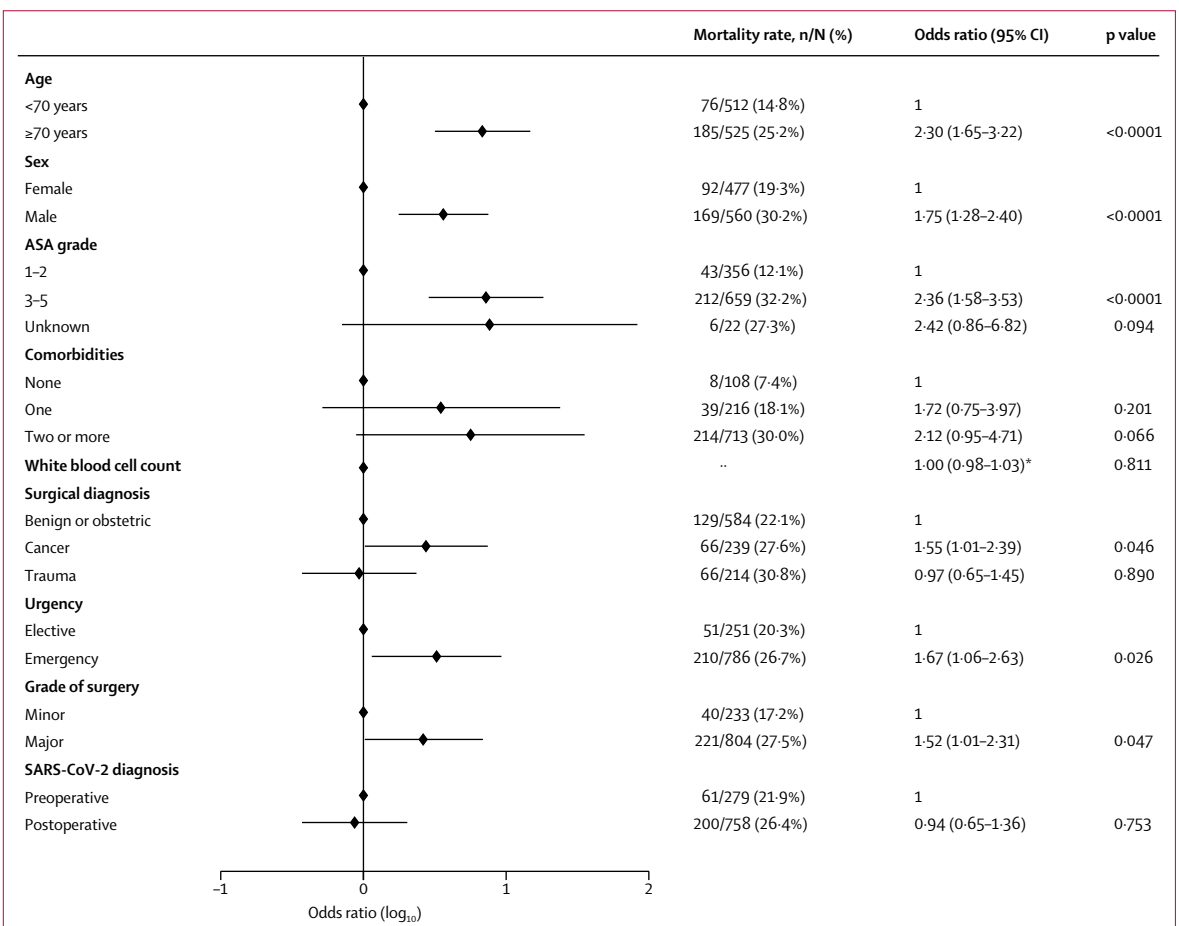

Figure 3: **Adjusted model of predictors for 30-day mortality**

1037 patients with complete data were included in the adjusted model. Of the patients excluded because of missing data, seven had died and 84 patients had not died at 30 days. ASA=American Society of Anesthesiologists. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. *Adjusted odds ratio reported per unit increase in white blood cell count (×10^9).

	Urgency			Grade of surgery		
	Elective (n=280)	Emergency (n=835)	p value	Minor (n=251)	Major (n=841)	p value
Mortality						
7-day	7 (2·5%)	52 (6·2%)	0·015	8 (3·2%)	51 (6·1%)	0·074
30-day	53 (18·9%)	214 (25·6%)	0·020	41 (16·3%)	226 (26·9%)	0·00055
Missing	2 (0·7%)	11 (1·3%)	..	1 (0·4%)	8 (1·0%)	..
Pulmonary complications						
Composite of pulmonary complications	147 (52·5%)	428 (51·3%)	0·873	116 (46·2%)	455 (54·1%)	0·022
Pneumonia	118 (42·1%)	334 (40·0%)	0·527	94 (37·5%)	355 (42·2%)	0·178
Acute respiratory distress syndrome	41 (14·6%)	119 (14·3%)	0·872	33 (13·2%)	127 (15·1%)	0·442
Unexpected postoperative ventilation	..	..	0·262	..	..	0·160
Non-invasive ventilation	23	31	..	12	41	..
Invasive ventilation	40	156	..	41	153	..
Missing	3	21	..	4	14	..
Duration of invasive ventilation	..	..	0·049	..	..	0·023
1–23 h	16	32	..	7	41	..
24–47 h	5	27	..	3	28	..
48–71 h	2	21	..	3	20	..
≥72 h	17	79	..	29	66	..
Missing	240	676	..	209	686	..
Pulmonary embolism						
30-day	4 (1·4%)	18 (2·2%)	0·449	8 (3·2%)	14 (1·7%)	0·132
Missing	3	21	..	4	14	..
Postoperative intensive care unit admission	..	..	0·0034	..	..	0·177
None	158 (56·4%)	570 (68·3%)	..	177 (70·5%)	538 (64·0%)	..
Planned	64 (22·9%)	189 (22·6%)	..	46 (18·3%)	203 (24·1%)	..
Unplanned from theatre	16 (5·7%)	25 (3·0%)	..	10 (4·0%)	31 (3·7%)	..
Unplanned from ward	23 (8·2%)	38 (4·6%)	..	17 (6·8%)	43 (5·1%)	..
Missing	19 (6·8%)	13 (1·6%)	..	1 (0·4%)	26 (3·1%)	..
Reoperation	..	..	0·0015	..	..	0·487
Reoperated	53 (18·9%)	101 (12·1%)	..	39 (15·5%)	115 (13·7%)	..
Not reoperated	209 (74·6%)	717 (85·9%)	..	207 (82·5%)	702 (83·5%)	..
Missing	18 (6·4%)	17 (2·0%)	..	5 (2·0%)	24 (2·9%)	..
Length of stay						
Median (IQR), days	13 (5–28)	16 (7–28)	0·012	10 (3–27)	17 (8–29)	<0·0001
>30 days	64 (22·9%)	168 (20·1%)	0·352	52 (20·7%)	176 (20·9%)	0·911
Missing	2 (0·7%)	11 (1·3%)	..	1 (0·4%)	8 (1·0%)	..

Urgency data missing for 13 patients and grade of surgery data missing for 36 patients. Percentages shown are based on the denominator of patients in the subgroup.

Table 4: **Postoperative outcomes**

806 (71·5%), with timing of diagnosis missing for 28 patients. SARS-CoV-2 diagnosis was confirmed by laboratory testing in 969 (85·9%) patients, radiological findings in 80 (7·1%), and clinical findings in 68 (6·0%), with method of diagnosis missing for 11 patients. Overall, 357 (31·6%) had preoperative thorax CT and the most common radiological finding was ground glass opacity (table 2).

Emergency surgery was done in 835 (74·0%) of 1128 patients and elective surgery in 280 (24·8%; table 3), with urgency missing for 13 patients. Indications for surgery were benign disease in 615 (54·5%), cancer in 278 (24·6%), and trauma in 227 (20·1%), with indication missing for eight patients. 251 (22·3%) procedures were categorised as minor and 841 (74·6%) as major, with grade of surgery missing for 36 patients. Procedures included gastrointestinal and general (373 [33·1%]), orthopaedic (302 [26·8%]), cardiothoracic (86 [7·6%]), hepatobiliary (62 [5·5%]), obstetric (51 [4·5%]), vascular (45 [4·0%]), head and neck (40 [3·5%]), neurosurgery (39 [3·5%]), urological (37 [3·3%]), and other (58 [5·1%]) surgeries. Procedure type was missing for 36 patients. A full breakdown of procedures is in the appendix (pp 11–14).

30-day mortality was 23·8% (268 of 1128). Men had higher 30-day mortality than women (28·4% [172 of 605] *vs* 18·2% [94 of 517], p<0·0001). Patients aged 70 years or

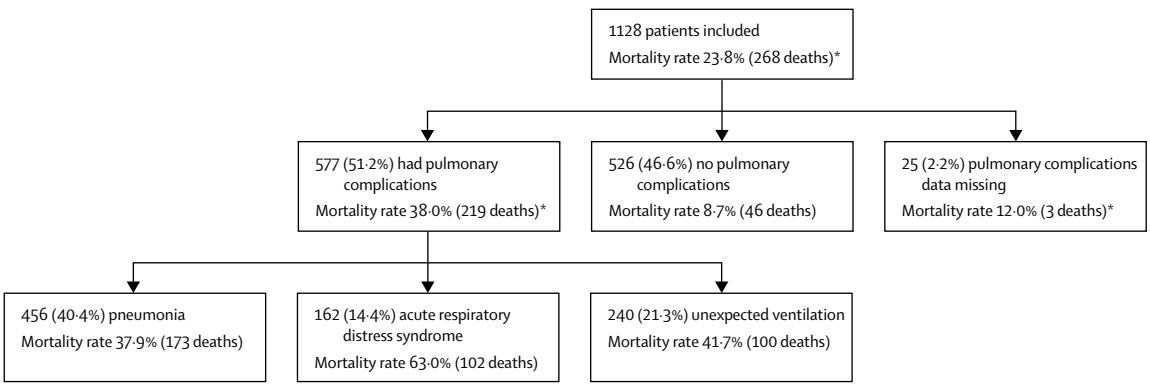

Figure 4: **30-day mortality rates associated with components of pulmonary complications**
Relationships between the pulmonary complications are in the appendix (p 20). *Mortality data were missing for 15 patients; pulmonary complications data were also missing for 14 of these patients; the other one patient had a pulmonary complication (unexpected ventilation).

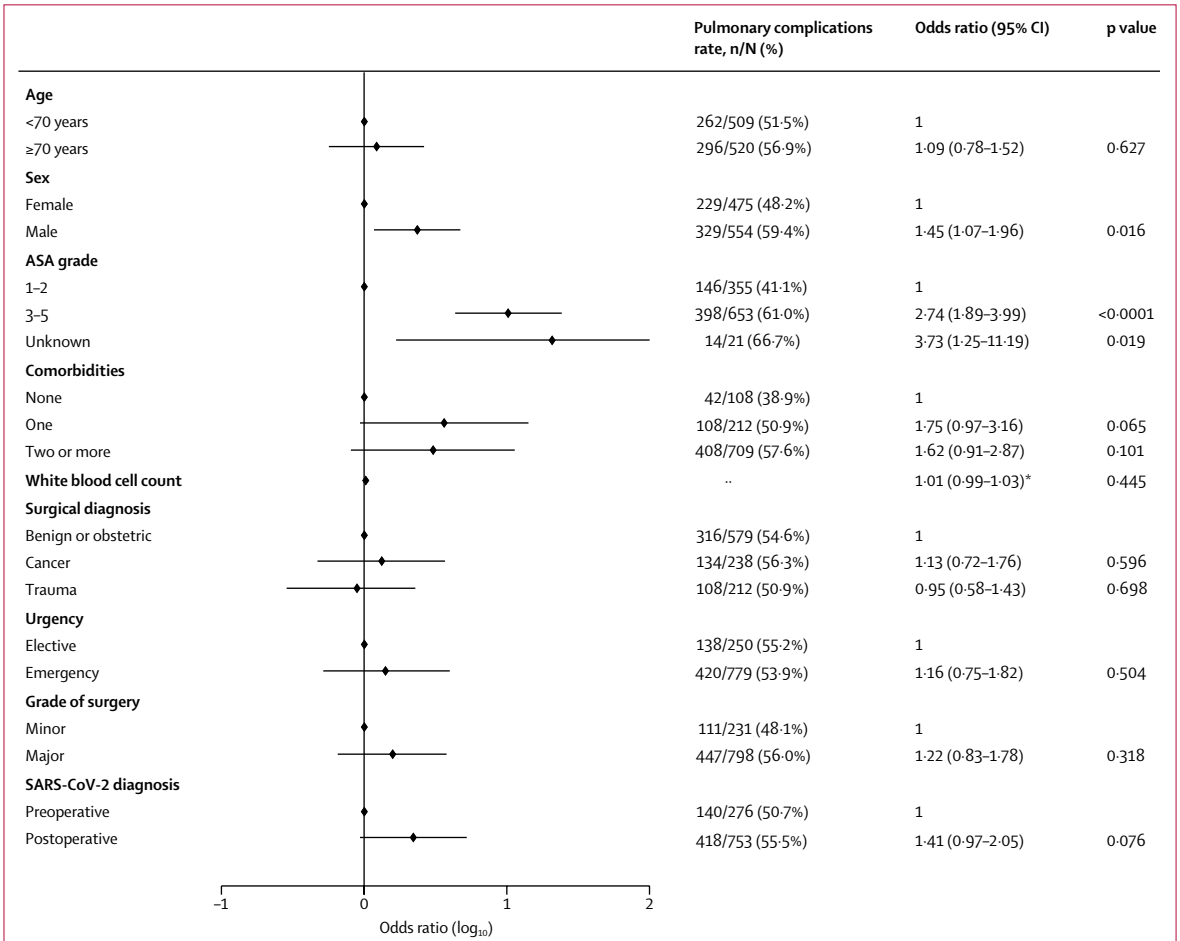

Figure 5: **Adjusted model of predictors for pulmonary complications**
1029 patients with complete data are included in the adjusted model. Of the patients excluded because of missing data, 19 developed pulmonary complications and 80 patients did not. ASA=American Society of Anesthesiologists. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. *Adjusted odds ratio reported per unit increase in white blood cell count (×10⁹).

older had higher mortality than patients younger than 70 years (33·7% [188 of 558] *vs* 13·9% [79 of 567], p<0·0001). Mortality was higher after emergency surgery (25·6% [214 of 835]) than elective surgery (18·9% [53 of 280]; p=0·023; figure 1). Men had higher mortality rates than women, and men and women aged 70 years or older

had higher rates than those younger than 70 years (figure 2).

In adjusted analyses (figure 3; appendix p 15), predictors of 30-day mortality were male sex (OR 1·75 [95% CI 1·28–2·40], p<0·0001), age 70 years or older versus younger than 70 years (2·30 [1·65–3·22], p<0·0001), ASA grades 3–5 versus grades 1–2 (2·35 [1·57–3·53], p<0·0001), malignant versus benign or obstetric diagnosis (1·55 [1·01–2·39], p=0·046), emergency versus elective surgery (1·67 [1·06–2·63], p=0·026), and major versus minor surgery (1·52, [1·01–2·31], p=0·047).

7-day mortality was 5·2% (59 of 1128; table 4). In adjusted analyses (appendix p 16), having ASA grades 3–5 versus grades 1–2 was associated with increased odds of 7-day mortality (OR 2·52 [95% CI 1·10–5·77], p<0·029), whereas postoperative diagnosis was associated with decreased risk (0·25 [0·13–0·46], p<0·0001).

577 (51·2%) of 1128 patients had at least one pulmonary complication (figure 4): 456 (40·4%) had pneumonia, 240 (21·3%) had unexpected ventilation, and 162 (14·4%) had ARDS. Patients who developed pulmonary complications had a higher 30-day mortality than those who did not (38·0% [219 of 577] versus 8·7% [46 of 526], p<0·0001). Pulmonary complications had occurred in 219 (81·7%) of 268 patients who died. Among patients who developed pulmonary complications, 30-day mortality was highest in those who developed ARDS (102 [63·0%] of 162). Pulmonary complications were associated with high 30-day mortality rates across elective patients with a postoperative SARS-CoV-2 diagnosis (39 [28·3%] of 138), emergency patients with a preoperative SARS-CoV-2 diagnosis (53 [39·6%] of 134), and emergency patients with a postoperative SARS-CoV-2 diagnosis (125 [43·1%] of 290; figure 1). Pulmonary complication rates were similar in patients with laboratory-confirmed and clinically diagnosed SARS-CoV-2 infection (493 [50·9%] of 969 *vs* 32 [47·1%] of 68, p=0·543).

In adjusted analyses (figure 5; appendix p 17) pulmonary complications were independently associated with ASA grades 3–5 versus grades 1–2 (2·74 [95% CI 1·89–3·99], p<0·0001).

At 30 days, pulmonary embolism had occurred in 22 (2·0%) of 1128 patients. The 30-day mortality rate in patients with pulmonary embolism was similar to that in patients who did not have pulmonary embolism (five [22·7%] of 22 *vs* 263 [23·8%] of 1106, p=0·909).

In a sensitivity analysis including only patients with laboratory-confirmed SARS-CoV-2, the overall 30-day mortality rate was 23·7% (230 of 969), and pulmonary complications occurred in 493 (50·9%) of 969 patients. In adjusted analyses (appendix p 18), predictors of 30-day mortality were consistent with the main analysis: male sex, age 70 years or older, ASA grades 3–5, cancer surgery, and emergency surgery. The only independent predictor for 30-day pulmonary complications was ASA grades 3–5.

In a sensitivity analysis including only patients with preoperatively diagnosed SARS-CoV-2, the overall 30-day mortality rate was 21·1% (62 of 294), and pulmonary complications occurred in 142 (48·3%) of 294 patients. In adjusted analyses (appendix p 19), predictors of 30-day mortality were male sex and ASA grades 3–5. The only independent predictor for 30-day pulmonary complications was ASA grades 3–5.

Discussion

This study identified that postoperative pulmonary complications occur in half of patients with perioperative SARS-CoV-2 infection and are associated with high mortality. This has direct implications for clinical practice around the world. The increased risks associated with SARS-CoV-2 infection should be balanced against the risks of delaying surgery in individual patients; this study identified men, people aged 70 years or older, those with comorbidities (ASA grades 3–5), those having cancer surgery, and those needing emergency or major surgery as being most vulnerable to adverse outcomes.

Thresholds for surgery during the SARS-CoV-2 pandemic should be higher than during normal practice. Men aged 70 years and over who have emergency or major elective surgery are at particularly high risk of mortality, although minor elective surgery is also associated with higher-than-usual mortality. During SARS-CoV-2 outbreaks, consideration should be given for postponing non-critical procedures and promoting non-operative treatment to delay or avoid the need for surgery.[18]

Postoperative outcomes in SARS-CoV-2-infected patients are substantially worse than pre-pandemic baseline rates of pulmonary complications and mortality. The overall 30-day mortality in this study was 23·8%, and was high across all patient subgroups; all-cause mortality rates were 18·9% in elective patients, 25·6% in emergency patients, 16·3% in patients who had minor surgery, and 26·9% in patients who had major surgery. SARS-CoV-2-infected patients had greater mortality than even the highest-risk subgroups of the UK's NELA. The 2019 NELA report presented 30-day mortality rates of 16·9% in patients with a high preoperative risk of death, 16·8% in patients with an unexpected critical care admission, and 23·4% in frail patients older than 70 years.[19] The mortality rates identified in this study are also higher than those previously reported across international settings; a study across 58 countries, including low-income and middle-income countries, reported a 30-day mortality of 14·9% in the high-risk subgroup who had emergency midline laparotomy.[20] Postoperative mortality rates in SARS-CoV-2-infected patients with postoperative pulmonary complications approach those of the sickest patients with community-acquired COVID-19 who are admitted to intensive care.[21]

Mortality in patients with SARS-CoV-2 was mainly in those who had postoperative pulmonary complications, which was about 50% of patients. This rate is far higher than the pre-pandemic baseline; in the POPULAR

multicentre, prospective, observational study of 211 hospitals from 28 European countries in 2014–15, the pulmonary complication rate was 8%.[5] In our study, ARDS had the highest mortality rate of the different complications (mortality 63·0%) and occurred much more frequently (20%) than reported in the pre-pandemic African Surgical Outcomes Study (0·05%).[22] In another study of high-risk ASA grade 3 patients undergoing non-cardiac surgery in seven US centres, 0·2% developed ARDS, with an overall mortality related to postoperative pulmonary complications of 2·3%.[23] Even considering differences in the case-mix, the incidence of and mortality associated with pulmonary complications in SARS-CoV-2-infected patients is disproportionately high.

This study has limitations. Protocols for laboratory testing and radiological interpretation were not standardised across participating centres. We describe outcomes in the early phases of the pandemic when routine testing was not available across all sites; setting study inclusion criteria requiring laboratory-confirmed SARS-CoV-2 would have excluded some infected patients. Therefore, patients who did not have a laboratory test or CT scan were eligible for inclusion on the basis of clinical diagnosis. Only a minority of patients (6·0%) were included on the basis of a clinical diagnosis and these patients had similar clinical outcomes to patients with laboratory-confirmed SARS-CoV-2. The limitations of laboratory testing mean that some infected patients were excluded from the study based on false negative laboratory test results. Future studies need to make recommendations on the role of preoperative testing in patient selection for surgery.

The study included patients having any type of surgery and although this has produced generalisable results, it is possible that in large hospitals investigators might have not identified all patients. To mitigate this, the importance of identifying and enrolling all eligible patients was highlighted in training packages for local site investigators and strategies to support comprehensive patient identification were shared regularly with all sites. Final case ascertainment and data completeness were confirmed with local principal investigators, creating as robust a dataset as possible. As far as we are aware, this is the first international study assessing mortality rates after surgery in patients with SARS-CoV-2 infection, and the first that reaches across all surgical specialties.[24–27] It was not feasible for all participating hospitals, many of which were experiencing significant stress, to collect data on all patients who had surgery during the pandemic period. Consequently, this study's findings should be interpreted with caution because they have been benchmarked against pulmonary complication and mortality rates from high-quality pre-pandemic studies, rather than against contemporaneous non-SARS-CoV-2-infected comparators.

Data were collected in hospitals with ongoing SARS-CoV-2 infection outbreaks, which were predominantly in Europe and North America at the time of this study. As the pandemic continues, the evidence this study provides will be relevant to countries where large-scale outbreaks might take place in the future. To facilitate rapid study approvals, this study has focused on key outcomes (mortality and pulmonary complications) that can be collected using routine data. To support decision making by patients and surgeons, future studies should collect longer-term and patient-centred outcomes.

When hospitals resume routine surgery, it is likely to be in environments that remain exposed to SARS-CoV-2. In the future, routine preoperative screening for SARS-CoV-2 might be possible with rapid tests that have low false positive rates, but hospital-acquired infection would remain a challenge.[12,28] Strategies are urgently required to minimise in-hospital SARS-CoV-2 transmission and mitigate the risk of postoperative pulmonary complications in SARS-CoV-2-infected patients whose surgery cannot be delayed.

Contributors

The writing group (appendix p 1) contributed to study conception, protocol development, data collection, data interpretation, and critical revision of the manuscript. AB is the guarantor.

Declaration of interests

We declare no competing interests.

Data sharing

Data sharing requests will be considered by the management group upon written request to the corresponding author. Deidentified participant data or other prespecified data will be available subject to a written proposal and a signed data sharing agreement.

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9.2 Chapter 4 publication

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Original Article

Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study

COVIDSurg Collaborative* and **GlobalSurg Collaborative***

NIHR Global Health Research Unit on Global Surgery, Birmingham, UK

Summary

Peri-operative SARS-CoV-2 infection increases postoperative mortality. The aim of this study was to determine the optimal duration of planned delay before surgery in patients who have had SARS-CoV-2 infection. This international, multicentre, prospective cohort study included patients undergoing elective or emergency surgery during October 2020. Surgical patients with pre-operative SARS-CoV-2 infection were compared with those without previous SARS-CoV-2 infection. The primary outcome measure was 30-day postoperative mortality. Logistic regression models were used to calculate adjusted 30-day mortality rates stratified by time from diagnosis of SARS-CoV-2 infection to surgery. Among 140,231 patients (116 countries), 3127 patients (2.2%) had a pre-operative SARS-CoV-2 diagnosis. Adjusted 30-day mortality in patients without SARS-CoV-2 infection was 1.5% (95%CI 1.4–1.5). In patients with a pre-operative SARS-CoV-2 diagnosis, mortality was increased in patients having surgery within 0–2 weeks, 3–4 weeks and 5–6 weeks of the diagnosis (odds ratio (95%CI) 4.1 (3.3–4.8), 3.9 (2.6–5.1) and 3.6 (2.0–5.2), respectively). Surgery performed ≥ 7 weeks after SARS-CoV-2 diagnosis was associated with a similar mortality risk to baseline (odds ratio (95%CI) 1.5 (0.9–2.1)). After a ≥ 7 week delay in undertaking surgery following SARS-CoV-2 infection, patients with ongoing symptoms had a higher mortality than patients whose symptoms had resolved or who had been asymptomatic (6.0% (95%CI 3.2–8.7) vs. 2.4% (95%CI 1.4–3.4) vs. 1.3% (95%CI 0.6–2.0), respectively). Where possible, surgery should be delayed for at least 7 weeks following SARS-CoV-2 infection. Patients with ongoing symptoms ≥ 7 weeks from diagnosis may benefit from further delay.

Correspondence to: D. Nepogodiev
Email: dnepogodiev@doctors.org.uk
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*Collaborating authors are listed in online Supporting Information Appendix S2.
Twitter: @CovidSurg; @GlobalSurg

Introduction

Patients with peri-operative SARS-CoV-2 infection are at increased risk of death and pulmonary complications following surgery [1–3]. As the cumulative number of people who have had SARS-CoV-2 infection rises, it will be increasingly common for patients needing surgery to have previously had SARS-CoV-2 infection. High-income countries that are already implementing vaccination programmes are likely to experience reductions in new SARS-CoV-2 case infection rates, but these countries already have tens of millions of SARS-CoV-2 infection survivors. Most low- and middle-income countries (LMICs) are likely to have limited access to SARS-CoV-2 vaccines until at least 2023 [4, 5]. Thus, pre-operative SARS-CoV-2 infection will remain a challenge for the foreseeable future.

Pre-pandemic studies suggest delaying surgery in patients who have experienced respiratory infection in the 4 weeks preceding surgery [6–8]. However, there is only

limited evidence regarding the optimal timing of surgery following SARS-CoV-2 infection. A prospective cohort study including 122 patients having surgical for cancer, found that surgery ≥ 4 weeks after a positive SARS-CoV-2 swab result was associated with a lower risk of postoperative mortality than earlier surgery [9]. A study in Brazil included 49 patients whose elective surgery was delayed following the pre-operative diagnosis of asymptomatic SARS-CoV-2 infection [10]. These patients subsequently underwent surgery following confirmation of a negative SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) nasopharyngeal swab result. The postoperative complication rates were comparable to patients without SARS-CoV-2 infection. However, the study did not assess the optimal duration of delay following SARS-CoV-2 diagnosis. Clinical guidelines support postponing non-emergency surgery for patients with pre-operative SARS-CoV-2 infection, but specific recommendations are conflicting, recommending delays ranging from 1 to 12 weeks [11–15].

More granular data are needed urgently to inform clinical practice, especially regarding the significance of symptomatic vs. asymptomatic pre-operative SARS-CoV-2 infection. The aim of this study was to determine the optimal timing of surgery following SARS-CoV-2 infection.

Methods

This was an international, multicentre, prospective cohort study that included patients undergoing any type of surgery. The study was registered at each participating hospital in accordance with local and national regulations. Informed patient consent was taken if required by local or national regulations. In the UK, this study was registered as either a clinical audit or service evaluation at each recruiting institution. Co-investigators were required to confirm that applicable local and national approvals were in place before uploading data to the online database. The study was compliant with guidelines for the reporting of observational studies [16]. In the conduct of this study, no changes were made to usual patient care. Routine, anonymised data were collected using a secure online database (REDCap, Vanderbilt University, Nashville, TN, USA).

Participating hospitals included consecutive patients undergoing elective or emergency surgery for any indication in October 2020. Surgery was defined as any procedure that is routinely performed in an operating theatre by a surgeon. A list of excluded procedures was provided to investigators and is available in online Supporting Information, Appendix S1. Before commencing data collection, hospitals defined which surgical specialties would be participating. Hospitals could choose to collect data in one or multiple surgical specialties, depending on local resources. Data could be collected over up to four blocks of 7 consecutive days (5 October 2020 – 1 November 2020).

Patients were classified as having pre-operative SARS-CoV-2 infection based on any one of the following criteria: (a) positive RT-PCR nasopharyngeal swab taken before surgery (even if the result became available after surgery); (b) positive rapid antigen test performed before surgery; (c) chest computed tomography (CT) scan performed before surgery showing changes consistent with pneumonitis secondary to SARS-CoV-2 infection; (d) positive pre-operative immunoglobulin G or immunoglobulin M antibody test; or (e) clinical diagnosis made before surgery (in the absence of negative RT-PCR swab results). Patients who were diagnosed with SARS-CoV-2 in the period between postoperative days 0 and 30 were not studied. Data were captured on whether patients had experienced SARS-CoV-2 symptoms, and if so, whether these symptoms had resolved by the time of surgery. Both respiratory and non-respiratory symptoms were considered. These were classified as follows: asymptomatic; symptomatic but symptoms now resolved; or symptomatic with ongoing symptoms. Time from the diagnosis of SARS-CoV-2 infection to day of surgery was collected as a categorical factor and pre-determined to be analysed in the following categories: 0–2 weeks; 3–4 weeks; 5–6 weeks; and ≥ 7 weeks.

The primary outcome measure was 30-day postoperative mortality. Patients were followed-up either in-person or by telephone, as soon after postoperative day 30 as possible. If it was not possible to complete 30-day follow-up, in-patient mortality status was recorded. The secondary outcome measure was the incidence of 30-day postoperative pulmonary complications. This was a composite of pneumonia, acute respiratory distress syndrome (ARDS) and/or unexpected postoperative ventilation. Full definitions are available in online Supporting Information, Appendix S1.

The following information was collected for each patient: age; sex; ASA physical status; revised cardiac risk index (RCRI); presence of respiratory comorbidities; indication for surgery; grade of surgery (major/minor); and surgical urgency (elective/emergency). For data protection purposes, age was collected as a categorical variable. Consistent with previous analyses, age was categorised as < 70 years or ≥ 70 years [1, 2]. American Society of Anesthesiologists physical status was classified as grades 1–2 or grades 3–5. Patients were recorded as having respiratory comorbidities if they had a diagnosis of asthma or chronic obstructive pulmonary disease (COPD).

Indications for surgery were classified as: benign disease; cancer; obstetrics; or trauma. Emergency surgery was defined as surgery on an unplanned admission, and elective surgery was defined as surgery on a planned admission. The RCRI calculation and grade of surgery classification are available in online Supporting Information, Appendix S1. National income was recorded for each participating country, based on the World Bank's classification [17].

To ensure consistent denominators, missing data were included in the descriptive analyses. Imputation for missing data was not planned as, based on previous studies, a < 2% rate of missing data was anticipated [1, 2]. For categorical variables, a chi-squared test was used to test for differences between groups.

To adjust time from SARS-CoV-2 diagnosis to surgery for confounding factors, logistic regression models were fitted with variables selected a priori. These were variables that have previously been identified as independent predictors of mortality in patients with peri-operative SARS-CoV-2 infection [1] and included: age; sex; ASA physical status; RCRI; indication for surgery; grade of surgery; urgency of surgery; presence of respiratory comorbidities; and national income. Average marginal effects were used to produce adjusted mortality estimates stratified by time from SARS-CoV-2 diagnosis to surgery. The main model included all patients.

Since delayed surgery is more likely for elective rather than emergency cases, a sensitivity analysis was performed including only elective patients. A further sensitivity analysis was performed including only patients who either had RT-PCR nasopharyngeal swab-proven pre-operative SARS-CoV-2 infection or who were not infected. To address further possible bias, average marginal effects were used to produce adjusted mortality rates by time from SARS-CoV-2 diagnosis to surgery, stratified by the following pre-selected variables: age; ASA physical status; urgency of surgery; and grade of surgery. In order to explore the association of pre-operative COVID-19 symptoms, a further logistic regression model was fitted. This included only those patients who had a pre-operative SARS-CoV-2 diagnosis, since COVID-19 symptom status was not applicable to patients who did not have pre-operative SARS-CoV-2. These models were fitted with a primary outcome of 30-day postoperative mortality. Further models were fitted for the secondary outcome of the incidence of 30-day postoperative pulmonary complications. Analyses were completed in Stata, version 15.1 (StataCorp, College Station, TX, USA).

Results

A total of 140,231 patients were included across 1674 hospitals in 116 countries (see online Supporting Information, Figure S1). Patient and surgical characteristics are shown in Table 1. Baseline characteristic data for patients having elective surgery are available in online Supporting Information (Table S1). In total, 3127 (2.2%) patients had a pre-operative SARS-CoV-2 diagnosis. The time from SARS-CoV-2 diagnosis to surgery was 0–2 weeks in 1138 patients (36.4%), 3–4 weeks in 461 patients (14.7%), 5–6 weeks in 326 patients (10.4%) and ≥ 7 weeks in 1202 patients (38.4%) (Table 1). The majority of patients were asymptomatic at the time of surgery (either having

Table 1 Baseline characteristics and outcomes for patients undergoing surgery stratified by time from diagnosis of SARS-CoV-2 infection. Values are number (proportion).

	No pre-operative SARS-CoV-2 infection (n = 137,104)	Pre-operative SARS-CoV-2 infection (by timing of diagnosis prior to surgery)			
		0–2 weeks (n = 1138)	3–4 weeks (n = 461)	5–6 weeks (n = 326)	≥ 7 weeks (n = 1202)
Age; years					
0–29	31,456 (22.9%)	331 (29.1%)	84 (18.2%)	62 (19.0%)	169 (14.1%)
30–49	37,673 (27.5%)	355 (31.2%)	149 (32.3%)	101 (31.0%)	364 (30.3%)
50–69	41,649 (30.4%)	265 (23.3%)	162 (35.1%)	109 (33.4%)	471 (39.2%)
70–79	17,577 (12.8%)	93 (8.2%)	52 (11.3%)	41 (12.6%)	121 (10.1%)
≥ 80	8747 (6.4%)	94 (8.3%)	14 (3.0%)	13 (4.0%)	77 (6.4%)
Missing	2 (0%)	–	–	–	–
Sex					
Female	71,375 (52.1%)	610 (53.6%)	220 (47.7%)	177 (54.3%)	634 (52.7%)
Missing	5 (0.0%)	–	–	–	–

(continued)

Table 1 (*continued*)

	No pre-operative SARS-CoV-2 infection (n = 137,104)	Pre-operative SARS-CoV-2 infection (by timing of diagnosis prior to surgery)			
		0–2 weeks (n = 1138)	3–4 weeks (n = 461)	5–6 weeks (n = 326)	≥ 7 weeks (n = 1202)
ASA physical status					
1–2	103,503 (75.5%)	779 (68.5%)	316 (68.5%)	227 (69.6%)	805 (67.0%)
3–5	33,553 (24.5%)	359 (31.5%)	145 (31.5%)	99 (30.4%)	397 (33.0%)
Missing	48 (0.0%)	–	–	–	–
Revised cardiac risk index					
0	61,379 (44.8%)	433 (38.0%)	176 (38.2%)	123 (37.7%)	446 (37.1%)
1	60,722 (44.3%)	512 (45.0%)	211 (45.8%)	145 (44.5%)	564 (46.9%)
2	11,116 (8.1%)	134 (11.8%)	50 (10.8%)	41 (12.6%)	129 (10.7%)
≥ 3	3818 (2.8%)	59 (5.2%)	24 (5.2%)	17 (5.2%)	62 (5.2%)
Missing	69 (0.1%)	–	–	–	1 (0.1%)
Respiratory comorbidities					
Yes	12,190 (8.9%)	114 (10.0%)	45 (9.8%)	31 (9.5%)	123 (10.2%)
Missing	111 (0.1%)	–	–	–	–
Indication for surgery					
Benign	86,764 (63.3%)	629 (55.3%)	273 (59.2%)	208 (63.8%)	822 (68.4%)
Cancer	23,612 (17.2%)	100 (8.8%)	117 (25.4%)	73 (22.4%)	234 (19.5%)
Trauma	17,048 (12.4%)	193 (17.0%)	48 (10.4%)	27 (8.3%)	96 (8.0%)
Obstetrics	9673 (7.1%)	216 (19.0%)	23 (5.0%)	18 (5.5%)	50 (4.2%)
Missing	7 (0.0%)	–	–	–	–
Grade of surgery					
Minor	55,301 (40.3%)	400 (35.1%)	131 (28.4%)	122 (37.4%)	462 (38.4%)
Major	81,771 (59.6%)	738 (64.9%)	330 (71.6%)	204 (62.6%)	739 (61.5%)
Missing	32 (0.0%)	–	–	–	1 (0.1%)
Urgency of surgery					
Elective	95,680 (69.8%)	338 (29.7%)	300 (65.1%)	232 (71.2%)	892 (74.2%)
Emergency	41,413 (30.2%)	800 (70.3%)	161 (34.9%)	94 (28.8%)	310 (25.8%)
Missing	11 (0.0%)	–	–	–	–
COVID-19 symptoms					
Asymptomatic	–	731 (64.2%)	203 (44.0%)	133 (40.8%)	317 (26.4%)
Symptomatic – resolved	–	124 (10.9%)	193 (41.9%)	163 (50.0%)	820 (68.2%)
Symptomatic – ongoing	–	277 (24.3%)	65 (14.1%)	28 (8.6%)	56 (4.7%)
Missing	–	6 (0.5%)	-	2 (0.6%)	9 (0.7%)
Country income					
High	90,024 (65.7%)	461 (40.5%)	159 (34.5%)	135 (41.4%)	696 (57.9%)
Low/middle	47,080 (34.3%)	677 (59.5%)	302 (65.5%)	191 (58.6%)	506 (42.1%)
30-day postoperative mortality					
Yes	1973 (1.4%)	104 (9.1%)	32 (6.9%)	18 (5.5%)	24 (2.0%)
Missing	92 (0.1%)	0 (0.0%)	–	–	2 (0.2%)
30-day postoperative pulmonary complications					
Yes	3654 (2.7%)	149 (13.1%)	60 (13.0%)	33 (10.1%)	42 (3.5%)
Missing	105 (0.1%)	–	–	–	3 (0.2%)

ASA, American Society of Anaesthesiologists.

Table 2 Unadjusted and adjusted model for 30-day postoperative mortality in all patients. Values are odds ratio (OR) (95%CI).

	Unadjusted		Adjusted	
	OR (95%CI)	**p value**	**OR (95%CI)**	**p value**
Age; years				
0–69	Reference	–	Reference	–
≥ 70	3.12 (2.86–3.40)	< 0.001	1.72 (1.56–1.90)	< 0.001
Sex				
Female	Reference	–	Reference	–
Male	1.41 (1.29–1.53)	< 0.001	1.09 (0.99–1.19)	0.068
ASA physical status				
1–2	Reference	–	Reference	–
3–5	8.96 (8.13–9.87)	< 0.001	5.32 (4.75–5.96)	< 0.001
Revised cardiac risk index				
0	Reference	–	Reference	–
1	2.33 (2.07–2.61)	< 0.001	1.43 (1.26–1.63)	< 0.001
2	6.50 (5.69–7.42)	< 0.001	1.82 (1.56–2.13)	< 0.001
≥ 3	12.81 (11.02–14.89)	< 0.001	2.78 (2.32–3.32)	< 0.001
Respiratory comorbidities				
No	Reference	–	Reference	–
Yes	1.71 (1.51–1.94)	< 0.001	1.02 (0.89–1.16)	0.767
Indication for surgery				
Benign	Reference	–	Reference	–
Cancer	1.62 (1.46–1.80)	< 0.001	1.98 (1.76–2.23)	< 0.001
Trauma	1.60 (1.43–1.80)	< 0.001	0.91 (0.79–1.04)	0.173
Obstetrics	0.27 (0.19–0.37)	< 0.001	0.23 (0.16–0.33)	< 0.001
Grade of surgery				
Minor	Reference	–	Reference	–
Major	3.25 (2.90–3.63)	< 0.001	2.37 (2.11–2.67)	< 0.001
Urgency of surgery				
Elective	Reference	–	Reference	–
Emergency	5.60 (5.10–6.15)	< 0.001	6.48 (5.83–7.21)	< 0.001
Country income				
High	Reference	–	Reference	–
Low/middle	1.76 (1.61–1.92)	< 0.001	2.96 (2.69–3.26)	< 0.001
Pre-operative SARS-CoV-2 by timing of pre-operative diagnosis				
No diagnosis	Reference	–	Reference	–
0–2 weeks	6.88 (5.60–8.46)	< 0.001	3.22 (2.55–4.07)	< 0.001
3–4 weeks	5.11 (3.56–7.33)	< 0.001	3.03 (2.03–4.52)	< 0.001
5–6 weeks	4.00 (2.48–6.45)	< 0.001	2.78 (1.64–4.71)	< 0.001
≥ 7 weeks	1.40 (0.93–2.10)	0.107	1.02 (0.66–1.56)	0.940

ASA, American Society of Anesthesiologists.

never had symptoms or symptoms having resolved) (Table 1).

Compared with patients who did not have SARS-CoV-2 infection, patients with pre-operative SARS-CoV-2 infection were more likely to be ASA physical status 3–5 (24.5% vs. 32.0%; $p < 0.001$), to undergo major surgery (59.6% vs. 64.2%; $p < 0.001$) and to undergo emergency surgery (30.2% vs. 43.7%; $p < 0.001$). However, there was lower proportion of patients aged ≥ 70 years in the cohort with SARS-CoV-2 infection (16.1% vs. 19.2%; $p < 0.001$).

The overall 30-day postoperative mortality rate was 1.5% (2151/140,231). When stratified by time from

SARS-CoV-2 diagnosis to surgery, 30-day postoperative mortality rates were as follows: 9.1% (104/1138) 0–2 weeks; 6.9% (32/461) 3–4 weeks; 5.5% (18/326) 5–6 weeks; and 2.0% (24/1202) at ≥ 7 weeks. The 30-day mortality rate in patients who did not have a pre-operative SARS-CoV-2 infection was 1.4% (1973/137,104).

In the adjusted model, there was a significantly higher risk of 30-day mortality in patients with pre-operative SARS-CoV-2 infection diagnosed 0–2 weeks, 3–4 weeks and 5–6 weeks before surgery compared with patients who did not have a pre-operative SARS-CoV-2 infection (Table 2). However, there was no significant difference in 30-day postoperative mortality rate in those patients diagnosed with SARS-CoV-2 infection ≥ 7 weeks before surgery (Table 2).

Adjusted 30-day mortality rate in patients who did not have SARS-CoV-2 infection was 1.5% (95%CI 1.4–1.5). This was increased in patients who had surgery at 0–2 weeks, 3–4 weeks and at 5–6 weeks after SARS-CoV-2 diagnosis (Fig. 1). In patients who had surgery ≥ 7 weeks after SARS-CoV-2 diagnosis, the 30-day mortality rate was similar to patients who did not have SARS-CoV-2 infection (Fig. 1).

Sensitivity analyses including only patients having elective surgery (available in online Supporting Information, Tables S1–S3) and only patients with RT-PCR nasopharyngeal swab-proven SARS-CoV-2 infection (available in online Supporting Information, Tables S4–S5) showed that patients having surgery 0–2 weeks, 3–4 weeks and 5–6 weeks after SARS-CoV-2 diagnosis had significantly higher adjusted 30-day postoperative mortality rates compared with patients who did not have SARS-CoV-2 infection (Fig. 1). Patients operated ≥ 7 weeks after SARS-CoV-2 infection had a similar mortality as patients without SARS-CoV-2 infection. These findings were also consistent across sub-groups stratified by age, ASA physical status, and grade and urgency of surgery (Fig. 2).

In the analysis restricted to patients who had experienced pre-operative SARS-CoV-2 infection, patients with ongoing COVID-19 symptoms had a higher adjusted 30-day mortality rate than patients whose

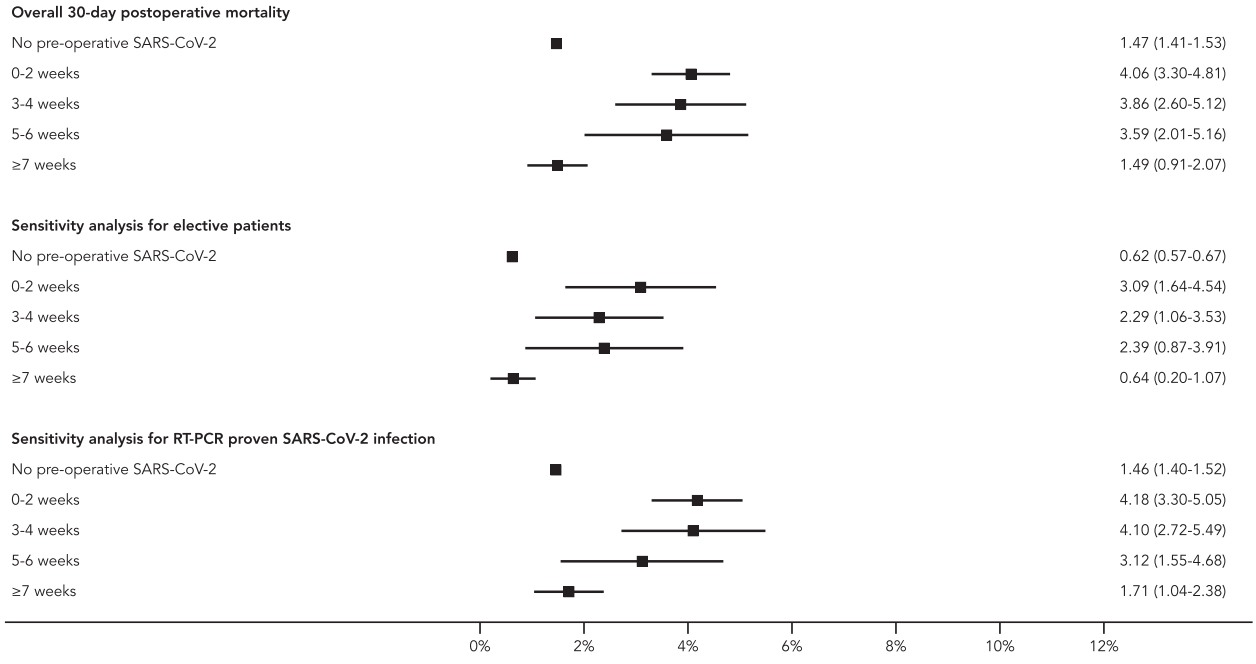

Figure 1 Overall adjusted 30-day postoperative mortality from main analysis and sensitivity analyses for patients having elective surgery and those patients with a reverse transcription polymerase chain reaction (RT-PCR) nasopharyngeal swab positive result for SARS-CoV-2. 'No pre-operative SARS-CoV-2' refers to patients without a diagnosis of SARS-CoV-2 infection. The time-periods relate to the timing of surgery following the diagnosis of SARS-CoV-2 infection. Sensitivity analysis for RT-PCR nasopharyngeal swab proven SARS-CoV-2 includes patients who either had RT-PCR nasopharyngeal swab proven SARS-CoV-2 or did not have a SARS-CoV-2 diagnosis; patients with a SARS-CoV-2 diagnosis which was not supported by a RT-PCR nasopharyngeal swab were not analysed. Full models and results are available in online Supporting Information (Appendix S1, Tables S3–S4 (elective patients), Tables S5–S6 (swab-proven SARS-CoV-2 infection)).

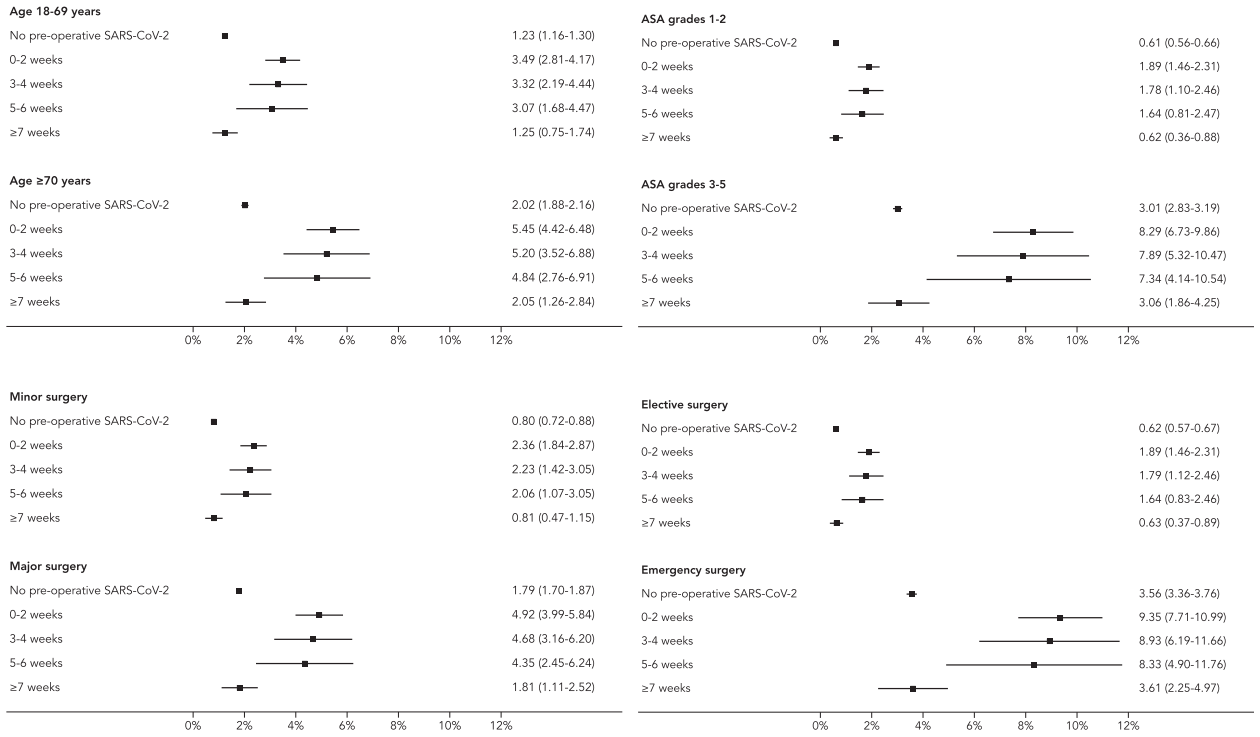

Figure 2 Adjusted 30-day postoperative mortality rates from main analysis, stratified by pre-defined sub-groups. 'No pre-operative SARS-CoV-2' refers to patients without a diagnosis of SARS-CoV-2 infection. The time-periods relate to the timing of surgery following the diagnosis of SARS-CoV-2 infection. Full models and results are available in online Supporting Information (Appendix S1, Table S2).

symptoms had resolved or who had been asymptomatic (Fig. 3). Following a ≥ 7-week delay between SARS-CoV-2 infection and surgery, patients with ongoing COVID-19 symptoms had a higher mortality rate than patients whose symptoms had resolved or who had been asymptomatic (Fig. 3).

Overall, 2.8% (3938/140,231) of patients developed a postoperative pulmonary complication within 30 days, including 1.7% (2387/140,231) who developed pneumonia, 0.8% (1100/140,231) who developed ARDS, and 0.8% (1137/140,231) who had an unexpected requirement for mechanical ventilation. In both the overall analysis and the sensitivity analysis for elective surgery, patients who had surgery 0–2 weeks, 3–4 weeks and 5–6 weeks after SARS-CoV-2 diagnosis had significantly higher adjusted 30-day postoperative pulmonary complication rates compared with patients who did not have SARS-CoV-2 infection. However, patients who had surgery ≥ 7 weeks after SARS-CoV-2 infection had similar rates of postoperative pulmonary complications as patients without SARS-CoV-2 infection (Fig. 4). Among patients operated ≥ 7 following SARS-CoV-2 diagnosis, those with ongoing COVID-19 symptoms were at greatest risk of 30-day postoperative pulmonary complications (Fig. 5).

Discussion

This study found that patients operated within 6 weeks of SARS-CoV-2 diagnosis were at an increased risk of 30-day postoperative mortality and 30-day postoperative pulmonary complications. These risks decreased to baseline in patients who underwent surgery ≥ 7 weeks after SARS-CoV-2 diagnosis. These findings were consistent across both low-risk (age < 70 years, ASA physical status 1–2, minor surgery) and high-risk (age ≥ 70 years, ASA physical status 3–5, major surgery) sub-groups. Therefore, surgery should be delayed for at least 7 weeks following SARS-CoV-2 infection to reduce the risk of postoperative mortality and pulmonary complications. In addition, we have shown that patients who are still symptomatic ≥ 7 weeks after SARS-CoV-2 infection and undergo surgery also have an increased mortality rate. As such, these patients may benefit from a further delay until their symptoms resolve.

Our findings that pre-operative SARS-CoV-2 infection increases the risk of postoperative mortality and pulmonary

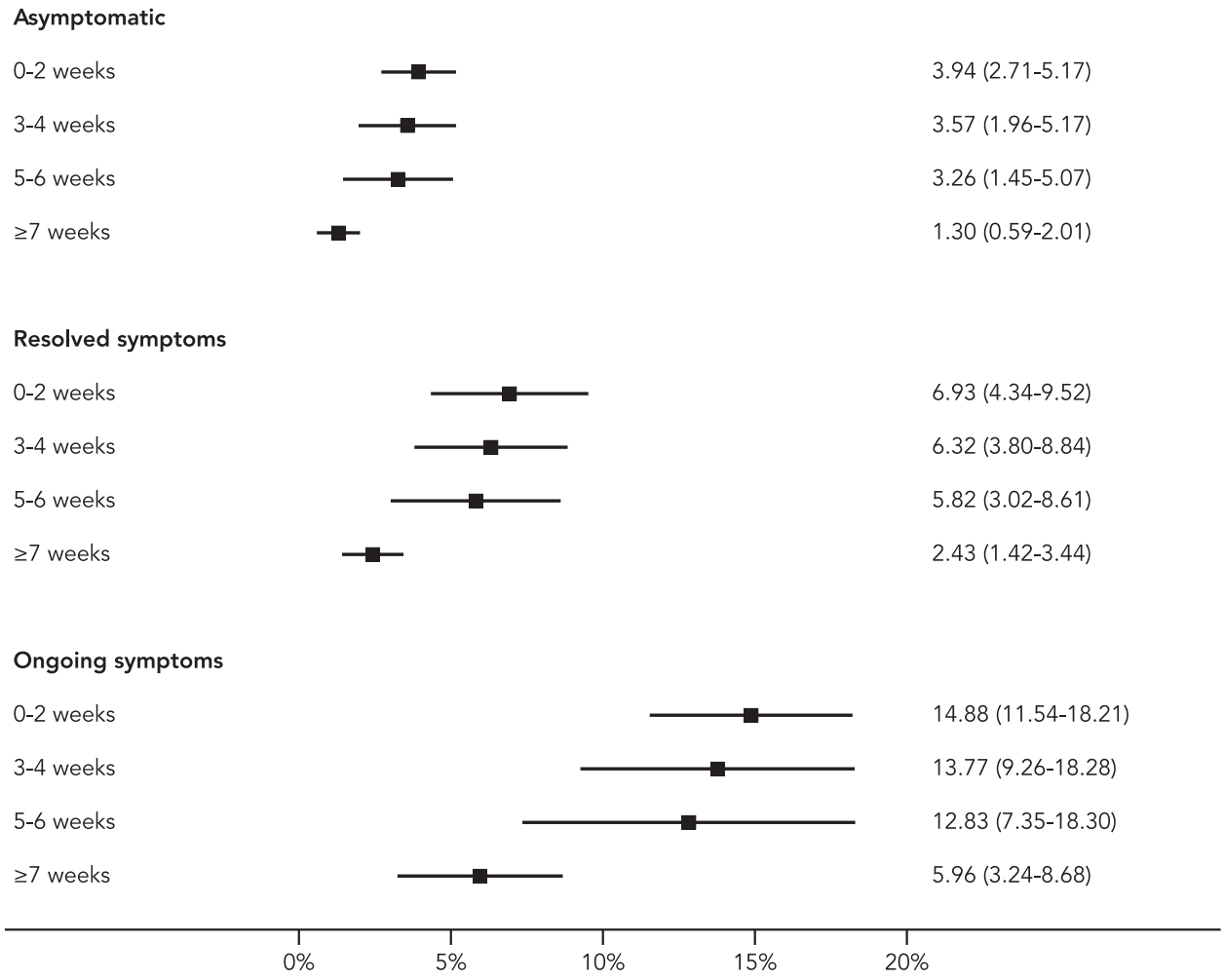

Figure 3 Adjusted 30-day postoperative mortality rates in patients with pre-operative SARS-CoV-2 infection stratified by COVID-19 symptoms. The time-periods relate to the timing of surgery following the diagnosis of SARS-CoV-2 infection. Full models and results are available in online Supporting Information (Appendix S1, Tables S7–S8).

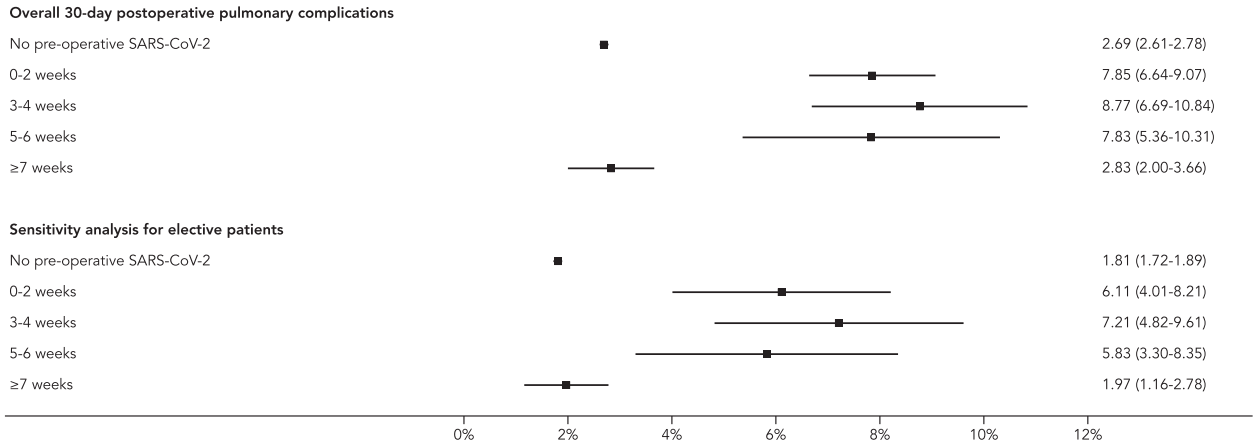

Figure 4 Overall adjusted 30-day postoperative pulmonary complications (PPC) rate from main analysis and sensitivity analysis for patients having elective surgery. 'No pre-operative SARS-CoV-2' refers to patients without a diagnosis of SARS-CoV-2 infection. The time-periods relate to the timing of surgery following the diagnosis of SARS-CoV-2 infection. Full models and results are shown in online Supporting Information (Appendix S1, Tables S9–S10).

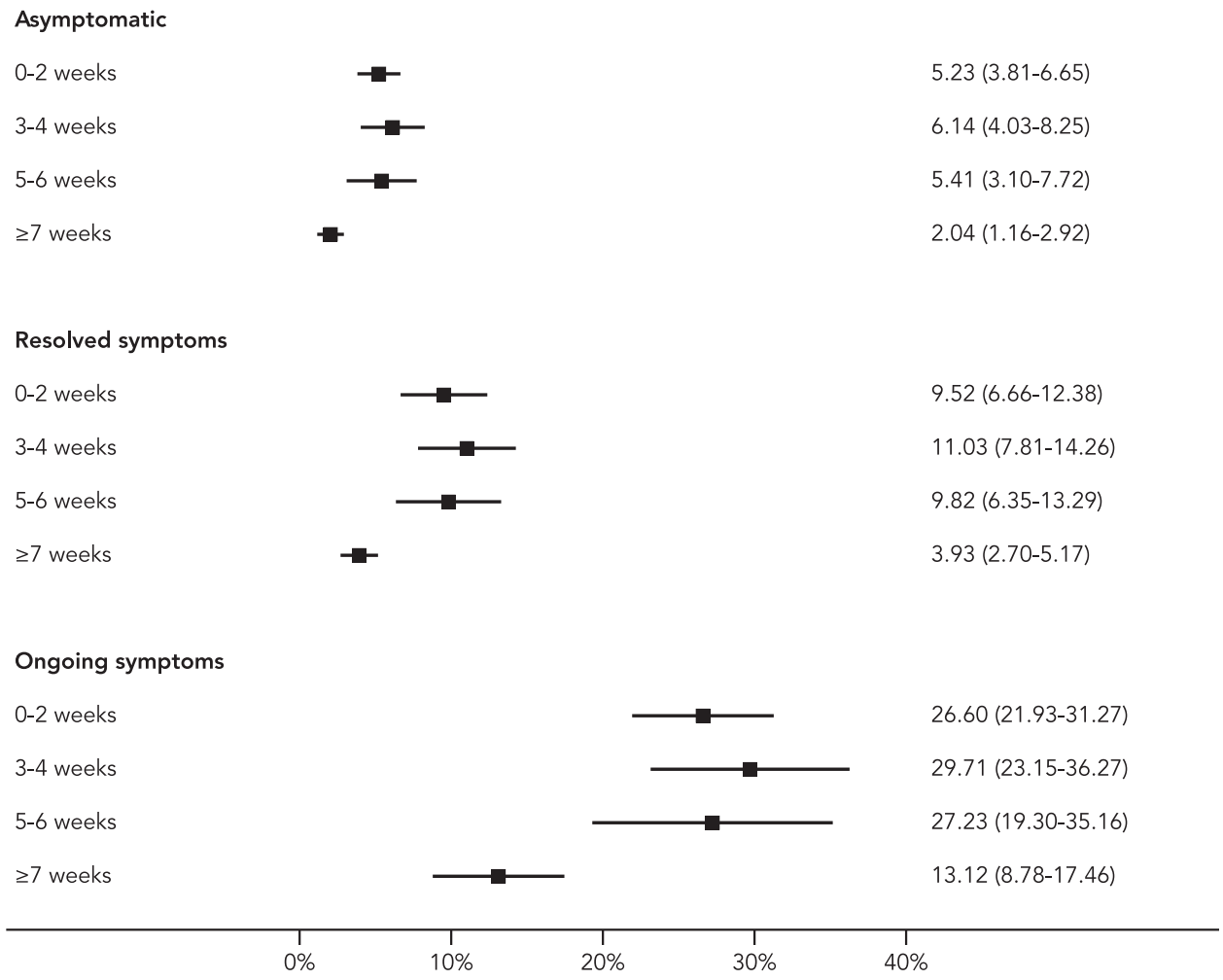

Figure 5 Adjusted 30-day postoperative pulmonary complications (PPC) rate in patients with pre-operative SARS-CoV-2 infection stratified by COVID-19 symptoms. The time-periods relate to the timing of surgery following the diagnosis of SARS-CoV-2 infection. Full model and results are available in online Supporting Information (Appendix S1, Tables S13–S14).

complications is line with previous work [1–3]. However, this is the first study to provide robust data regarding the optimal timing for surgery following SARS-CoV-2 infection. The greater granularity in this analysis compared with previous studies [9, 10] has enabled ≥ 7 weeks to be determined as the optimal cut-off. Whilst cut-offs beyond 7 weeks were not formally tested, they are unlikely to offer a significant advantage, since adjusted mortality rates for delay intervals ≥ 7 weeks were broadly stable (see online Supporting Information, Appendix S1). Moreover, overall mortality following a delay of ≥ 7 weeks was similar to mortality in patients who did not have pre-operative SARS-CoV-2 infection.

There is a backlog of tens of millions of elective operations that were cancelled during the early phase of the COVID-19 pandemic [18]. This study offers evidence to support the safe restarting of surgery in the context of a rapidly increasing number of people who have survived SARS-CoV-2. This study's findings should support informed shared decision-making by anaesthetists, surgeons and patients. Decisions should be tailored for each patient, since the possible advantages of delaying surgery for at least 7 weeks following SARS-CoV-2 diagnosis must be balanced against the potential risks of delay. For some urgent surgical procedures, such as resection of advanced tumours [19, 20], surgeons and patients may decide that the risks of delay are not justified.

This study has some limitations. Firstly, ascertainment of SARS-CoV-2 status was based on routine pre-operative tests. Therefore, it is possible that some patients who had previously experienced SARS-CoV-2 infection may have been misclassified as never having been infected. This

could be particularly likely for patients with asymptomatic infection who may be less likely to get tested. However, it is re-assuring that a high proportion of patients in this cohort were recorded as having had asymptomatic infection, suggesting that many such cases were detected. Secondly, this study was based on time from SARS-CoV-2 diagnosis to surgery, but it is possible that diagnosis was delayed in some patients, underestimating the true delay from when patients were infected to the date of surgery. This was addressed by a sensitivity analysis restricting SARS-CoV-2 diagnosis to those patients who had positive RT-PCR nasopharyngeal swab results, since swab-based diagnosis is likely to give the best approximation of date of infection. The results of this sensitivity analysis were consistent with the main analyses. Thirdly, it was not possible to conduct procedure-specific analyses, although exploration of results stratified by grade (minor vs. major) and urgency of surgery (elective vs. urgency) demonstrates that the overall findings were consistent across these groups. Finally, whilst both subgroup analyses by age, ASA physical status, urgency and grade of surgery, and sensitivity analyses for elective surgery were all consistent with the main analysis, there is a possibility of residual bias.

In conclusion, we performed an international, multicentre, prospective cohort study of 140,231 patients undergoing surgery in 116 countries, in order to determine the optimal timing of surgery after SARS-CoV-2 infection. We found that risks of postoperative morbidity and mortality are greatest if patients are operated within 6 weeks of diagnosis of SARS-CoV-2 infection. Our results suggest that, where possible, surgery should be delayed for at least 7 weeks following SARS-CoV-2 infection. Patients with ongoing symptoms at $\geq$ 7 weeks from diagnosis may benefit from further delay.

Acknowledgements

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Supporting Information

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

Appendix S1. Supporting information.

Table S1. Baseline characteristics and outcomes in elective patients.

Table S2. Unadjusted and adjusted 30-day postoperative mortality (95%CI) in key sub-groups from main analysis.

Table S3. Sensitivity analysis for elective patients with unadjusted and adjusted models for 30-day postoperative mortality.

Table S4. Sensitivity analysis for elective patients with unadjusted and adjusted 30-day postoperative mortality (95%CI) in key sub-groups.

Table S5. Sensitivity analysis for RT-PCR nasopharyngeal swab proven SARS-CoV-2 infection, with unadjusted and adjusted models for 30-day postoperative mortality.

Table S6. Sensitivity analysis for RT-PCR nasopharyngeal swab proven SARS-CoV-2 infection with unadjusted and adjusted 30-day postoperative mortality in key sub-groups.

Table S7. Unadjusted and adjusted models for 30-day postoperative mortality in patients with pre-operative SARS-CoV-2 infection.

Table S8. Unadjusted and adjusted 30-day postoperative mortality in patients with pre-operative SARS-CoV-2 infection in key sub-groups.

Table S9. Unadjusted and adjusted model for 30-day postoperative pulmonary complications in all patients.

Table S10. Unadjusted and adjusted 30-day postoperative pulmonary complications in key sub-groups from main analysis.

Table S11. Sensitivity analysis for elective patients with unadjusted and adjusted model for 30-day postoperative pulmonary complications.

Table S12. Sensitivity analysis for elective patients with unadjusted and adjusted 30-day postoperative pulmonary complications in key sub-groups.

Table S13. Unadjusted and adjusted models for 30-day postoperative pulmonary complications in patients with pre-operative SARS-CoV-2 infection.

Table S14. Unadjusted and adjusted 30-day postoperative pulmonary complications in patients with pre-operative SARS-CoV-2 infection in key sub-groups.

Table S15. List of excluded procedures.

Table S16. 30-day postoperative mortality and postoperative pulmonary complication rates stratified by timing of surgery after SARS-CoV-2 diagnosis.

Table S17. 30-day postoperative mortality and postoperative pulmonary complication rates in patients operated ≥ 3 weeks after SARS-CoV-2 diagnosis, stratified by results of most recent repeat RT-PCR nasopharyngeal swab.

Figure S1. Study flowchart.

Figure S2. Adjusted 30-day postoperative mortality rates from sensitivity analysis for elective patients, stratified by pre-defined sub-groups.

Appendix S2. COVIDSurg Collaborative and GlobalSurg Collaborative authors (all PubMed indexed co-authors).

9.3 Appendix 1: Supplemental tables to Chapter 6

Table 9.1: Categorisation of included OPCS codes

OPCS code	Procedure	Sub-specialty	Specialty	Day-case surgery
K13	Interventional cardiology	Cardiology	Cardiology	No
K16	Interventional cardiology	Cardiology	Cardiology	No
K35	Interventional cardiology	Cardiology	Cardiology	No
K49	Interventional cardiology	Cardiology	Cardiology	Yes
K50	Interventional cardiology	Cardiology	Cardiology	No
K51	Interventional cardiology	Cardiology	Cardiology	Yes
K56	Interventional cardiology	Cardiology	Cardiology	No
K57	Interventional cardiology	Cardiology	Cardiology	Yes
K58	Interventional cardiology	Cardiology	Cardiology	Yes
K59	Interventional cardiology	Cardiology	Cardiology	Yes
K60	Interventional cardiology	Cardiology	Cardiology	Yes
K61	Interventional cardiology	Cardiology	Cardiology	Yes
K62	Interventional cardiology	Cardiology	Cardiology	Yes
K63	Interventional cardiology	Cardiology	Cardiology	Yes
K65	Interventional cardiology	Cardiology	Cardiology	Yes
K73	Interventional cardiology	Cardiology	Cardiology	Yes
K74	Interventional cardiology	Cardiology	Cardiology	Yes
K75	Interventional cardiology	Cardiology	Cardiology	Yes
K76	Interventional cardiology	Cardiology	Cardiology	No
K77	Interventional cardiology	Cardiology	Cardiology	No
L03	Interventional cardiology	Cardiology	Cardiology	No
L13	Interventional cardiology	Cardiology	Cardiology	No
K40	Coronary artery surgery	Cardiac surgery	Cardiothoracic Surgery	No
K41	Coronary artery surgery	Cardiac surgery	Cardiothoracic Surgery	No
K42	Coronary artery surgery	Cardiac surgery	Cardiothoracic Surgery	Yes
K43	Coronary artery surgery	Cardiac surgery	Cardiothoracic Surgery	No
K44	Coronary artery surgery	Cardiac surgery	Cardiothoracic Surgery	No
K45	Coronary artery surgery	Cardiac surgery	Cardiothoracic Surgery	No
K47	Coronary artery surgery	Cardiac surgery	Cardiothoracic Surgery	No
K48	Coronary artery surgery	Cardiac surgery	Cardiothoracic Surgery	No
K64	Other day-case cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	Yes
K66	Other day-case cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	Yes
E61	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
E62	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K04	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K07	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K08	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K09	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K10	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K11	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K12	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K14	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K15	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K17	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K18	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K19	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K20	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K22	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K23	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K24	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K37	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K38	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K46	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K52	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K53	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K54	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K55	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K67	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K68	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K69	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
K71	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No
L02	Other inpatient cardiac surgery	Cardiac surgery	Cardiothoracic Surgery	No

K05	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
K06	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
K33	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L01	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L04	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L05	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L06	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L07	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L08	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L09	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L10	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L12	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L77	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
L79	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	Yes
L80	Surgery on the great vessels	Cardiac surgery	Cardiothoracic Surgery	No
K01	Transplant surgery	Cardiac surgery	Cardiothoracic Surgery	No
K02	Transplant surgery	Cardiac surgery	Cardiothoracic Surgery	No
K25	Valvular heart surgery	Cardiac surgery	Cardiothoracic Surgery	No
K26	Valvular heart surgery	Cardiac surgery	Cardiothoracic Surgery	No
K27	Valvular heart surgery	Cardiac surgery	Cardiothoracic Surgery	No
K28	Valvular heart surgery	Cardiac surgery	Cardiothoracic Surgery	No
K29	Valvular heart surgery	Cardiac surgery	Cardiothoracic Surgery	No
K30	Valvular heart surgery	Cardiac surgery	Cardiothoracic Surgery	No
K31	Valvular heart surgery	Cardiac surgery	Cardiothoracic Surgery	No
K32	Valvular heart surgery	Cardiac surgery	Cardiothoracic Surgery	No
K34	Valvular heart surgery	Cardiac surgery	Cardiothoracic Surgery	No
K36	Valvular heart surgery	Cardiac surgery	Cardiothoracic Surgery	No
E59	Biopsy of lung	Thoracic surgery	Cardiothoracic Surgery	Yes
E49	Bronchoscopy	Thoracic surgery	Cardiothoracic Surgery	Yes
E51	Bronchoscopy	Thoracic surgery	Cardiothoracic Surgery	No
E63	Bronchoscopy	Thoracic surgery	Cardiothoracic Surgery	Yes
T10	Bronchoscopy	Thoracic surgery	Cardiothoracic Surgery	No
E54	Lung resection	Thoracic surgery	Cardiothoracic Surgery	No
E67	Other day-case thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	Yes
T01	Other day-case thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	Yes
T14	Other day-case thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	Yes
E39	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E40	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E41	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E43	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E44	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E46	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E47	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E48	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E50	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E52	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E55	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E57	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
G23	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
T02	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
T03	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
T05	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
T07	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
T08	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
T09	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
T11	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
T15	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
T16	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
T17	Other inpatient thoracic surgery	Thoracic surgery	Cardiothoracic Surgery	No
E53	Transplant surgery	Thoracic surgery	Cardiothoracic Surgery	No
B27	Excision of breast	Breast surgery	General Surgery	No
B28	Excision of breast	Breast surgery	General Surgery	Yes
B41	Excision of breast	Breast surgery	General Surgery	Yes
B30	Other day-case breast surgery	Breast surgery	General Surgery	Yes
B31	Other day-case breast surgery	Breast surgery	General Surgery	Yes
B32	Other day-case breast surgery	Breast surgery	General Surgery	Yes
B33	Other day-case breast surgery	Breast surgery	General Surgery	Yes
B34	Other day-case breast surgery	Breast surgery	General Surgery	Yes
B35	Other day-case breast surgery	Breast surgery	General Surgery	Yes
B36	Other day-case breast surgery	Breast surgery	General Surgery	Yes
B37	Other day-case breast surgery	Breast surgery	General Surgery	Yes

B40	Other day-case breast surgery	Breast surgery	General Surgery	Yes
B29	Other inpatient breast surgery	Breast surgery	General Surgery	No
G49	Colorectal resection	Colorectal surgery	General Surgery	No
G58	Colorectal resection	Colorectal surgery	General Surgery	No
G69	Colorectal resection	Colorectal surgery	General Surgery	No
H04	Colorectal resection	Colorectal surgery	General Surgery	No
H05	Colorectal resection	Colorectal surgery	General Surgery	No
H06	Colorectal resection	Colorectal surgery	General Surgery	No
H07	Colorectal resection	Colorectal surgery	General Surgery	No
H08	Colorectal resection	Colorectal surgery	General Surgery	No
H09	Colorectal resection	Colorectal surgery	General Surgery	No
H10	Colorectal resection	Colorectal surgery	General Surgery	No
H11	Colorectal resection	Colorectal surgery	General Surgery	No
H29	Colorectal resection	Colorectal surgery	General Surgery	No
H33	Colorectal resection	Colorectal surgery	General Surgery	No
H14	Ileostomy, colostomy	Colorectal surgery	General Surgery	No
H15	Ileostomy, colostomy	Colorectal surgery	General Surgery	No
H32	Ileostomy, colostomy	Colorectal surgery	General Surgery	No
G62	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
H18	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
H19	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
H30	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
H40	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
H41	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
H42	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
H46	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
H47	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
H62	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
H66	Other day-case colorectal surgery	Colorectal surgery	General Surgery	Yes
G71	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H02	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H03	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H12	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H13	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H16	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H17	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H34	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H35	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H36	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H50	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
T37	Other inpatient colorectal surgery	Colorectal surgery	General Surgery	No
H31	Other interventional radiology	Colorectal surgery	General Surgery	No
H44	Proctology	Colorectal surgery	General Surgery	Yes
H48	Proctology	Colorectal surgery	General Surgery	Yes
H49	Proctology	Colorectal surgery	General Surgery	Yes
H51	Proctology	Colorectal surgery	General Surgery	Yes
H52	Proctology	Colorectal surgery	General Surgery	Yes
H53	Proctology	Colorectal surgery	General Surgery	Yes
H54	Proctology	Colorectal surgery	General Surgery	Yes
H55	Proctology	Colorectal surgery	General Surgery	Yes
H56	Proctology	Colorectal surgery	General Surgery	Yes
H57	Proctology	Colorectal surgery	General Surgery	Yes
H58	Proctology	Colorectal surgery	General Surgery	Yes
H59	Proctology	Colorectal surgery	General Surgery	Yes
H60	Proctology	Colorectal surgery	General Surgery	Yes
H20	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H21	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H22	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H23	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H24	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H25	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H26	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H27	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H28	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H37	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H68	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H69	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H70	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	Yes
H71	Sigmoidoscopy, colonoscopy	Colorectal surgery	General Surgery	No
J09	Diagnostic laparoscopy	General surgery	General Surgery	Yes
J51	Diagnostic laparoscopy	General surgery	General Surgery	Yes

J73	Diagnostic laparoscopy	General surgery	General Surgery	Yes
Q39	Diagnostic laparoscopy	General surgery	General Surgery	Yes
Q50	Diagnostic laparoscopy	General surgery	General Surgery	Yes
T42	Diagnostic laparoscopy	General surgery	General Surgery	Yes
T43	Diagnostic laparoscopy	General surgery	General Surgery	Yes
T85	Excision of lymph node	General surgery	General Surgery	No
T86	Excision of lymph node	General surgery	General Surgery	Yes
T87	Excision of lymph node	General surgery	General Surgery	Yes
T88	Excision of lymph node	General surgery	General Surgery	Yes
T91	Excision of lymph node	General surgery	General Surgery	Yes
B08	Excision of thyroid, parathyroid	General surgery	General Surgery	No
B14	Excision of thyroid, parathyroid	General surgery	General Surgery	No
T19	Groin hernia repair	General surgery	General Surgery	Yes
T20	Groin hernia repair	General surgery	General Surgery	Yes
T21	Groin hernia repair	General surgery	General Surgery	Yes
T22	Groin hernia repair	General surgery	General Surgery	Yes
T23	Groin hernia repair	General surgery	General Surgery	Yes
B12	Other day-case endocrine surgery	General surgery	General Surgery	Yes
B23	Other day-case endocrine surgery	General surgery	General Surgery	Yes
B25	Other day-case endocrine surgery	General surgery	General Surgery	Yes
T29	Other day-case general surgery	General surgery	General Surgery	Yes
T31	Other day-case general surgery	General surgery	General Surgery	Yes
T48	Other day-case general surgery	General surgery	General Surgery	Yes
T51	Other day-case general surgery	General surgery	General Surgery	Yes
T92	Other day-case general surgery	General surgery	General Surgery	Yes
T96	Other day-case general surgery	General surgery	General Surgery	Yes
X03	Other day-case general surgery	General surgery	General Surgery	Yes
X55	Other day-case general surgery	General surgery	General Surgery	Yes
B01	Other inpatient endocrine surgery	General surgery	General Surgery	No
B02	Other inpatient endocrine surgery	General surgery	General Surgery	No
B04	Other inpatient endocrine surgery	General surgery	General Surgery	No
B06	Other inpatient endocrine surgery	General surgery	General Surgery	No
B09	Other inpatient endocrine surgery	General surgery	General Surgery	No
B10	Other inpatient endocrine surgery	General surgery	General Surgery	No
B16	Other inpatient endocrine surgery	General surgery	General Surgery	No
B18	Other inpatient endocrine surgery	General surgery	General Surgery	No
B20	Other inpatient endocrine surgery	General surgery	General Surgery	No
B22	Other inpatient endocrine surgery	General surgery	General Surgery	No
H01	Other inpatient general surgery	General surgery	General Surgery	No
J72	Other inpatient general surgery	General surgery	General Surgery	No
T28	Other inpatient general surgery	General surgery	General Surgery	No
T30	Other inpatient general surgery	General surgery	General Surgery	No
T32	Other inpatient general surgery	General surgery	General Surgery	No
T33	Other inpatient general surgery	General surgery	General Surgery	No
T34	Other inpatient general surgery	General surgery	General Surgery	No
T38	Other inpatient general surgery	General surgery	General Surgery	No
T39	Other inpatient general surgery	General surgery	General Surgery	No
T41	Other inpatient general surgery	General surgery	General Surgery	No
T50	Other inpatient general surgery	General surgery	General Surgery	No
T89	Other inpatient general surgery	General surgery	General Surgery	No
X14	Other inpatient general surgery	General surgery	General Surgery	No
X17	Other inpatient general surgery	General surgery	General Surgery	No
X46	Other inpatient general surgery	General surgery	General Surgery	No
T45	Other interventional radiology	General surgery	General Surgery	No
T90	Other interventional radiology	General surgery	General Surgery	Yes
B17	Transplant surgery	General surgery	General Surgery	No
X04	Transplant surgery	General surgery	General Surgery	Yes
X45	Transplant surgery	General surgery	General Surgery	No
T24	Ventral hernia repair	General surgery	General Surgery	Yes
T25	Ventral hernia repair	General surgery	General Surgery	No
T26	Ventral hernia repair	General surgery	General Surgery	No
T27	Ventral hernia repair	General surgery	General Surgery	Yes
T97	Ventral hernia repair	General surgery	General Surgery	Yes
T98	Ventral hernia repair	General surgery	General Surgery	Yes
J18	Cholecystectomy	Hepatobiliary surgery	General Surgery	Yes
J13	Diagnostic percutaneous operations on liver	Hepatobiliary surgery	General Surgery	Yes
J17	ERCP & related procedures	Hepatobiliary surgery	General Surgery	Yes
J38	ERCP & related procedures	Hepatobiliary surgery	General Surgery	Yes
J39	ERCP & related procedures	Hepatobiliary surgery	General Surgery	Yes
J40	ERCP & related procedures	Hepatobiliary surgery	General Surgery	No
J41	ERCP & related procedures	Hepatobiliary surgery	General Surgery	Yes

J42	ERCP & related procedures	Hepatobiliary surgery	General Surgery	No
J43	ERCP & related procedures	Hepatobiliary surgery	General Surgery	Yes
J44	ERCP & related procedures	Hepatobiliary surgery	General Surgery	Yes
J45	ERCP & related procedures	Hepatobiliary surgery	General Surgery	Yes
J49	ERCP & related procedures	Hepatobiliary surgery	General Surgery	No
J53	ERCP & related procedures	Hepatobiliary surgery	General Surgery	Yes
J74	ERCP & related procedures	Hepatobiliary surgery	General Surgery	Yes
J02	Excision of liver, pancreas, spleen	Hepatobiliary surgery	General Surgery	No
J55	Excision of liver, pancreas, spleen	Hepatobiliary surgery	General Surgery	No
J56	Excision of liver, pancreas, spleen	Hepatobiliary surgery	General Surgery	No
J57	Excision of liver, pancreas, spleen	Hepatobiliary surgery	General Surgery	No
J69	Excision of liver, pancreas, spleen	Hepatobiliary surgery	General Surgery	No
J70	Excision of liver, pancreas, spleen	Hepatobiliary surgery	General Surgery	No
J16	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J19	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J23	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J26	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J31	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J34	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J36	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J37	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J60	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J63	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J68	Other day-case hepatobiliary surgery	Hepatobiliary surgery	General Surgery	Yes
J03	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J04	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J05	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J07	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J08	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J20	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J21	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J27	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J28	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J29	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J30	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J32	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J33	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J35	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J52	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J58	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J59	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J61	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J62	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J65	Other inpatient hepatobiliary surgery	Hepatobiliary surgery	General Surgery	No
J06	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J10	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J11	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J12	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J14	Other interventional radiology	Hepatobiliary surgery	General Surgery	Yes
J15	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J24	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J25	Other interventional radiology	Hepatobiliary surgery	General Surgery	Yes
J46	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J47	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J48	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J50	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J66	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J67	Other interventional radiology	Hepatobiliary surgery	General Surgery	Yes
J77	Other interventional radiology	Hepatobiliary surgery	General Surgery	No
J01	Transplant surgery	Hepatobiliary surgery	General Surgery	No
J54	Transplant surgery	Hepatobiliary surgery	General Surgery	No
G12	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G14	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G15	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G16	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G17	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G18	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G19	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G20	Gastroscopy	Oesophagogastric surgery	General Surgery	No
G21	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G42	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes

G43	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G44	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G45	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G46	Gastroscopy	Oesophagogastric surgery	General Surgery	No
G54	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G55	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G64	Gastroscopy	Oesophagogastric surgery	General Surgery	No
G65	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G79	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G80	Gastroscopy	Oesophagogastric surgery	General Surgery	Yes
G34	Gastrostomy, jejunostomy	Oesophagogastric surgery	General Surgery	No
G60	Gastrostomy, jejunostomy	Oesophagogastric surgery	General Surgery	No
G74	Ileostomy, colostomy	Oesophagogastric surgery	General Surgery	No
G75	Ileostomy, colostomy	Oesophagogastric surgery	General Surgery	No
G01	Oesophagogastric resection	Oesophagogastric surgery	General Surgery	No
G02	Oesophagogastric resection	Oesophagogastric surgery	General Surgery	No
G03	Oesophagogastric resection	Oesophagogastric surgery	General Surgery	No
G27	Oesophagogastric resection	Oesophagogastric surgery	General Surgery	No
G28	Oesophagogastric resection	Oesophagogastric surgery	General Surgery	No
G10	Other day-case oesophagogastric surgery	Oesophagogastric surgery	General Surgery	Yes
G30	Other day-case oesophagogastric surgery	Oesophagogastric surgery	General Surgery	Yes
G48	Other day-case oesophagogastric surgery	Oesophagogastric surgery	General Surgery	Yes
G67	Other day-case oesophagogastric surgery	Oesophagogastric surgery	General Surgery	Yes
T36	Other day-case oesophagogastric surgery	Oesophagogastric surgery	General Surgery	Yes
G04	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G05	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G06	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G07	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G08	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G09	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G11	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G13	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G24	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G25	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G29	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G31	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G32	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G33	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G35	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G36	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G38	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G40	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G41	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G50	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G51	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G52	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G53	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G57	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G59	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G61	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G63	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G70	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G72	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G73	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G76	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G78	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G82	Other inpatient oesophagogastric surgery	Oesophagogastric surgery	General Surgery	No
G26	Transplant surgery	Oesophagogastric surgery	General Surgery	No
G68	Transplant surgery	Oesophagogastric surgery	General Surgery	No
X09	Amputation of lower limb	Vascular surgery	General Surgery	No
X10	Amputation of lower limb	Vascular surgery	General Surgery	No
X11	Amputation of lower limb	Vascular surgery	General Surgery	No
X07	Amputation of upper limb	Vascular surgery	General Surgery	No
X08	Amputation of upper limb	Vascular surgery	General Surgery	Yes
L16	Aortic surgery	Vascular surgery	General Surgery	No
L18	Aortic surgery	Vascular surgery	General Surgery	No
L19	Aortic surgery	Vascular surgery	General Surgery	No
L20	Aortic surgery	Vascular surgery	General Surgery	No
L21	Aortic surgery	Vascular surgery	General Surgery	No
L22	Aortic surgery	Vascular surgery	General Surgery	No
L23	Aortic surgery	Vascular surgery	General Surgery	No

L25	Aortic surgery	Vascular surgery	General Surgery	No
L74	Arteriovenous shunt	Vascular surgery	General Surgery	Yes
L75	Arteriovenous shunt	Vascular surgery	General Surgery	Yes
L83	Other day-case vascular surgery	Vascular surgery	General Surgery	Yes
L93	Other day-case vascular surgery	Vascular surgery	General Surgery	Yes
L98	Other day-case vascular surgery	Vascular surgery	General Surgery	Yes
L81	Other inpatient vascular surgery	Vascular surgery	General Surgery	No
L82	Other inpatient vascular surgery	Vascular surgery	General Surgery	No
L90	Other inpatient vascular surgery	Vascular surgery	General Surgery	No
L97	Other inpatient vascular surgery	Vascular surgery	General Surgery	No
O15	Other inpatient vascular surgery	Vascular surgery	General Surgery	No
X12	Other inpatient vascular surgery	Vascular surgery	General Surgery	No
L29	Surgery on arteries	Vascular surgery	General Surgery	No
L30	Surgery on arteries	Vascular surgery	General Surgery	No
L37	Surgery on arteries	Vascular surgery	General Surgery	No
L38	Surgery on arteries	Vascular surgery	General Surgery	No
L41	Surgery on arteries	Vascular surgery	General Surgery	No
L42	Surgery on arteries	Vascular surgery	General Surgery	No
L45	Surgery on arteries	Vascular surgery	General Surgery	No
L46	Surgery on arteries	Vascular surgery	General Surgery	No
L48	Surgery on arteries	Vascular surgery	General Surgery	No
L49	Surgery on arteries	Vascular surgery	General Surgery	No
L50	Surgery on arteries	Vascular surgery	General Surgery	No
L51	Surgery on arteries	Vascular surgery	General Surgery	No
L52	Surgery on arteries	Vascular surgery	General Surgery	No
L53	Surgery on arteries	Vascular surgery	General Surgery	No
L56	Surgery on arteries	Vascular surgery	General Surgery	No
L57	Surgery on arteries	Vascular surgery	General Surgery	No
L58	Surgery on arteries	Vascular surgery	General Surgery	No
L59	Surgery on arteries	Vascular surgery	General Surgery	No
L60	Surgery on arteries	Vascular surgery	General Surgery	No
L62	Surgery on arteries	Vascular surgery	General Surgery	No
L65	Surgery on arteries	Vascular surgery	General Surgery	No
L67	Surgery on arteries	Vascular surgery	General Surgery	Yes
L68	Surgery on arteries	Vascular surgery	General Surgery	Yes
L69	Surgery on arteries	Vascular surgery	General Surgery	No
L70	Surgery on arteries	Vascular surgery	General Surgery	Yes
L84	Varicose vein surgery	Vascular surgery	General Surgery	Yes
L85	Varicose vein surgery	Vascular surgery	General Surgery	Yes
L86	Varicose vein surgery	Vascular surgery	General Surgery	Yes
L87	Varicose vein surgery	Vascular surgery	General Surgery	Yes
K78	Vascular interventional radiology	Vascular surgery	General Surgery	No
L26	Vascular interventional radiology	Vascular surgery	General Surgery	No
L27	Vascular interventional radiology	Vascular surgery	General Surgery	No
L28	Vascular interventional radiology	Vascular surgery	General Surgery	No
L31	Vascular interventional radiology	Vascular surgery	General Surgery	No
L39	Vascular interventional radiology	Vascular surgery	General Surgery	No
L43	Vascular interventional radiology	Vascular surgery	General Surgery	No
L47	Vascular interventional radiology	Vascular surgery	General Surgery	No
L54	Vascular interventional radiology	Vascular surgery	General Surgery	Yes
L63	Vascular interventional radiology	Vascular surgery	General Surgery	Yes
L66	Vascular interventional radiology	Vascular surgery	General Surgery	No
L71	Vascular interventional radiology	Vascular surgery	General Surgery	No
L72	Vascular interventional radiology	Vascular surgery	General Surgery	No
L73	Vascular interventional radiology	Vascular surgery	General Surgery	No
L76	Vascular interventional radiology	Vascular surgery	General Surgery	No
L88	Vascular interventional radiology	Vascular surgery	General Surgery	Yes
L94	Vascular interventional radiology	Vascular surgery	General Surgery	Yes
L95	Vascular interventional radiology	Vascular surgery	General Surgery	Yes
L96	Vascular interventional radiology	Vascular surgery	General Surgery	No
L99	Vascular interventional radiology	Vascular surgery	General Surgery	Yes
O01	Vascular interventional radiology	Vascular surgery	General Surgery	No
O02	Vascular interventional radiology	Vascular surgery	General Surgery	No
O03	Vascular interventional radiology	Vascular surgery	General Surgery	No
O04	Vascular interventional radiology	Vascular surgery	General Surgery	No
O20	Vascular interventional radiology	Vascular surgery	General Surgery	Yes
P05	Excision of vulva, vagina, cervix	Gynaecology	Gynaecology	Yes
Q01	Excision of vulva, vagina, cervix	Gynaecology	Gynaecology	Yes
Q27	Female sterilisation	Gynaecology	Gynaecology	Yes
Q28	Female sterilisation	Gynaecology	Gynaecology	Yes
Q35	Female sterilisation	Gynaecology	Gynaecology	Yes

Q37	Female sterilisation	Gynaecology	Gynaecology	Yes
Q07	Hysterectomy, salpingoophrectomy	Gynaecology	Gynaecology	No
Q08	Hysterectomy, salpingoophrectomy	Gynaecology	Gynaecology	No
Q22	Hysterectomy, salpingoophrectomy	Gynaecology	Gynaecology	No
Q23	Hysterectomy, salpingoophrectomy	Gynaecology	Gynaecology	No
Q24	Hysterectomy, salpingoophrectomy	Gynaecology	Gynaecology	Yes
Q25	Hysterectomy, salpingoophrectomy	Gynaecology	Gynaecology	Yes
Q43	Hysterectomy, salpingoophrectomy	Gynaecology	Gynaecology	No
Q17	Hysteroscopy & related procedures	Gynaecology	Gynaecology	Yes
Q18	Hysteroscopy & related procedures	Gynaecology	Gynaecology	Yes
M53	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
M57	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
M58	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P01	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P03	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P06	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P07	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P09	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P11	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P13	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P14	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P15	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P17	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P19	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P20	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P26	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P27	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P29	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P31	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
P32	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q02	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q03	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q05	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q10	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q16	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q19	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q20	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q26	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q29	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q30	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q31	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q32	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q34	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q36	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q38	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q41	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q52	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q54	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q55	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q56	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
Q57	Other day-case gynaecology	Gynaecology	Gynaecology	Yes
M51	Other inpatient gynaecology	Gynaecology	Gynaecology	No
M52	Other inpatient gynaecology	Gynaecology	Gynaecology	No
M55	Other inpatient gynaecology	Gynaecology	Gynaecology	No
P18	Other inpatient gynaecology	Gynaecology	Gynaecology	No
P21	Other inpatient gynaecology	Gynaecology	Gynaecology	No
P24	Other inpatient gynaecology	Gynaecology	Gynaecology	No
P25	Other inpatient gynaecology	Gynaecology	Gynaecology	No
P30	Other inpatient gynaecology	Gynaecology	Gynaecology	No
Q09	Other inpatient gynaecology	Gynaecology	Gynaecology	No
Q44	Ovarian surgery	Gynaecology	Gynaecology	Yes
Q45	Ovarian surgery	Gynaecology	Gynaecology	Yes
Q47	Ovarian surgery	Gynaecology	Gynaecology	No
Q49	Ovarian surgery	Gynaecology	Gynaecology	Yes
Q51	Ovarian surgery	Gynaecology	Gynaecology	Yes
P22	Repair of prolapse of vagina	Gynaecology	Gynaecology	No
P23	Repair of prolapse of vagina	Gynaecology	Gynaecology	No
P28	Repair of prolapse of vagina	Gynaecology	Gynaecology	Yes
E20	Adenoidectomy	Head & Neck surgery	Head & Neck surgery	Yes
E24	Laryngoscopy	Head & Neck surgery	Head & Neck surgery	No
E25	Laryngoscopy	Head & Neck surgery	Head & Neck surgery	Yes

E35	Laryngoscopy	Head & Neck surgery	Head & Neck surgery	Yes
D10	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
D12	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
E12	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
E13	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
E16	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
F18	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
F29	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	No
V06	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	No
V07	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
V08	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	No
V09	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
V10	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	No
V11	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
V13	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	No
V14	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	No
V15	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	No
V16	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	No
V17	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
V18	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	No
V19	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
V20	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	No
V21	Maxillofacial surgery	Head & Neck surgery	Head & Neck surgery	Yes
D01	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D02	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D03	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D04	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D05	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D06	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D07	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D08	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D13	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D14	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D15	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D16	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D17	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D19	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D20	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D22	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D23	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
D24	Operations on ear	Head & Neck surgery	Head & Neck surgery	No
D26	Operations on ear	Head & Neck surgery	Head & Neck surgery	No
D28	Operations on ear	Head & Neck surgery	Head & Neck surgery	Yes
E19	Operations on neck	Head & Neck surgery	Head & Neck surgery	No
E21	Operations on neck	Head & Neck surgery	Head & Neck surgery	No
E23	Operations on neck	Head & Neck surgery	Head & Neck surgery	No
E27	Operations on neck	Head & Neck surgery	Head & Neck surgery	Yes
E28	Operations on neck	Head & Neck surgery	Head & Neck surgery	No
E29	Operations on neck	Head & Neck surgery	Head & Neck surgery	No
E30	Operations on neck	Head & Neck surgery	Head & Neck surgery	No
E31	Operations on neck	Head & Neck surgery	Head & Neck surgery	No
E33	Operations on neck	Head & Neck surgery	Head & Neck surgery	Yes
E34	Operations on neck	Head & Neck surgery	Head & Neck surgery	Yes
E38	Operations on neck	Head & Neck surgery	Head & Neck surgery	Yes
E42	Operations on neck	Head & Neck surgery	Head & Neck surgery	No
E01	Operations on nose	Head & Neck surgery	Head & Neck surgery	No
E02	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E03	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E04	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E05	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E08	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E09	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E10	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E11	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E14	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E15	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E17	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E64	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
E66	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
T94	Operations on nose	Head & Neck surgery	Head & Neck surgery	Yes
F20	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes

F22	Oral surgery	Head & Neck surgery	Head & Neck surgery	No
F23	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F24	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F26	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F28	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F30	Oral surgery	Head & Neck surgery	Head & Neck surgery	No
F32	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F38	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F39	Oral surgery	Head & Neck surgery	Head & Neck surgery	No
F40	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F42	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F44	Oral surgery	Head & Neck surgery	Head & Neck surgery	No
F45	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F46	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F48	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F50	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F51	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F52	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F53	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F55	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F56	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F58	Oral surgery	Head & Neck surgery	Head & Neck surgery	Yes
F34	Tonsillectomy	Head & Neck surgery	Head & Neck surgery	Yes
F36	Tonsillectomy	Head & Neck surgery	Head & Neck surgery	Yes
A01	Brain tissue surgery	Neurosurgery	Neurosurgery	No
A02	Brain tissue surgery	Neurosurgery	Neurosurgery	No
A03	Brain tissue surgery	Neurosurgery	Neurosurgery	No
A04	Brain tissue surgery	Neurosurgery	Neurosurgery	No
A05	Brain tissue surgery	Neurosurgery	Neurosurgery	No
A06	Brain tissue surgery	Neurosurgery	Neurosurgery	No
A08	Brain tissue surgery	Neurosurgery	Neurosurgery	No
A10	Brain tissue surgery	Neurosurgery	Neurosurgery	Yes
A11	Brain tissue surgery	Neurosurgery	Neurosurgery	No
A12	Brain ventricular surgery	Neurosurgery	Neurosurgery	No
A13	Brain ventricular surgery	Neurosurgery	Neurosurgery	No
A14	Brain ventricular surgery	Neurosurgery	Neurosurgery	No
A16	Brain ventricular surgery	Neurosurgery	Neurosurgery	No
A17	Brain ventricular surgery	Neurosurgery	Neurosurgery	No
A18	Brain ventricular surgery	Neurosurgery	Neurosurgery	No
A20	Brain ventricular surgery	Neurosurgery	Neurosurgery	No
A24	Cranial nerve surgery	Neurosurgery	Neurosurgery	No
A25	Cranial nerve surgery	Neurosurgery	Neurosurgery	No
A26	Cranial nerve surgery	Neurosurgery	Neurosurgery	Yes
A27	Cranial nerve surgery	Neurosurgery	Neurosurgery	No
A28	Cranial nerve surgery	Neurosurgery	Neurosurgery	Yes
A29	Cranial nerve surgery	Neurosurgery	Neurosurgery	No
A30	Cranial nerve surgery	Neurosurgery	Neurosurgery	No
A31	Cranial nerve surgery	Neurosurgery	Neurosurgery	Yes
A32	Cranial nerve surgery	Neurosurgery	Neurosurgery	No
A34	Cranial nerve surgery	Neurosurgery	Neurosurgery	No
A36	Cranial nerve surgery	Neurosurgery	Neurosurgery	Yes
A07	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
A22	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
A38	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
A39	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
A40	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
A41	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
A42	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
A43	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
O05	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
V03	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
V04	Cranium and dural surgery	Neurosurgery	Neurosurgery	Yes
V05	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
V12	Cranium and dural surgery	Neurosurgery	Neurosurgery	No
L35	Neurovascular interventional radiology	Neurosurgery	Neurosurgery	Yes
L33	Other inpatient neurosurgery	Neurosurgery	Neurosurgery	No
L34	Other inpatient neurosurgery	Neurosurgery	Neurosurgery	No
C71	Cataract surgery	Opthalmology	Ophthalmology	Yes
C72	Cataract surgery	Opthalmology	Ophthalmology	Yes
C73	Cataract surgery	Opthalmology	Ophthalmology	Yes
C74	Cataract surgery	Opthalmology	Ophthalmology	Yes

C75	Cataract surgery	Opthalmology	Ophthalmology	Yes
C77	Cataract surgery	Opthalmology	Ophthalmology	Yes
C59	Glaucoma surgery	Opthalmology	Ophthalmology	Yes
C60	Glaucoma surgery	Opthalmology	Ophthalmology	Yes
C62	Glaucoma surgery	Opthalmology	Ophthalmology	Yes
C64	Glaucoma surgery	Opthalmology	Ophthalmology	Yes
C65	Glaucoma surgery	Opthalmology	Ophthalmology	Yes
C79	Operations on vitreous body of eye	Opthalmology	Ophthalmology	Yes
C02	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C03	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C04	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C09	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C11	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C24	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C25	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C26	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C27	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C29	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C31	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C32	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C33	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C34	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C35	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C37	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C39	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C40	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C41	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C43	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C44	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C45	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C46	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C47	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C49	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C51	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C52	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C53	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C54	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C55	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C57	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C61	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C66	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C67	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C69	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C80	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C81	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C82	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C84	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C85	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C86	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C87	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C88	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C89	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C90	Other day-case ophthalmology	Opthalmology	Ophthalmology	Yes
C01	Other inpatient ophthalmology	Opthalmology	Ophthalmology	No
C05	Other inpatient ophthalmology	Opthalmology	Ophthalmology	No
C06	Other inpatient ophthalmology	Opthalmology	Ophthalmology	No
C08	Other inpatient ophthalmology	Opthalmology	Ophthalmology	No
C83	Other inpatient ophthalmology	Opthalmology	Ophthalmology	No
C91	Other inpatient ophthalmology	Opthalmology	Ophthalmology	No
S04	Excision of lesion of skin	Plastic surgery	Plastic Surgery	Yes
S06	Excision of lesion of skin	Plastic surgery	Plastic Surgery	Yes
S08	Excision of lesion of skin	Plastic surgery	Plastic Surgery	Yes
S10	Excision of lesion of skin	Plastic surgery	Plastic Surgery	Yes
S11	Excision of lesion of skin	Plastic surgery	Plastic Surgery	Yes
A59	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
A62	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
A64	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
A75	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
C10	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
E07	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S01	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes

S03	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S05	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S22	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S23	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S26	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S27	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S28	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S30	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S31	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S33	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S35	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S36	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S37	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S38	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S39	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S40	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S41	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S42	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S43	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S47	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S49	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S54	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S55	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S56	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S57	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S60	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S62	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
S63	Other day-case plastic surgery	Plastic surgery	Plastic Surgery	Yes
A63	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
B38	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
B39	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S02	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S17	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S18	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S19	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S20	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S21	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S24	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S25	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S29	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S32	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S34	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
S48	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
V01	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
V02	Other inpatient plastic surgery	Plastic surgery	Plastic Surgery	No
C12	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
C13	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
C14	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
C15	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
C16	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
C17	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
C18	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
C19	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
C20	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
C22	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
C23	Procedure on eyelid	Plastic surgery	Plastic Surgery	Yes
F01	Procedure on lip	Plastic surgery	Plastic Surgery	Yes
F02	Procedure on lip	Plastic surgery	Plastic Surgery	Yes
F03	Procedure on lip	Plastic surgery	Plastic Surgery	No
F04	Procedure on lip	Plastic surgery	Plastic Surgery	Yes
F05	Procedure on lip	Plastic surgery	Plastic Surgery	Yes
F06	Procedure on lip	Plastic surgery	Plastic Surgery	Yes
O19	Arthroscopic procedures	Orthopaedics	Orthopaedics	Yes
W82	Arthroscopic procedures	Orthopaedics	Orthopaedics	Yes
W83	Arthroscopic procedures	Orthopaedics	Orthopaedics	Yes
W84	Arthroscopic procedures	Orthopaedics	Orthopaedics	Yes
W85	Arthroscopic procedures	Orthopaedics	Orthopaedics	Yes
W86	Arthroscopic procedures	Orthopaedics	Orthopaedics	Yes
W87	Arthroscopic procedures	Orthopaedics	Orthopaedics	Yes
W88	Arthroscopic procedures	Orthopaedics	Orthopaedics	Yes
W89	Arthroscopic procedures	Orthopaedics	Orthopaedics	Yes

O27	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W44	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W45	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W53	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W54	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W55	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W56	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W57	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W69	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W71	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W77	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W78	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W79	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W80	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W81	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W91	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
W92	day-case procedures on joint	Orthopaedics	Orthopaedics	Yes
V22	Decompression of cervical spine	Orthopaedics	Orthopaedics	No
V25	Decompression of lumbar spine	Orthopaedics	Orthopaedics	No
O29	Division or excision of bone	Orthopaedics	Orthopaedics	Yes
W06	Division or excision of bone	Orthopaedics	Orthopaedics	Yes
W07	Division or excision of bone	Orthopaedics	Orthopaedics	Yes
W08	Division or excision of bone	Orthopaedics	Orthopaedics	Yes
W09	Division or excision of bone	Orthopaedics	Orthopaedics	Yes
W12	Division or excision of bone	Orthopaedics	Orthopaedics	No
W13	Division or excision of bone	Orthopaedics	Orthopaedics	Yes
W14	Division or excision of bone	Orthopaedics	Orthopaedics	Yes
W15	Division or excision of bone	Orthopaedics	Orthopaedics	Yes
W16	Division or excision of bone	Orthopaedics	Orthopaedics	No
T59	Excision of ganglion	Orthopaedics	Orthopaedics	Yes
T60	Excision of ganglion	Orthopaedics	Orthopaedics	Yes
T61	Excision of ganglion	Orthopaedics	Orthopaedics	Yes
T52	Fasciectomy, fasciotomy	Orthopaedics	Orthopaedics	Yes
T53	Fasciectomy, fasciotomy	Orthopaedics	Orthopaedics	Yes
T54	Fasciectomy, fasciotomy	Orthopaedics	Orthopaedics	Yes
T55	Fasciectomy, fasciotomy	Orthopaedics	Orthopaedics	Yes
T56	Fasciectomy, fasciotomy	Orthopaedics	Orthopaedics	Yes
T57	Fasciectomy, fasciotomy	Orthopaedics	Orthopaedics	Yes
O17	Fracture-related surgery	Orthopaedics	Orthopaedics	Yes
W19	Fracture-related surgery	Orthopaedics	Orthopaedics	Yes
W20	Fracture-related surgery	Orthopaedics	Orthopaedics	No
W21	Fracture-related surgery	Orthopaedics	Orthopaedics	Yes
W22	Fracture-related surgery	Orthopaedics	Orthopaedics	Yes
W23	Fracture-related surgery	Orthopaedics	Orthopaedics	No
W24	Fracture-related surgery	Orthopaedics	Orthopaedics	Yes
W25	Fracture-related surgery	Orthopaedics	Orthopaedics	No
W26	Fracture-related surgery	Orthopaedics	Orthopaedics	Yes
W28	Fracture-related surgery	Orthopaedics	Orthopaedics	Yes
W30	Fracture-related surgery	Orthopaedics	Orthopaedics	Yes
W65	Fracture-related surgery	Orthopaedics	Orthopaedics	Yes
W66	Fracture-related surgery	Orthopaedics	Orthopaedics	Yes
W67	Fracture-related surgery	Orthopaedics	Orthopaedics	No
W59	Fusion of joint	Orthopaedics	Orthopaedics	Yes
W62	Fusion of joint	Orthopaedics	Orthopaedics	Yes
O18	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
O32	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W37	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W38	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W39	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W40	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W41	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W42	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W46	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W47	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W48	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W93	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W94	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
W95	Lower limb joint replacement	Orthopaedics	Orthopaedics	No
T62	Operations on bursa	Orthopaedics	Orthopaedics	Yes
O09	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
O10	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes

W02	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
W11	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
W17	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
W29	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
W33	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
W68	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
W70	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
X01	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
X02	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
X20	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
X21	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
X27	Other day-case orthopaedics	Orthopaedics	Orthopaedics	Yes
A48	Other day-case spinal surgery	Orthopaedics	Orthopaedics	Yes
V47	Other day-case spinal surgery	Orthopaedics	Orthopaedics	Yes
V50	Other day-case spinal surgery	Orthopaedics	Orthopaedics	Yes
V52	Other day-case spinal surgery	Orthopaedics	Orthopaedics	Yes
V54	Other day-case spinal surgery	Orthopaedics	Orthopaedics	Yes
V55	Other day-case spinal surgery	Orthopaedics	Orthopaedics	Yes
O35	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W01	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W05	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W10	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W18	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W27	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W31	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W32	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W43	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W52	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W60	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W61	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W63	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
W64	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
X05	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
X19	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
X22	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
X23	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
X24	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
X25	Other inpatient orthopaedics	Orthopaedics	Orthopaedics	No
A44	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
A45	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
A47	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
A49	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
A51	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V23	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V24	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V26	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V27	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V28	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V29	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V30	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V31	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V32	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V33	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V34	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V35	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V36	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V40	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V41	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V42	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V43	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V44	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V45	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V46	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V49	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V51	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V56	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V57	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V67	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V68	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V69	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No
V70	Other inpatient spinal surgery	Orthopaedics	Orthopaedics	No

W58	Other reconstruction of joint	Orthopaedics	Orthopaedics	No
S64	Procedures on nail, nail bed	Orthopaedics	Orthopaedics	Yes
S66	Procedures on nail, nail bed	Orthopaedics	Orthopaedics	Yes
S68	Procedures on nail, nail bed	Orthopaedics	Orthopaedics	Yes
S70	Procedures on nail, nail bed	Orthopaedics	Orthopaedics	Yes
A60	Procedures on peripheral nerves	Orthopaedics	Orthopaedics	Yes
A61	Procedures on peripheral nerves	Orthopaedics	Orthopaedics	Yes
A65	Procedures on peripheral nerves	Orthopaedics	Orthopaedics	Yes
A66	Procedures on peripheral nerves	Orthopaedics	Orthopaedics	Yes
A67	Procedures on peripheral nerves	Orthopaedics	Orthopaedics	Yes
A68	Procedures on peripheral nerves	Orthopaedics	Orthopaedics	Yes
A69	Procedures on peripheral nerves	Orthopaedics	Orthopaedics	Yes
A73	Procedures on peripheral nerves	Orthopaedics	Orthopaedics	Yes
W03	Reconstruction of foot	Orthopaedics	Orthopaedics	Yes
W04	Reconstruction of foot	Orthopaedics	Orthopaedics	No
V37	Spinal fusion	Orthopaedics	Orthopaedics	No
V38	Spinal fusion	Orthopaedics	Orthopaedics	No
V39	Spinal fusion	Orthopaedics	Orthopaedics	No
V66	Spinal fusion	Orthopaedics	Orthopaedics	No
A57	Spinal nerve root procedure	Orthopaedics	Orthopaedics	Yes
V48	Spinal nerve root procedure	Orthopaedics	Orthopaedics	Yes
T64	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T65	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T67	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T68	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T69	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T70	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T71	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T72	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T74	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T76	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	No
T77	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	No
T79	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T80	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T81	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
T83	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
W72	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
W73	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
W74	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
W75	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
W76	Surgery on ligament, tendon, muscle	Orthopaedics	Orthopaedics	Yes
O06	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O07	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O08	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O21	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O22	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O23	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O24	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O25	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O26	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O37	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O38	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O39	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
O40	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
W49	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
W50	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
W51	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
W96	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
W97	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
W98	Upper limb joint replacement	Orthopaedics	Orthopaedics	No
N30	Circumcision, prepuceplasty	Urology	Urology	Yes
M34	Cystectomy	Urology	Urology	No
M35	Cystectomy	Urology	Urology	No
M14	Extracorporeal fragmentation of calculus of kidney	Urology	Urology	Yes
N17	Male sterilisation	Urology	Urology	Yes
M02	Nephrectomy, uretectomy	Urology	Urology	No
M03	Nephrectomy, uretectomy	Urology	Urology	No
M18	Nephrectomy, uretectomy	Urology	Urology	No
M36	Operations on bladder	Urology	Urology	No
M37	Operations on bladder	Urology	Urology	No
M43	Operations on bladder	Urology	Urology	Yes

M48	Operations on bladder	Urology	Urology	Yes
M49	Operations on bladder	Urology	Urology	Yes
M65	Operations on bladder	Urology	Urology	No
M70	Operations on bladder	Urology	Urology	Yes
M16	Other day-case urology	Urology	Urology	Yes
M22	Other day-case urology	Urology	Urology	Yes
M28	Other day-case urology	Urology	Urology	Yes
M31	Other day-case urology	Urology	Urology	Yes
M32	Other day-case urology	Urology	Urology	Yes
M62	Other day-case urology	Urology	Urology	Yes
M71	Other day-case urology	Urology	Urology	Yes
M75	Other day-case urology	Urology	Urology	Yes
M79	Other day-case urology	Urology	Urology	Yes
M81	Other day-case urology	Urology	Urology	Yes
M83	Other day-case urology	Urology	Urology	Yes
N01	Other day-case urology	Urology	Urology	Yes
N20	Other day-case urology	Urology	Urology	Yes
N22	Other day-case urology	Urology	Urology	Yes
N24	Other day-case urology	Urology	Urology	Yes
N27	Other day-case urology	Urology	Urology	Yes
N28	Other day-case urology	Urology	Urology	Yes
N32	Other day-case urology	Urology	Urology	Yes
N34	Other day-case urology	Urology	Urology	Yes
M04	Other inpatient urology	Urology	Urology	No
M05	Other inpatient urology	Urology	Urology	No
M06	Other inpatient urology	Urology	Urology	No
M08	Other inpatient urology	Urology	Urology	No
M15	Other inpatient urology	Urology	Urology	No
M19	Other inpatient urology	Urology	Urology	No
M20	Other inpatient urology	Urology	Urology	No
M21	Other inpatient urology	Urology	Urology	No
M23	Other inpatient urology	Urology	Urology	No
M24	Other inpatient urology	Urology	Urology	No
M25	Other inpatient urology	Urology	Urology	No
M38	Other inpatient urology	Urology	Urology	No
M39	Other inpatient urology	Urology	Urology	No
M41	Other inpatient urology	Urology	Urology	No
M54	Other inpatient urology	Urology	Urology	No
M60	Other inpatient urology	Urology	Urology	No
M64	Other inpatient urology	Urology	Urology	No
N26	Other inpatient urology	Urology	Urology	No
N29	Other inpatient urology	Urology	Urology	No
X15	Other inpatient urology	Urology	Urology	No
X16	Other inpatient urology	Urology	Urology	No
M12	Other interventional radiology	Urology	Urology	Yes
M13	Percutaneous puncture of kidney	Urology	Urology	No
M61	Prostatectomy	Urology	Urology	No
N03	Scrotal surgery	Urology	Urology	Yes
N05	Scrotal surgery	Urology	Urology	Yes
N06	Scrotal surgery	Urology	Urology	Yes
N07	Scrotal surgery	Urology	Urology	Yes
N08	Scrotal surgery	Urology	Urology	Yes
N09	Scrotal surgery	Urology	Urology	Yes
N10	Scrotal surgery	Urology	Urology	Yes
N11	Scrotal surgery	Urology	Urology	Yes
N13	Scrotal surgery	Urology	Urology	Yes
N15	Scrotal surgery	Urology	Urology	Yes
N18	Scrotal surgery	Urology	Urology	Yes
N19	Scrotal surgery	Urology	Urology	Yes
M01	Transplant surgery	Urology	Urology	No
M17	Transplant surgery	Urology	Urology	Yes
M33	Ureteric stent procedures	Urology	Urology	No
M07	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	No
M09	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M10	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	No
M11	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M26	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	No

M27	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M29	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M30	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M42	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	No
M44	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	No
M45	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M56	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M66	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	No
M67	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M68	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M76	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M77	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M85	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M86	Ureteroscopy, cystoscopy & related procedures	Urology	Urology	Yes
M72	Urethral surgery	Urology	Urology	No
M73	Urethral surgery	Urology	Urology	Yes

Table 9.2: Baseline data taken from Annual Hospital Episode Statistics Hospital Admitted Patient Care Activity (AHES-APC) datasets

OPCS code	Estimated number of elective procedures		Mean length of hospital stay in 2018-19	Proportion of procedures completed as day-cases in 2018-19	Average wait (days) on the waiting list for patients operated in 2018-19
	2018-19	2020-21			
A01	216	130	7.7	0.5%	72.4
A02	3,963	3,531	6.9	0.2%	23.1
A03	39	16	3.3	0.0%	63.5
A04	526	387	6.0	9.9%	13.3
A05	139	127	17.5	0.7%	29.9
A06	27	22	3.9	11.2%	65.0
A07	98	69	14.4	1.0%	95.9
A08	642	536	5.4	10.0%	10.9
A10	773	460	5.3	71.9%	19.3
A11	502	318	10.4	0.6%	61.6
A12	1,376	928	10.6	1.0%	59.0
A13	356	298	5.3	7.6%	34.9
A14	819	1,107	5.9	31.4%	36.9
A16	93	116	11.6	0.0%	38.8
A17	306	274	7.3	0.3%	40.6
A18	14	9	8.2	0.0%	20.6
A20	614	380	13.1	13.7%	62.5
A22	26	9	9.8	38.0%	33.8
A24	38	12	5.4	7.9%	116.8
A25	8	4	4.6	12.5%	139.6
A26	427	267	0.9	70.5%	66.9
A27	5	5	4.3	41.7%	24.3
A28	54	30	1.1	76.0%	54.8
A29	374	254	8.5	4.3%	87.3
A30	20	16	2.8	29.6%	66.9
A31	48	14	1.0	64.6%	30.4
A32	511	268	3.9	2.9%	106.3
A34	8	0	3.3	12.9%	66.3
A36	557	438	0.5	84.7%	85.1
A38	1,303	1,182	8.6	0.2%	49.7
A39	192	93	7.0	2.1%	86.4
A40	55	22	10.9	0.0%	121.8
A41	973	663	10.7	0.4%	15.7
A42	47	41	7.4	10.6%	43.8
A43	205	174	11.5	0.5%	56.0
A44	612	491	9.0	0.3%	46.5
A45	84	30	11.1	4.8%	64.0
A47	27	21	2.0	22.2%	18.3
A48	3,869	1,847	0.9	73.9%	86.9
A49	278	173	7.6	1.1%	99.6
A51	305	236	8.3	19.7%	98.4
A57	48,974	19,695	0.4	98.0%	104.8
A59	417	178	0.7	84.8%	98.2
A60	5,976	3,802	0.2	98.5%	135.1
A61	4,052	1,539	0.3	88.4%	92.4
A62	2,453	2,110	0.7	87.6%	10.2
A63	36	23	2.1	42.2%	47.5
A64	960	727	0.4	91.4%	5.2
A65	44,564	20,323	0.0	99.0%	72.3
A66	117	43	0.4	80.3%	86.0

A67	4,739	2,200	0.1	93.0%	86.3
A68	1,197	533	0.5	78.3%	86.1
A69	1,479	604	0.1	95.6%	91.7
A73	37,046	16,201	0.3	97.6%	108.8
A75	170	41	1.5	56.0%	78.9
B01	147	71	6.4	0.0%	55.6
B02	0	0	-	0.0%	0.0
B04	1,116	878	5.7	0.3%	65.0
B06	26	29	6.6	0.0%	25.3
B08	11,210	7,799	1.7	5.6%	72.2
B09	19	9	2.3	0.0%	33.8
B10	860	388	1.1	28.6%	102.8
B12	2,246	1,532	1.2	88.6%	27.3
B14	4,751	2,753	1.2	23.8%	107.9
B16	85	65	1.1	29.4%	103.7
B17	4	9	17.3	0.0%	1.0
B18	411	339	4.1	1.0%	33.7
B20	25	24	7.5	28.0%	49.2
B22	870	633	3.6	1.3%	62.5
B23	2	4	1.0	50.0%	5.0
B25	219	185	3.1	56.6%	17.0
B27	17,937	15,009	1.8	19.6%	33.3
B28	42,943	32,922	0.2	80.4%	25.3
B29	1,416	392	1.9	34.6%	123.6
B30	3,639	1,575	1.0	53.9%	91.7
B31	3,963	1,544	0.9	36.1%	106.2
B32	4,806	3,136	1.6	90.4%	19.5
B33	700	384	1.6	62.1%	47.4
B34	2,511	1,671	0.1	93.1%	36.0
B35	1,165	535	0.1	96.0%	46.6
B36	2,859	727	0.1	94.5%	121.3
B37	4,958	2,428	0.7	79.3%	119.1
B38	7	4	3.6	28.6%	19.8
B39	1,032	284	5.0	2.0%	229.7
B40	9	0	0.0	100.0%	59.6
B41	986	615	0.2	80.9%	23.5
C01	679	497	2.6	17.4%	47.3
C02	268	153	0.9	64.3%	74.4
C03	129	58	0.4	71.3%	96.0
C04	119	57	0.6	70.7%	70.9
C05	262	100	1.0	41.7%	61.1
C06	688	410	1.6	39.9%	68.5
C08	690	292	1.2	26.7%	25.1
C09	436	232	0.0	97.0%	98.5
C10	3,814	2,491	0.3	96.6%	66.7
C11	6,113	3,919	0.1	97.8%	66.7
C12	20,984	10,211	0.0	98.8%	60.8
C13	3,396	1,580	0.0	98.2%	100.9
C14	2,010	1,287	0.2	94.2%	63.8
C15	12,855	6,635	0.0	98.7%	83.7
C16	761	422	1.0	93.4%	55.2
C17	731	506	0.5	93.7%	67.6
C18	5,349	2,406	0.0	98.6%	111.3
C19	504	193	0.5	96.4%	57.1
C20	86	43	1.7	88.5%	56.7
C22	6,730	3,142	0.1	99.2%	58.5
C23	253	113	0.1	96.5%	97.3
C24	301	197	0.3	87.1%	63.2

C25	3,617	1,016	0.2	80.5%	127.4
C26	102	47	0.5	84.6%	74.4
C27	2,880	793	0.0	98.2%	90.2
C29	3,688	1,211	0.0	99.3%	76.4
C31	6,848	2,536	0.0	96.7%	126.2
C32	2,465	881	0.0	96.9%	121.0
C33	1,066	357	0.0	97.6%	114.0
C34	250	82	0.0	98.8%	95.3
C35	312	128	0.0	97.8%	109.9
C37	816	379	0.1	97.9%	100.0
C39	2,710	1,193	0.1	96.9%	71.6
C40	386	215	0.4	90.4%	62.5
C41	44	18	0.5	91.0%	80.7
C43	1,166	620	0.2	98.3%	44.4
C44	2,569	1,498	0.4	71.9%	113.1
C45	1,557	883	0.3	97.5%	80.6
C46	3,462	1,910	0.7	77.1%	97.9
C47	1,787	1,080	0.6	96.8%	59.7
C49	203	106	0.0	97.5%	78.7
C51	3,002	1,952	0.6	97.8%	80.2
C52	465	321	0.0	96.8%	59.8
C53	25	8	0.0	96.0%	67.3
C54	716	553	0.2	85.3%	27.1
C55	39	33	1.2	74.7%	27.6
C57	249	182	0.7	84.9%	27.9
C59	116	76	0.4	88.1%	47.0
C60	9,246	6,723	0.1	92.3%	65.5
C61	2,573	2,117	0.0	97.6%	66.7
C62	2,936	1,796	0.2	98.3%	62.0
C64	229	150	0.1	95.8%	65.4
C65	3,619	2,356	0.0	97.2%	40.1
C66	2,782	2,394	0.1	98.4%	36.4
C67	39	66	1.3	82.1%	38.0
C69	915	567	0.8	90.6%	24.2
C71	3,811	1,260	0.1	98.5%	51.3
C72	29	15	0.0	96.6%	92.6
C73	17,893	18,361	0.0	99.6%	66.1
C74	278	242	0.7	75.9%	37.4
C75	423,494	233,483	0.0	99.4%	81.6
C77	150	65	0.0	97.6%	55.1
C79	106,809	98,757	0.1	97.4%	41.1
C80	1,208	917	0.2	88.2%	60.9
C81	857	578	0.2	93.5%	26.9
C82	8,536	6,158	0.3	96.8%	45.9
C83	0	2	-	0.0%	0.0
C84	241	149	0.7	66.4%	31.6
C85	1,811	1,099	0.1	93.5%	23.9
C86	4,117	1,887	0.3	97.4%	67.3
C87	1,058	1,571	0.4	97.7%	61.5
C88	59	38	0.0	100.0%	4.3
C89	2,247	1,953	0.0	99.2%	38.2
C90	39	21	0.0	97.4%	97.9
C91	0	4	-	0.0%	0.0
D01	2,088	1,178	0.3	93.3%	71.3
D02	16,307	11,422	0.1	98.2%	53.7
D03	1,584	528	0.4	80.9%	115.8
D04	172	83	1.4	79.8%	19.0
D05	31	12	2.3	90.6%	75.2

D06	3,503	2,114	0.5	96.8%	39.6
D07	3,849	1,688	1.4	93.0%	32.9
D08	940	333	1.8	81.9%	69.4
D10	3,076	1,419	1.2	53.8%	123.9
D12	1,191	525	0.9	64.3%	125.6
D13	1,930	560	0.1	94.2%	95.0
D14	8,614	3,191	0.3	78.8%	126.2
D15	23,216	4,385	0.3	95.3%	86.4
D16	1,334	419	0.2	78.9%	133.6
D17	682	219	0.3	72.0%	133.7
D19	797	326	0.7	81.3%	81.2
D20	2,986	847	0.3	96.1%	69.0
D22	399	108	0.2	95.5%	114.2
D23	184	35	0.2	91.3%	61.2
D24	1,392	823	1.0	38.3%	65.8
D26	97	26	1.3	43.3%	114.6
D28	1,263	425	0.3	96.1%	70.9
E01	101	107	4.0	13.9%	35.5
E02	3,180	1,086	0.5	65.3%	132.9
E03	19,887	5,878	0.2	85.2%	98.4
E04	4,424	1,431	0.2	88.0%	107.3
E05	2,338	808	1.7	82.2%	71.9
E07	2,382	546	0.3	77.8%	143.8
E08	7,490	2,928	0.4	81.4%	86.5
E09	27,351	19,272	0.1	97.8%	64.4
E10	605	363	0.3	95.9%	41.1
E11	27	26	0.4	77.8%	64.1
E12	86	36	0.8	80.3%	75.7
E13	4,944	2,072	0.5	79.1%	96.8
E14	3,283	1,279	0.6	75.0%	107.6
E15	363	182	1.8	60.0%	92.2
E16	158	69	1.9	59.6%	89.3
E17	759	431	0.7	76.3%	86.5
E19	361	335	17.6	4.1%	20.5
E20	6,155	1,454	0.2	87.7%	99.9
E21	166	61	2.3	6.0%	135.9
E23	331	144	5.4	23.0%	80.3
E24	1,076	502	2.0	40.4%	73.3
E25	7,539	4,549	1.2	84.0%	29.1
E27	650	376	2.9	71.8%	46.4
E28	260	119	2.0	33.9%	90.1
E29	369	359	21.2	7.0%	22.9
E30	47	19	3.8	42.9%	55.1
E31	141	91	6.1	20.6%	56.9
E33	566	251	1.1	75.1%	81.0
E34	5,286	3,020	0.8	75.3%	44.9
E35	1,893	1,157	1.7	64.7%	48.6
E38	1,005	624	0.2	94.7%	64.7
E39	34	36	6.6	32.1%	59.9
E40	25	16	7.5	8.0%	76.5
E41	232	151	3.8	42.7%	50.3
E42	1,992	1,813	19.0	26.1%	44.7
E43	158	84	4.9	24.7%	74.0
E44	0	2	-	0.0%	0.0
E46	76	58	6.2	5.3%	32.6
E47	33	26	13.8	27.4%	14.1
E48	1,270	819	2.9	41.1%	22.4
E49	36,042	15,554	1.5	81.4%	15.4

E50	804	607	3.1	33.7%	25.4
E51	1,200	727	2.0	46.9%	50.0
E52	170	92	4.2	10.6%	26.7
E53	52	32	37.6	1.9%	15.5
E54	10,201	7,986	6.5	0.1%	22.6
E55	1,809	1,166	6.1	0.1%	33.8
E57	51	25	7.4	5.9%	25.2
E59	12,095	9,925	1.0	76.9%	12.2
E61	463	394	5.6	11.9%	29.4
E62	80	57	2.6	10.0%	45.8
E63	16,673	13,000	0.6	88.8%	10.6
E64	877	689	0.4	80.4%	96.1
E66	366	329	0.3	85.8%	64.1
E67	29	2	3.4	62.1%	27.9
F01	124	87	1.3	83.1%	46.7
F02	9,189	5,182	0.1	97.6%	56.3
F03	663	374	1.2	20.7%	105.4
F04	146	83	0.9	72.1%	74.3
F05	1,438	804	0.3	94.0%	61.7
F06	2,832	1,558	0.2	97.8%	40.0
F18	3,095	1,621	0.2	90.7%	78.4
F20	3,170	1,899	0.1	97.4%	43.9
F22	1,014	899	8.2	10.2%	27.5
F23	4,035	2,435	0.4	84.5%	40.9
F24	6,717	3,968	0.2	94.7%	25.0
F26	4,566	2,009	1.0	71.0%	68.4
F28	1,682	907	0.6	86.7%	49.6
F29	1,178	688	1.5	3.5%	127.4
F30	240	98	1.6	19.6%	145.0
F32	2,734	1,219	0.2	91.5%	48.5
F34	45,021	15,636	0.4	65.9%	96.2
F36	1,793	1,150	1.1	81.0%	29.4
F38	4,178	2,112	1.3	82.5%	46.3
F39	74	44	4.7	37.9%	87.3
F40	108	50	0.8	85.3%	72.6
F42	8,050	3,703	0.4	97.0%	35.3
F44	4,332	2,484	1.8	12.2%	81.0
F45	1,072	547	0.8	44.5%	77.3
F46	55	34	3.6	65.0%	83.3
F48	1,742	1,193	1.3	92.7%	44.7
F50	14	7	0.5	50.0%	131.8
F51	535	196	0.2	88.1%	86.9
F52	44	14	0.8	65.9%	127.3
F53	77	50	1.1	79.1%	86.5
F55	285	86	0.1	93.7%	114.2
F56	134	39	0.3	92.6%	80.8
F58	171	103	2.2	84.9%	92.5
G01	1,403	1,008	12.7	0.1%	31.2
G02	87	62	12.6	0.0%	22.9
G03	212	163	12.9	1.9%	25.7
G04	27	21	5.5	3.7%	72.8
G05	18	12	11.9	0.0%	57.5
G06	25	11	12.8	27.9%	63.1
G07	169	137	18.8	5.9%	38.6
G08	16	16	16.3	30.8%	35.4
G09	531	311	2.9	5.1%	98.5
G10	38	16	1.3	84.3%	37.5
G11	14	10	8.6	21.4%	12.5

G12	63	59	0.5	79.4%	29.3
G13	8	7	4.4	12.3%	21.8
G14	426	214	0.7	83.3%	50.7
G15	4,876	3,885	2.1	65.5%	32.6
G16	9,655	6,265	0.9	86.8%	28.3
G17	15	7	0.9	73.3%	32.5
G18	462	257	1.0	61.6%	55.8
G19	512	265	1.0	83.2%	39.3
G20	7	23	3.7	27.8%	7.5
G21	9,211	4,318	0.8	86.4%	43.9
G23	1,975	990	3.7	7.0%	123.8
G24	2,628	960	3.0	13.1%	129.3
G25	219	114	3.6	12.4%	115.1
G26	1	0	49.7	0.0%	0.0
G27	349	324	11.3	0.3%	24.9
G28	3,307	1,283	3.9	0.7%	118.9
G29	296	236	4.2	4.4%	41.9
G30	1,384	362	0.9	59.0%	82.1
G31	30	23	9.6	6.7%	143.4
G32	1,840	626	2.6	3.2%	135.4
G33	2,363	913	5.8	6.6%	101.1
G34	7,423	5,754	6.0	47.2%	42.1
G35	8	7	8.1	0.0%	79.3
G36	90	47	8.1	10.0%	82.3
G38	932	592	2.8	47.7%	86.8
G40	178	174	3.7	4.5%	48.1
G41	13	14	8.8	46.4%	24.3
G42	1,965	1,527	0.3	80.3%	40.4
G43	18,182	11,949	2.1	69.5%	37.2
G44	26,398	18,781	4.6	59.4%	32.8
G45	685,821	415,882	0.5	91.8%	28.5
G46	402	352	4.1	41.8%	32.7
G48	515	231	1.3	77.0%	77.4
G49	55	59	15.0	10.9%	31.9
G50	39	26	8.2	10.2%	42.0
G51	96	80	14.3	1.0%	49.4
G52	5	9	8.7	0.0%	9.0
G53	109	94	11.2	4.6%	62.4
G54	327	270	4.8	51.6%	26.8
G55	283	148	0.7	73.4%	25.6
G57	37	16	5.1	35.1%	29.7
G58	205	215	13.0	1.9%	55.4
G59	20	22	9.5	10.2%	32.5
G60	1,045	1,059	8.9	43.3%	33.0
G61	59	39	10.2	3.4%	99.9
G62	4	2	0.5	75.0%	72.0
G63	68	19	10.8	36.7%	28.1
G64	1,658	449	5.9	38.2%	18.1
G65	199	134	1.5	74.8%	49.8
G67	978	2,149	6.6	56.6%	31.8
G68	1	0	22.1	0.0%	0.0
G69	1,403	1,011	13.2	1.1%	60.3
G70	128	89	7.0	10.9%	60.9
G71	64	45	13.1	0.0%	51.7
G72	146	71	12.1	0.0%	130.1
G73	353	291	11.9	4.5%	72.8
G74	1,045	748	14.3	0.1%	59.1
G75	5,015	2,628	7.4	2.6%	90.0

G76	48	24	8.5	0.0%	64.5
G78	138	96	11.0	13.8%	67.8
G79	139	94	3.2	66.9%	48.6
G80	11,448	6,940	0.5	92.8%	36.1
G82	61	16	4.0	35.8%	46.8
H01	827	798	2.8	16.8%	43.2
H02	1,386	1,263	2.7	32.8%	71.4
H03	163	104	5.0	28.9%	101.4
H04	563	383	10.6	0.0%	74.0
H05	484	358	11.7	0.8%	57.5
H06	1,406	1,344	10.2	0.1%	24.2
H07	8,399	7,668	8.4	0.1%	28.8
H08	175	143	12.1	0.0%	35.2
H09	1,135	938	9.4	0.1%	29.1
H10	1,937	1,382	9.2	0.2%	49.6
H11	552	351	12.4	1.1%	54.3
H12	99	74	3.3	37.3%	48.7
H13	36	28	13.8	0.0%	27.6
H14	151	116	5.1	45.7%	79.9
H15	4,394	2,783	8.7	2.7%	84.2
H16	17	15	8.8	17.9%	75.9
H17	46	16	5.6	28.3%	39.1
H18	14	4	2.1	79.6%	47.8
H19	152	82	9.3	51.2%	45.8
H20	196,045	150,592	0.1	97.7%	39.0
H21	1,062	785	1.7	76.8%	37.7
H22	419,132	280,442	0.1	97.6%	35.8
H23	58,210	25,684	0.1	97.9%	25.7
H24	1,863	1,512	3.3	65.7%	30.8
H25	310,417	132,825	0.4	94.5%	25.6
H26	685	279	0.6	93.7%	31.1
H27	86	62	4.1	69.7%	36.7
H28	702	346	1.6	86.7%	54.3
H29	606	553	12.4	2.1%	54.7
H30	283	87	4.6	59.1%	67.9
H31	104	57	5.4	39.5%	17.8
H32	38	16	15.5	0.0%	106.0
H33	11,502	9,781	9.5	0.2%	37.3
H34	548	299	1.7	29.2%	110.3
H35	899	342	2.5	16.7%	153.4
H36	485	190	3.7	5.8%	106.6
H37	15	6	0.0	100.0%	33.3
H40	190	129	1.5	60.2%	51.8
H41	4,194	2,684	1.9	53.7%	56.0
H42	1,166	524	1.7	52.3%	105.4
H44	3,600	1,989	2.0	82.1%	66.4
H46	2,868	1,403	0.9	93.0%	62.6
H47	16	8	4.7	50.0%	85.3
H48	8,718	3,732	0.1	94.0%	75.1
H49	557	376	0.3	90.8%	77.9
H50	288	239	3.9	12.8%	96.3
H51	8,256	3,243	0.3	86.7%	91.1
H52	20,018	8,963	0.1	97.5%	55.6
H53	361	134	0.8	83.2%	91.0
H54	800	464	0.9	85.6%	59.2
H55	13,277	7,603	0.4	90.6%	79.4
H56	10,140	4,948	0.2	94.2%	69.1
H57	113	32	0.5	89.4%	130.6

H58	2,508	1,850	1.5	72.6%	31.3
H59	5,556	2,171	0.4	85.1%	86.5
H60	2,820	1,807	0.6	85.3%	57.0
H62	1,202	618	1.9	79.5%	48.8
H66	354	162	2.9	72.6%	105.2
H68	323	205	0.6	96.4%	64.5
H69	1,274	684	0.3	96.5%	62.8
H70	48	19	1.2	79.7%	59.5
H71	0	48		0.0%	0.0
J01	385	227	13.2	0.3%	95.7
J02	2,533	2,221	6.9	0.8%	32.3
J03	425	288	5.7	2.8%	38.9
J04	11	4	5.8	27.0%	52.8
J05	86	67	6.6	10.5%	28.4
J06	20	19	5.7	5.0%	19.6
J07	9	15	11.6	0.0%	34.2
J08	79	50	3.3	8.9%	43.6
J09	279	210	1.9	58.2%	27.3
J10	1,887	1,659	2.3	4.6%	21.1
J11	469	378	4.6	26.0%	24.6
J12	1,507	1,547	7.0	11.5%	23.0
J13	13,173	10,155	2.2	70.8%	20.8
J14	1,022	700	3.0	58.6%	20.5
J15	12	23	7.5	0.0%	39.5
J16	11	2	4.5	53.8%	82.8
J17	284	253	1.0	81.4%	18.8
J18	65,581	37,868	1.5	57.6%	90.6
J19	8	5	4.1	51.9%	111.2
J20	22	23	4.5	18.3%	64.5
J21	161	166	9.8	15.6%	146.5
J23	34	24	3.0	56.4%	64.8
J24	77	128	10.8	24.7%	19.8
J25	35	41	2.3	69.4%	16.1
J26	21	21	4.3	51.9%	70.0
J27	80	40	7.6	1.3%	37.8
J28	29	16	5.1	13.9%	41.4
J29	187	135	12.0	0.0%	43.6
J30	53	19	7.8	11.3%	47.4
J31	32	42	4.1	59.8%	41.1
J32	17	3	7.6	17.5%	87.0
J33	84	68	8.5	8.3%	48.4
J34	157	46	2.0	60.0%	44.4
J35	60	53	3.1	40.1%	27.5
J36	117	121	1.2	74.6%	35.1
J37	85	33	3.7	61.4%	43.3
J38	18,379	14,319	3.6	51.2%	24.5
J39	298	1,140	2.5	52.3%	43.5
J40	6,007	4,263	3.6	50.0%	28.0
J41	4,027	2,774	1.9	60.5%	42.9
J42	847	647	2.8	46.5%	26.4
J43	2,385	1,674	3.3	52.5%	25.2
J44	498	308	2.5	55.1%	31.4
J45	131	123	2.9	61.2%	21.8
J46	62	58	6.0	6.4%	16.5
J47	731	578	10.0	6.3%	15.2
J48	903	735	9.5	13.2%	16.5
J49	10	7	6.3	20.7%	125.3
J50	447	416	6.8	13.4%	13.7

J51	13	9	0.5	61.5%	106.0
J52	15	6	6.7	48.0%	28.4
J53	2,759	1,647	0.4	91.3%	30.8
J54	10	0	7.2	0.0%	0.0
J55	119	81	15.8	0.0%	33.5
J56	1,199	1,077	12.7	0.1%	25.9
J57	611	572	15.8	2.1%	31.6
J58	38	12	7.3	15.9%	34.2
J59	29	7	7.9	3.5%	73.0
J60	94	87	2.4	77.6%	37.9
J61	414	438	8.0	37.5%	19.1
J62	0	0	-	0.0%	0.0
J63	3	0	10.3	66.7%	23.5
J65	36	85	7.1	41.5%	24.0
J66	286	166	11.2	43.3%	21.7
J67	193	147	2.4	69.3%	14.0
J68	29	49	0.5	73.2%	51.1
J69	310	180	7.2	0.3%	52.3
J70	53	19	2.9	11.4%	64.2
J72	242	225	5.4	36.8%	21.1
J73	51	44	0.2	90.2%	28.4
J74	9,951	7,069	0.4	92.2%	21.9
J77	0	0	1.0	0.0%	0.0
K01	3	2	28.2	0.0%	0.0
K02	72	73	60.3	4.2%	51.8
K04	214	206	5.7	0.0%	60.8
K05	2	4	20.5	0.0%	34.0
K06	138	124	8.8	0.0%	98.8
K07	36	23	8.7	0.0%	34.9
K08	25	20	11.1	0.0%	79.0
K09	211	163	8.6	0.9%	82.3
K10	379	219	5.8	0.8%	81.9
K11	431	351	6.3	0.5%	47.8
K12	4	3	5.6	28.6%	126.0
K13	653	427	1.5	9.5%	89.2
K14	26	15	7.8	3.9%	75.3
K15	3	2	5.8	40.0%	24.0
K16	426	909	2.4	34.7%	55.3
K17	200	158	14.4	0.0%	93.5
K18	122	118	6.4	2.5%	93.0
K19	79	29	9.3	1.3%	77.7
K20	72	39	4.2	4.2%	72.5
K22	160	124	7.6	8.1%	44.2
K23	53	199	9.0	28.3%	30.5
K24	210	167	7.7	2.4%	88.2
K25	3,243	2,070	11.8	0.5%	86.0
K26	8,936	7,677	7.8	0.1%	61.2
K27	161	86	12.6	0.6%	97.4
K28	176	110	5.7	1.7%	104.8
K29	14	14	15.0	14.4%	41.4
K30	373	278	12.1	0.8%	100.6
K31	23	23	5.1	4.3%	79.4
K32	0	3	-	0.0%	0.0
K33	397	302	10.4	0.0%	105.6
K34	93	55	11.5	1.1%	80.2
K35	894	561	5.3	13.9%	62.6
K36	1	2	4.5	0.0%	95.0
K37	127	91	4.1	0.0%	84.2

K38	6	9	4.1	0.0%	77.3
K40	1,695	940	11.7	0.2%	76.9
K41	15	16	7.3	0.0%	56.6
K42	3	1	2.4	80.0%	176.0
K43	0	3	-	0.0%	0.0
K44	28	32	7.6	10.5%	54.6
K45	13,829	8,141	9.2	0.0%	67.5
K46	1	3	9.0	0.0%	0.0
K47	15	12	8.7	13.2%	85.0
K48	34	24	8.7	5.9%	67.1
K49	2,606	2,109	2.5	44.7%	61.3
K50	119	77	3.0	30.1%	55.1
K51	543	367	0.9	77.0%	54.1
K52	120	52	3.9	9.2%	60.7
K53	9	4	4.7	31.8%	109.8
K54	99	59	45.8	0.0%	4.8
K55	29	36	8.4	6.8%	35.5
K56	146	92	5.5	10.3%	46.3
K57	11,290	7,204	0.9	51.7%	101.7
K58	2,638	1,686	0.9	75.4%	95.6
K59	10,578	8,645	2.5	52.8%	60.9
K60	33,064	28,817	2.4	51.8%	49.3
K61	1,739	1,666	3.7	40.5%	45.2
K62	10,003	7,507	0.8	42.6%	119.7
K63	113,544	69,061	1.5	71.8%	46.0
K64	29	19	1.3	55.4%	97.0
K65	2,735	1,862	2.6	52.5%	45.0
K66	5	7	2.3	80.0%	47.5
K67	110	73	9.9	0.9%	54.5
K68	270	213	5.9	5.5%	27.4
K69	113	73	8.2	0.9%	31.2
K71	29	23	5.1	14.0%	17.5
K73	2,600	2,437	0.5	83.5%	57.4
K74	352	537	0.7	77.9%	43.2
K75	36,418	27,012	2.2	48.9%	52.8
K76	87	74	6.0	12.7%	74.2
K77	126	114	5.7	12.7%	43.5
K78	8	3	1.6	12.7%	71.0
L01	32	26	12.6	9.4%	33.6
L02	175	117	10.5	16.0%	38.2
L03	504	390	2.1	25.0%	77.0
L04	191	111	14.3	0.0%	1.0
L05	10	7	18.2	20.0%	44.8
L06	20	8	8.9	0.0%	69.1
L07	32	16	10.6	0.0%	69.3
L08	16	15	13.1	6.3%	44.0
L09	141	125	9.1	0.0%	45.9
L10	43	29	6.4	0.0%	53.5
L12	104	69	10.6	0.0%	45.2
L13	583	470	3.0	18.0%	84.4
L16	106	80	12.8	0.0%	44.3
L18	80	82	10.9	2.5%	45.0
L19	2,357	1,545	10.2	0.1%	58.9
L20	42	55	14.0	0.0%	22.7
L21	198	111	11.7	0.5%	63.4
L22	46	36	15.1	4.4%	45.1
L23	393	295	7.1	0.0%	53.1
L25	84	45	6.2	2.4%	54.0

L26	793	496	2.7	45.5%	65.1
L27	3,041	1,765	4.6	0.5%	51.2
L28	84	62	5.0	6.0%	41.6
L29	3,136	2,129	3.1	0.2%	14.8
L30	103	52	4.4	10.7%	58.2
L31	456	415	3.2	41.9%	37.3
L33	348	268	13.1	1.4%	72.6
L34	16	15	4.1	6.4%	55.8
L35	3,405	2,410	2.3	65.9%	39.8
L37	57	38	6.1	0.0%	47.5
L38	91	75	4.9	25.3%	36.1
L39	318	252	3.2	46.2%	45.0
L41	4	3	8.0	0.0%	54.0
L42	8	4	4.6	12.4%	47.3
L43	824	563	4.1	31.3%	37.9
L45	16	26	8.6	0.0%	54.9
L46	14	9	7.9	22.0%	41.6
L47	458	338	5.5	24.5%	35.4
L48	1	3	9.4	0.0%	0.0
L49	56	26	8.3	3.6%	39.7
L50	8	6	14.9	0.0%	55.6
L51	456	221	8.6	0.0%	54.9
L52	90	36	5.7	0.0%	36.9
L53	48	39	8.0	8.3%	71.6
L54	4,130	2,717	2.3	58.3%	55.1
L56	6	1	13.2	0.0%	24.0
L57	246	154	6.6	2.8%	49.4
L58	49	62	15.1	2.0%	28.5
L59	2,180	1,405	9.8	0.8%	39.1
L60	2,147	1,297	6.5	0.4%	52.5
L62	282	181	8.4	4.6%	41.1
L63	10,703	7,213	3.6	53.4%	41.2
L65	22	10	11.9	8.9%	31.4
L66	1,427	781	4.3	49.9%	39.2
L67	4,019	2,157	0.7	93.0%	9.6
L68	139	118	3.1	52.4%	20.6
L69	75	78	5.5	16.0%	60.9
L70	3,700	1,391	1.2	81.8%	98.6
L71	3,877	2,230	4.1	21.9%	57.8
L72	470	304	4.0	48.6%	40.9
L73	8	1	1.0	37.5%	55.3
L74	14,277	11,067	1.3	72.4%	38.6
L75	1,691	827	2.4	64.5%	77.8
L76	4	0	7.0	0.0%	68.0
L77	4	13	20.5	0.0%	129.0
L79	1,801	1,198	4.8	53.5%	40.1
L80	31	27	5.8	16.4%	75.9
L81	16	6	7.8	12.4%	82.3
L82	9	8	2.6	33.8%	83.3
L83	48	10	2.1	83.3%	98.9
L84	3,077	586	0.1	90.3%	97.7
L85	254	90	0.3	86.3%	100.2
L86	6,123	1,886	0.1	99.1%	94.3
L87	4,471	1,264	0.1	95.7%	91.4
L88	14,886	4,600	0.1	97.9%	100.0
L90	25	17	6.9	32.0%	33.1
L93	379	209	2.5	71.8%	57.2
L94	10,297	10,576	1.6	81.0%	26.4

L95	1,549	766	1.5	79.0%	53.2
L96	49	38	5.2	22.3%	8.3
L97	471	209	4.7	46.1%	70.2
L98	21	14	2.0	60.5%	100.8
L99	24,285	21,446	7.6	50.5%	14.4
M01	1,064	516	8.6	0.0%	36.9
M02	7,013	5,235	4.4	0.3%	40.8
M03	1,803	1,527	3.4	0.4%	42.1
M04	157	81	1.9	21.7%	96.9
M05	625	467	2.7	2.1%	71.1
M06	358	333	6.9	20.4%	42.7
M07	0	3,265	-	0.0%	0.0
M08	57	43	4.6	35.0%	48.0
M09	8,956	4,238	1.0	52.1%	81.6
M10	1,045	606	1.9	19.5%	83.2
M11	913	640	0.8	64.6%	63.6
M12	6	0	4.0	83.3%	20.5
M13	13,869	11,130	4.3	49.6%	21.4
M14	16,278	9,222	0.0	98.8%	46.7
M15	387	271	3.7	49.7%	22.1
M16	6,758	6,210	2.5	54.4%	63.0
M17	108	28	0.2	98.7%	23.2
M18	139	99	7.4	2.9%	45.8
M19	480	299	7.8	21.0%	98.1
M20	231	191	5.4	2.2%	94.0
M21	74	53	6.6	2.7%	74.7
M22	6	5	0.9	31.3%	83.3
M23	23	15	1.8	39.1%	49.9
M24	0	22	-	0.0%	0.0
M25	244	230	2.6	30.0%	95.9
M26	317	271	2.7	41.6%	51.9
M27	16,199	13,763	1.2	58.5%	62.8
M28	1,222	11	1.3	54.4%	58.7
M29	23,155	16,862	1.7	68.2%	53.5
M30	1,479	1,064	0.8	67.0%	62.5
M31	2,851	3,970	0.2	95.6%	20.7
M32	684	522	0.5	75.8%	80.7
M33	1,769	1,840	4.8	40.3%	33.8
M34	1,871	1,535	9.3	1.4%	39.3
M35	142	118	5.5	4.2%	72.2
M36	78	33	9.2	0.0%	123.0
M37	115	72	8.6	3.5%	88.5
M38	3,133	1,643	3.1	44.9%	88.2
M39	184	86	5.6	2.7%	106.1
M41	62	54	2.9	25.9%	102.1
M42	36,776	30,973	1.5	37.3%	36.3
M43	11,846	5,331	0.2	91.6%	111.0
M44	5,229	3,139	1.9	36.6%	94.8
M45	94,771	59,570	0.4	91.8%	45.5
M48	296	165	2.0	71.4%	71.2
M49	58,213	31,974	0.4	96.6%	53.6
M51	81	21	4.5	4.9%	129.0
M52	854	490	2.5	2.5%	121.7
M53	1,188	191	1.0	51.8%	111.0
M54	30	10	6.0	23.4%	108.8
M55	47	13	3.3	21.3%	107.5
M56	3,006	1,392	0.1	90.9%	105.4
M57	70	32	1.2	51.4%	95.9

M58	144	51	0.1	89.6%	82.1
M60	70	30	3.2	12.9%	88.9
M61	9,778	6,226	1.7	2.0%	41.4
M62	34	24	3.6	53.2%	62.3
M64	541	161	1.8	12.0%	113.8
M65	21,043	11,074	2.0	8.5%	106.1
M66	1,396	699	1.1	30.0%	101.9
M67	531	340	1.6	59.0%	75.8
M68	1,317	546	0.2	84.7%	93.3
M70	42,833	27,558	0.1	93.5%	31.0
M71	589	425	0.9	46.5%	38.3
M72	475	253	1.3	30.1%	104.8
M73	3,086	1,181	0.7	56.4%	146.3
M75	90	46	1.2	53.2%	72.9
M76	12,132	6,765	0.5	77.2%	76.2
M77	1,620	1,038	0.4	92.6%	40.8
M79	6,764	2,773	0.3	86.9%	69.9
M81	2,950	1,603	0.4	87.2%	72.8
M83	95	82	0.4	89.3%	19.2
M85	185	80	1.4	73.1%	94.7
M86	154	83	1.2	65.8%	71.4
N01	1,378	624	1.0	91.1%	82.2
N03	567	302	2.1	69.6%	75.1
N05	93	46	0.8	63.2%	54.6
N06	3,629	2,774	0.8	76.9%	38.0
N07	245	142	0.6	87.3%	92.7
N08	943	585	0.4	85.2%	112.7
N09	5,500	2,654	0.2	92.7%	107.0
N10	241	71	0.2	86.4%	117.0
N11	5,844	2,764	0.2	88.2%	98.4
N13	521	325	0.7	84.1%	77.6
N15	2,823	1,142	0.2	93.5%	99.8
N17	8,775	2,499	0.0	99.3%	87.6
N18	26	17	0.5	84.6%	95.0
N19	1,674	918	0.1	96.4%	70.8
N20	235	82	0.3	89.5%	78.5
N22	43	9	0.6	74.4%	67.0
N24	432	183	3.8	64.4%	71.3
N26	465	377	4.4	10.3%	21.1
N27	1,453	734	0.5	86.9%	63.0
N28	3,277	1,078	0.5	81.5%	107.9
N29	501	148	2.1	4.4%	100.2
N30	28,358	12,766	0.2	94.6%	90.6
N32	1,944	1,095	0.6	90.8%	55.0
N34	569	220	0.0	96.7%	85.3
O01	838	623	9.9	4.5%	48.2
O02	294	168	10.5	2.4%	61.6
O03	368	303	6.2	0.8%	56.5
O04	348	320	6.4	8.0%	55.3
O05	245	199	7.5	1.2%	40.0
O06	143	33	4.1	2.1%	118.9
O07	832	309	2.1	0.5%	127.6
O08	48	11	2.9	2.1%	102.0
O09	26	31	2.6	53.8%	111.8
O10	59	15	0.7	67.8%	98.7
O15	1,011	702	14.6	6.5%	0.0
O17	1,381	962	2.3	71.6%	10.0
O18	173	71	6.2	1.2%	117.0

O19	465	167	0.2	89.0%	85.7
O20	1	1	0.0	100.0%	113.0
O21	480	200	4.4	1.5%	123.6
O22	22	8	2.4	0.0%	89.9
O23	80	57	6.4	10.0%	87.1
O24	46	20	2.6	28.5%	49.3
O25	229	217	2.0	37.9%	64.5
O26	134	131	2.1	44.1%	51.0
O27	4,560	2,117	0.5	69.9%	99.8
O29	19,760	5,750	0.2	81.6%	95.9
O32	961	340	2.9	2.9%	128.8
O35	0	30	-	0.0%	0.0
O37	0	36	-	0.0%	0.0
O38	0	84	-	0.0%	0.0
O39	0	54	-	0.0%	0.0
O40	0	111	-	0.0%	0.0
P01	93	49	0.5	74.4%	61.8
P03	1,866	878	0.5	87.3%	59.5
P05	5,064	2,950	1.1	74.4%	47.4
P06	1,561	800	0.2	92.3%	56.1
P07	241	98	0.3	88.5%	83.2
P09	4,206	1,812	0.6	90.7%	42.6
P11	463	168	1.2	84.3%	73.8
P13	1,896	644	1.0	82.0%	83.9
P14	28	15	0.4	82.1%	90.5
P15	461	228	0.2	94.1%	74.9
P17	129	77	1.7	58.1%	68.0
P18	383	156	1.9	11.0%	108.2
P19	208	95	0.3	76.5%	71.3
P20	2,414	1,433	0.4	85.6%	64.1
P21	61	29	3.4	47.7%	89.3
P22	257	76	1.5	7.8%	131.6
P23	18,069	6,023	1.5	8.8%	115.8
P24	1,216	337	1.8	4.7%	130.5
P25	415	135	2.0	24.3%	110.7
P26	669	492	2.0	73.2%	60.8
P27	518	279	0.7	88.5%	46.3
P28	69	27	0.9	52.2%	91.0
P29	1,547	780	0.7	79.3%	47.9
P30	29	36	3.0	37.9%	80.6
P31	1,234	685	0.5	78.3%	93.8
P32	26	9	1.1	50.0%	118.4
Q01	10,670	6,692	0.1	94.8%	37.5
Q02	2,232	650	0.1	96.5%	62.0
Q03	2,764	1,221	0.5	93.6%	31.7
Q05	873	531	0.5	83.9%	53.5
Q07	28,748	19,517	2.8	2.0%	75.3
Q08	5,305	2,889	1.7	3.0%	91.1
Q09	2,965	1,464	2.5	9.6%	110.5
Q10	1,884	1,141	0.3	90.9%	34.1
Q16	8,981	3,698	0.1	92.9%	75.5
Q17	30,458	17,991	0.2	90.8%	50.9
Q18	39,233	21,084	0.1	94.1%	44.9
Q19	3	0	0.0	100.0%	112.7
Q20	1,550	777	1.0	86.2%	59.9
Q22	8,106	5,482	1.3	45.1%	76.1
Q23	6,107	3,710	1.6	37.7%	76.4
Q24	251	188	1.4	52.9%	75.1

Q25	272	163	1.1	66.1%	79.1
Q26	2	2	0.0	100.0%	60.5
Q27	252	88	0.2	82.5%	92.8
Q28	73	27	0.3	84.9%	69.4
Q29	9	5	0.9	33.3%	45.7
Q30	115	40	0.8	78.5%	98.2
Q31	140	77	2.2	51.5%	89.8
Q32	191	86	0.6	75.9%	80.4
Q34	12	10	2.9	66.7%	104.2
Q35	6,006	1,757	0.1	88.0%	88.0
Q36	157	41	0.1	89.8%	94.9
Q37	37	15	0.1	83.8%	69.3
Q38	310	101	0.6	78.3%	92.7
Q39	82	18	0.4	87.8%	40.3
Q41	4,206	1,342	0.1	91.5%	70.5
Q43	1,561	962	4.1	36.3%	80.5
Q44	88	44	1.0	74.8%	87.9
Q45	21	11	1.4	67.4%	56.5
Q47	204	171	3.3	41.2%	63.2
Q49	7,940	4,342	0.9	62.2%	90.2
Q50	159	151	2.1	64.8%	43.7
Q51	151	94	3.1	67.4%	49.5
Q52	203	100	0.7	66.1%	93.9
Q54	1,553	795	0.6	59.4%	100.6
Q55	7,103	4,495	1.2	81.9%	44.0
Q56	15	16	0.5	46.7%	94.4
Q57	8	3	0.4	75.0%	80.8
S01	547	175	0.4	74.0%	115.0
S02	477	101	4.4	6.1%	124.1
S03	136	48	1.0	59.6%	108.0
S04	1,032	260	0.6	79.1%	79.2
S05	2,630	1,943	0.0	98.3%	92.7
S06	203,861	141,448	0.1	96.6%	51.8
S08	6,905	5,251	0.2	98.1%	45.6
S10	320	173	0.6	94.3%	59.0
S11	400	231	0.7	89.3%	62.3
S17	42	28	17.2	4.7%	61.7
S18	126	93	10.3	1.6%	77.0
S19	8	12	9.6	35.5%	52.8
S20	30	24	16.3	13.4%	116.8
S21	5	2	11.9	21.4%	29.5
S22	18	15	2.2	66.6%	3.0
S23	399	138	0.4	83.0%	139.0
S24	80	56	18.0	17.4%	48.8
S25	90	43	10.0	15.6%	44.2
S26	86	47	7.5	60.4%	32.3
S27	1,218	1,141	1.6	90.9%	51.5
S28	5	5	0.6	80.0%	25.3
S29	0	4	-	0.0%	0.0
S30	303	145	1.3	72.6%	63.7
S31	405	180	2.1	74.2%	108.3
S32	0	1	-	0.0%	0.0
S33	264	0	0.1	100.0%	135.2
S34	0	0	-	0.0%	0.0
S35	2,488	1,309	6.5	52.0%	24.6
S36	843	670	1.2	91.7%	49.5
S37	105	57	9.9	57.0%	57.7
S38	1	1	0.0	100.0%	228.0

S39	36	9	0.5	69.4%	123.1
S40	66	56	1.8	74.4%	18.4
S41	765	581	1.4	86.4%	11.1
S42	4,850	3,569	1.2	86.7%	4.9
S43	2,000	974	1.5	87.8%	51.6
S47	8,141	5,094	2.2	73.0%	21.6
S48	226	48	1.1	37.2%	105.3
S49	440	127	0.9	65.6%	67.4
S54	176	85	3.1	63.6%	29.9
S55	1,655	943	2.3	73.3%	4.6
S56	666	365	2.6	74.7%	24.5
S57	12,819	9,758	5.4	62.6%	19.8
S60	3,125	1,235	0.8	84.2%	90.7
S62	1,477	628	0.5	81.7%	109.9
S63	13	11	10.1	61.5%	88.7
S64	2,268	803	0.1	96.7%	68.5
S66	5,217	3,223	0.2	96.9%	15.5
S68	3,630	1,507	0.3	96.3%	65.6
S70	1,941	920	0.4	96.0%	50.4
T01	700	481	2.5	55.4%	47.7
T02	555	200	4.1	18.2%	108.2
T03	212	100	10.0	2.8%	43.5
T05	981	646	5.0	28.3%	45.5
T07	813	424	9.4	0.0%	23.6
T08	336	211	8.0	3.6%	69.4
T09	713	411	5.5	3.6%	18.5
T10	1,753	1,018	6.1	4.6%	12.9
T11	973	735	2.6	21.2%	12.6
T14	884	824	2.5	65.7%	10.3
T15	0	5	6.9	0.0%	0.0
T16	294	141	8.6	0.0%	54.0
T17	34	43	3.5	8.8%	53.8
T19	4,866	2,652	0.9	83.0%	78.5
T20	61,350	26,396	0.5	79.3%	82.7
T21	5,115	2,002	0.8	71.7%	90.5
T22	1,754	766	2.8	72.0%	73.4
T23	160	56	2.0	68.8%	87.5
T24	19,454	7,430	0.7	83.6%	86.4
T25	7,747	2,935	3.5	28.5%	113.2
T26	1,424	513	4.0	22.3%	121.4
T27	6,533	2,331	1.2	73.8%	91.5
T28	418	202	9.1	22.2%	109.7
T29	735	410	1.1	81.1%	77.2
T30	691	416	7.4	17.5%	66.4
T31	2,338	1,573	4.0	61.1%	56.6
T32	391	225	7.9	5.4%	153.7
T33	284	222	7.0	18.3%	53.5
T34	192	131	9.1	24.5%	47.1
T36	1,774	1,668	3.4	54.4%	21.9
T37	236	209	4.7	34.3%	32.1
T38	72	56	4.8	25.0%	32.6
T39	393	381	6.7	28.3%	29.7
T41	1,925	1,342	8.1	31.0%	67.7
T42	9,049	4,578	1.2	70.2%	92.7
T43	14,430	6,717	0.8	81.3%	69.1
T45	1,522	1,277	10.1	39.6%	15.8
T48	206	226	1.9	81.9%	32.3
T50	11	3	1.4	9.1%	85.1

T51	10	10	6.7	60.0%	141.2
T52	14,308	5,098	0.1	95.5%	99.4
T53	450	384	0.9	78.0%	61.0
T54	1,904	860	0.5	95.6%	94.2
T55	617	184	4.1	68.1%	107.6
T56	737	309	0.3	87.1%	115.3
T57	2,122	507	0.4	95.6%	77.8
T59	7,315	2,102	0.0	97.7%	75.6
T60	267	99	0.1	95.1%	95.5
T61	616	178	0.1	99.1%	66.8
T62	12,317	3,589	0.4	96.2%	83.3
T64	1,686	742	0.8	64.4%	112.3
T65	943	436	0.8	82.4%	82.1
T67	10,607	7,386	0.9	77.3%	30.2
T68	447	232	1.5	67.6%	80.3
T69	2,870	908	0.2	89.1%	94.6
T70	4,323	1,684	0.7	71.2%	103.0
T71	480	156	0.3	93.1%	80.0
T72	11,614	4,692	0.4	96.3%	77.7
T74	7,994	2,432	0.2	97.1%	76.9
T76	90	30	10.2	6.6%	135.4
T77	2,109	1,367	2.8	49.5%	71.3
T79	9,691	4,310	0.5	70.9%	78.8
T80	524	222	0.6	70.0%	110.8
T81	2,221	1,359	2.0	83.7%	70.4
T83	830	666	6.7	63.8%	81.7
T85	4,593	4,245	3.1	21.1%	20.9
T86	342	238	2.0	65.1%	18.5
T87	14,277	11,131	2.1	73.6%	16.7
T88	162	106	3.2	70.6%	17.5
T89	28	15	11.3	46.7%	175.7
T90	5	13	0.0	40.0%	0.0
T91	108	51	0.6	78.7%	17.9
T92	309	161	2.3	70.6%	65.6
T94	610	378	0.9	41.2%	74.7
T96	6,870	4,468	1.8	79.7%	63.9
T97	1,237	470	1.1	65.5%	92.5
T98	588	222	1.5	62.8%	96.5
V01	914	487	8.8	2.3%	86.8
V02	127	78	5.5	2.4%	88.5
V03	211	180	16.2	1.9%	49.8
V04	20	7	0.4	80.0%	45.7
V05	563	324	5.0	32.1%	72.5
V06	493	405	5.8	22.1%	37.7
V07	225	124	2.3	56.9%	70.2
V08	104	73	2.8	15.4%	5.4
V09	6,816	1,522	0.3	86.1%	6.0
V10	1,936	506	1.6	2.2%	136.9
V11	541	232	0.9	65.5%	52.5
V12	208	150	4.7	9.1%	88.1
V13	659	324	1.0	37.5%	96.4
V14	1,077	868	7.3	36.2%	53.3
V15	453	229	2.1	18.5%	6.2
V16	853	306	1.4	3.6%	130.0
V17	1,224	632	1.3	77.3%	59.1
V18	153	109	1.7	44.5%	73.8
V19	924	492	1.5	68.3%	61.0
V20	201	76	1.9	6.0%	148.1

V21	2,205	762	0.3	87.8%	109.8
V22	6,097	3,499	4.8	1.7%	91.2
V23	170	86	4.7	1.8%	122.9
V24	470	393	11.6	0.0%	77.7
V25	16,795	8,118	2.8	8.8%	103.1
V26	1,934	936	3.8	7.3%	113.4
V27	55	12	4.5	7.3%	135.5
V28	51	11	2.3	5.9%	130.7
V29	2,464	1,003	3.6	6.7%	102.6
V30	33	15	3.1	6.1%	167.8
V31	75	37	11.6	0.0%	88.9
V32	1	0	6.0	0.0%	316.0
V33	3,812	1,582	2.2	16.9%	88.1
V34	561	227	2.4	13.5%	112.1
V35	13	9	2.7	7.8%	134.8
V36	229	86	1.8	1.7%	94.6
V37	94	67	9.0	1.1%	96.3
V38	1,834	911	4.4	1.5%	154.9
V39	263	113	5.9	0.4%	189.8
V40	2,098	977	7.8	2.7%	120.8
V41	2,536	1,528	6.1	8.2%	143.4
V42	87	48	10.2	1.1%	102.2
V43	243	151	6.8	9.0%	72.3
V44	1,495	599	3.8	36.3%	54.8
V45	19	11	9.2	36.9%	84.1
V46	441	259	11.2	3.9%	100.4
V47	624	587	6.9	55.0%	27.3
V48	16,597	7,088	0.0	99.4%	172.6
V49	26	12	8.4	15.4%	83.4
V50	372	168	2.9	76.7%	80.2
V51	170	111	7.8	0.6%	121.1
V52	343	142	6.6	68.0%	111.7
V54	44,683	11,200	0.2	99.0%	124.9
V55	3	7	0.0	100.0%	85.7
V56	3	0	1.0	33.3%	65.0
V57	1	0	1.0	0.0%	37.0
V66	2	4	16.3	0.0%	141.0
V67	1,591	663	2.7	5.0%	103.5
V68	133	57	2.4	0.8%	96.1
V69	0	505	-	0.0%	0.0
V70	0	10	-	0.0%	0.0
W01	61	28	1.5	39.3%	177.0
W02	202	80	0.7	60.9%	126.6
W03	3,162	957	0.9	62.6%	115.7
W04	2,222	816	3.2	9.8%	136.1
W05	641	459	14.2	3.3%	68.3
W06	6,616	2,700	0.6	83.3%	112.1
W07	79	14	1.7	50.6%	112.7
W08	8,114	3,149	1.3	76.4%	97.7
W09	2,385	1,358	2.0	59.8%	83.4
W10	105	55	4.5	32.4%	93.5
W11	8	4	0.4	75.0%	139.6
W12	1,671	414	1.4	44.6%	109.9
W13	6,572	2,250	0.9	65.1%	100.0
W14	542	213	1.0	70.1%	138.4
W15	5,283	1,566	0.4	80.6%	105.4
W16	2,460	1,057	2.3	34.3%	123.4
W17	591	254	3.0	50.4%	115.5

W18	182	84	5.2	30.8%	73.2
W19	6,968	4,829	6.0	59.9%	25.9
W20	15,417	11,699	3.8	50.0%	14.4
W21	1,142	1,020	3.8	54.9%	15.3
W22	122	80	7.1	67.0%	13.5
W23	6,198	5,319	3.6	49.4%	21.6
W24	6,839	4,238	7.2	74.0%	6.3
W25	404	277	6.9	49.5%	9.0
W26	3,776	2,107	1.5	88.3%	6.1
W27	1,048	784	1.3	39.6%	96.1
W28	29,995	13,779	1.1	79.9%	82.2
W29	46	10	13.8	54.0%	33.7
W30	2,650	1,432	3.9	66.0%	40.9
W31	244	108	2.0	41.4%	82.2
W32	104	49	4.3	35.6%	89.5
W33	1,911	1,080	4.3	62.2%	55.3
W37	29,288	10,574	5.0	0.6%	114.0
W38	29,501	10,358	3.9	0.4%	108.5
W39	1,341	1,026	6.5	1.0%	117.0
W40	82,315	26,232	3.9	0.4%	118.7
W41	2,419	844	4.1	0.4%	118.0
W42	1,826	1,145	10.2	7.1%	119.4
W43	137	58	4.3	19.0%	142.2
W44	1,073	326	0.4	73.6%	126.0
W45	725	250	0.9	74.5%	129.4
W46	291	283	12.1	0.0%	98.5
W47	98	55	12.8	6.1%	111.1
W48	45	22	12.5	8.9%	123.9
W49	245	121	6.5	1.6%	69.0
W50	428	128	3.1	3.3%	108.7
W51	101	31	4.7	3.0%	107.9
W52	110	66	6.4	13.7%	106.3
W53	172	47	0.9	61.1%	122.3
W54	339	128	0.5	80.3%	129.6
W55	786	287	0.2	86.8%	119.2
W56	784	277	0.3	81.6%	112.2
W57	2,663	935	3.4	78.8%	97.5
W58	10,535	4,381	2.5	6.1%	122.8
W59	9,349	2,980	0.3	79.2%	105.6
W60	740	312	1.7	32.2%	132.8
W61	1,029	359	1.7	32.8%	114.9
W62	5,573	2,029	1.2	57.7%	123.6
W63	428	164	2.5	41.1%	113.5
W64	72	26	6.7	34.7%	108.1
W65	1,376	1,015	3.5	50.9%	9.8
W66	1,207	821	2.5	78.1%	11.2
W67	1,146	1,113	4.5	45.8%	9.1
W68	59	67	1.6	67.6%	6.3
W69	2,523	1,062	1.7	79.0%	82.9
W70	123	81	1.2	68.3%	96.0
W71	2,508	849	0.3	81.3%	99.0
W72	165	161	0.9	53.4%	85.4
W73	189	72	1.0	58.2%	87.3
W74	13,849	6,838	0.6	54.1%	108.1
W75	1,571	851	0.6	82.8%	55.3
W76	689	240	0.3	88.4%	83.3
W77	3,713	1,698	1.0	58.2%	110.4
W78	5,189	1,793	0.4	79.5%	91.8

W79	5,337	1,500	0.2	82.5%	110.8
W80	4,786	1,771	5.0	69.7%	93.0
W81	2,265	817	2.8	74.2%	98.1
W82	41,591	14,938	0.1	93.0%	73.1
W83	5,645	1,658	0.3	81.5%	94.8
W84	5,633	2,249	0.4	75.4%	101.1
W85	2,618	1,154	4.2	78.4%	77.1
W86	622	257	0.5	84.9%	95.1
W87	2,469	811	0.4	89.7%	86.7
W88	984	346	0.4	88.7%	94.7
W89	2,518	802	0.2	88.9%	95.8
W91	5,892	1,734	1.3	68.9%	87.9
W92	1,784	817	0.9	90.0%	64.9
W93	2,592	922	4.3	0.4%	103.8
W94	20,787	9,304	4.1	0.4%	107.6
W95	580	438	5.4	0.3%	129.3
W96	1,982	625	3.4	1.5%	119.4
W97	3,439	1,166	2.9	1.2%	129.0
W98	707	285	4.8	1.7%	123.8
X01	14	9	5.3	55.8%	7.8
X02	3	0	0.6	40.0%	59.5
X03	5	2	3.1	80.0%	144.3
X04	1	0	0.0	100.0%	0.0
X05	8	3	4.3	25.0%	33.8
X07	64	56	11.5	3.1%	40.7
X08	2,093	1,501	1.7	84.8%	46.0
X09	1,996	1,474	21.1	0.1%	48.2
X10	740	572	14.2	15.3%	30.8
X11	4,701	2,668	7.0	49.0%	48.1
X12	997	514	9.0	37.5%	66.3
X14	671	643	13.9	0.1%	29.2
X15	287	152	6.6	0.0%	161.7
X16	52	24	1.1	32.7%	81.2
X17	0	0	3.0	0.0%	0.0
X19	22	18	2.0	4.5%	122.4
X20	11	6	1.0	54.5%	89.1
X21	1,276	657	0.4	91.3%	98.0
X22	1,013	623	3.9	5.8%	113.7
X23	28	20	2.5	28.6%	133.4
X24	147	81	1.4	20.4%	137.6
X25	385	169	1.1	34.3%	128.6
X27	481	175	0.2	91.7%	134.4
X45	696	314	3.6	0.6%	33.4
X46	136	74	1.3	32.4%	19.9
X55	1,010	948	2.7	72.5%	11.8

The number of elective procedures was estimated from raw AHES-APC data as described in the methods

Table 9.3: Procedural costs mapped to Health Resource Groups

Procedure	Health Resource Group	Cost per procedure
Breast surgery		
Excision of breast	Malignant Breast Disorders with Interventions, with CC Score 0-2	£3,724
Other daycase breast surgery	Non-Malignant Breast Disorders with Interventions	£27,863
Other inpatient breast surgery	Non-Malignant Breast Disorders with Interventions	£27,863
Cardiac surgery		
Coronary artery surgery	Standard Coronary Artery Bypass Graft with CC Score 0-4	£11,292
Other daycase cardiac surgery	Standard, Other Operations on Heart or Pericardium, with CC Score 0-4	£7,612
Other inpatient cardiac surgery	Standard, Other Operations on Heart or Pericardium, with CC Score 0-4	£7,612
Surgery on the great vessels	Standard Repair of Aortic Root with CC Score 0-6	£14,559
Valvular heart surgery	Standard, Single Heart Valve Replacement or Repair, with CC Score 0-5	£12,082
Cardiology		
Interventional cardiology	Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 0-3	£2,885
Colorectal surgery		
Colorectal resection	Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 0-2	£3,544
Ileostomy, colostomy	Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 0-2	£3,710
Other daycase colorectal surgery	Intermediate Anal Procedures, 19 years and over, with CC Score 1-2	£2,200
Other inpatient colorectal surgery	Non-Malignant Gastrointestinal Tract Disorders with Single Intervention, with CC Score 0-2	£3,710
Proctology	Minor Anal Procedures	£1,728
Sigmoidoscopy, colonospy	Diagnostic Colonoscopy with Biopsy, 19 years and over	£1,176
General surgery		
Diagnositic laparoscopy	Intermediate Therapeutic General Abdominal Procedures, 19 years and over, with CC Score 1-2	£4,237
Excision of lymph node	Minor Therapeutic or Diagnostic, General Abdominal Procedures, 19 years and over	£1,392
Excision of thyroid, parathyroid	Thyroid Procedures with CC Score 0-1	£4,515
Groin hernia repair	Inguinal, Umbilical or Femoral Hernia Procedures, 19 years and over, with CC Score 1-2	£3,132
Other daycase endocrine surgery	Thyroid Procedures with CC Score 0-1	£4,515
Other daycase general surgery	Minor Therapeutic or Diagnostic, General Abdominal Procedures, 19 years and over	£1,392
Other inpatient endocrine surgery	Adrenal Procedures with CC Score 0-1	£6,123
Other inpatient general surgery	Major General Abdominal Procedures, 19 years and over, with CC Score 1-2	£5,785
Other interventional radiology	Percutaneous Single Drainage of Abdominal Abscess, with CC Score 0-1	£2,285
Ventral hernia repair	Abdominal Hernia Procedures, 19 years and over, with CC Score 1-3	£4,725
Gynaecology		
Excision of vulva, vagina, cervix	Major Open Lower Genital Tract Procedures with CC Score 0-2	£3,484

Female sterilisation	Minor, Laparoscopic or Endoscopic, Upper Genital Tract Procedures	£2,624
Hysterectomy, salpingoophrectomy	Major Open Upper Genital Tract Procedures with CC Score 0-2	£4,897
Hysteroscopy & related procedures	Diagnostic Hysteroscopy	£1,853
Other daycase gynaecology	Minor Lower Genital Tract Procedures	£2,002
Other inpatient gynaecology	Intermediate, Laparoscopic or Endoscopic, Upper Genital Tract Procedures, with CC Score 0-1	£3,194
Ovarian surgery	Major, Laparoscopic or Endoscopic, Upper Genital Tract Procedures, with CC Score 0-1	£4,507
Repair of prolapse of vagina	Intermediate Open Lower Genital Tract Procedures with CC Score 0-2	£2,829
Head & Neck surgery		
Adenoidectomy	Adenoidectomy	£1,961
Laryngoscopy	Diagnostic, Laryngoscopy or Pharyngoscopy, 19 years and over	£1,854
Maxillofacial surgery	Major Maxillofacial Procedures, 19 years and over, with CC Score 1+	£6,101
Operations on ear	Intermediate Ear Procedures, 19 years and over	£3,102
Operations on larynx, pharynx	Major, Mouth or Throat Procedures, 19 years and over, with CC Score 0-1	£3,818
Operations on nose	Intermediate Nose Procedures	£2,666
Oral surgery	Intermediate, Mouth or Throat Procedures, 19 years and over, with CC Score 0-1	£2,743
Tonsillectomy	Tonsillectomy, 4 years and over	£2,183
Hepatobiliary surgery		
Cholecystectomy	Laparoscopic Cholecystectomy, 19 years and over, with CC Score 1-3	£3,939
Diagnostic percutaneous operations on liver	Non-Malignant, Hepatobiliary or Pancreatic Disorders, with Single Intervention, with CC Score 0-3	£3,195
ERCP & related procedures	Intermediate Therapeutic Endoscopic Retrograde Cholangiopancreatography with CC Score 0-1	£1,947
Excision of liver, pancreas, spleen	Very Major, Hepatobiliary or Pancreatic Procedures, with CC Score 0-2	£8,088
Other daycase hepatobiliary surgery	Minor, Hepatobiliary or Pancreatic Procedures, with CC Score 1+	£4,603
Other inpatient hepatobiliary surgery	Very Major, Hepatobiliary or Pancreatic Procedures, with CC Score 0-2	£8,088
Other interventional radiology	Other Percutaneous Therapeutic, Hepatobiliary or Pancreatic Procedures, with CC Score 0-2	£2,772
Neurosurgery		
Brain tissue surgery	Complex Intracranial Procedures, 18 years and under, with CC Score 0-3	£12,140
Brain ventricular surgery	Complex Intracranial Procedures, 18 years and under, with CC Score 0-3	£12,140
Cranial nerve surgery	Very Major Intracranial Procedures, 18 years and under, with CC Score 0-3	£7,233
Cranium and dural surgery	Very Major Intracranial Procedures, 18 years and under, with CC Score 0-3	£7,233
Neurovascular interventional radiology	Percutaneous Transluminal Embolisation of, Single Small or Medium, Intracranial or Extracranial Aneurysm, with CC Score 0-3	£5,568
Other inpatient neurosurgery	Major Intracranial Procedures, 18 years and under, with CC Score 0-3	£8,188
Oesophagogastric surgery		
Gastroscopy	Diagnostic Endoscopic Upper Gastrointestinal Tract Procedures, 19 years and over	£999
Gastrostomy, jejunostomy	Radiological Insertion of Gastrostomy Tube, 19 years and over	£1,496

Oesophagogastric resection	Complex, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 0-1	£6,840
Other daycase oesophagogastric surgery	Intermediate Upper Gastrointestinal Tract Procedures, 19 years and over	£1,464
Other inpatient oesophagogastric surgery	Major, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 0-1	£5,091
Opthalmology		
Cataract surgery	Intermediate, Cataract or Lens Procedures, with CC Score 0-1	£3,557
Glaucoma surgery	Minor, Glaucoma or Iris Procedures	£1,432
Operations on vitreous body of eye	Intermediate Vitreous Retinal Procedures, 19 years and over, with CC Score 0-1	£1,320
Other daycase ophthalmology	Intermediate Oculoplastics Procedures, 19 years and over, with CC Score 0-1	£2,087
Other inpatient ophthalmology	Major, Orbit or Lacrimal Procedures, 19 years and over, with CC Score 1+	£3,096
Orthopaedics		
Arthroscopic procedures	Minor Knee Procedures for Non-Trauma, 19 years and over	£2,262
Daycase procedures on joint	General orthopaedics (non-trauma)*	£3,960
Decompression of cervical spine	Percutaneous Vertebroplasty of One Level of Spine	£3,697
Decompression of lumbar spine	Percutaneous Vertebroplasty of One Level of Spine	£3,697
Denervation of spinal facet joint	Denervation or Injection around Spinal Facet, for Pain Management	£916
Division or excision of bone	Malignancy, of Bone or Connective Tissue, with CC Score 0-1	£2,179
Excision of ganglion	Soft Tissue Disorders with CC Score 0-2	£1,001
Fasciectomy, fasciotomy	Soft Tissue Disorders with CC Score 0-2	£1,001
Fracture-related surgery	General orthopaedics (trauma)*	£3,710
Fusion of joint	General orthopaedics (non-trauma)*	£3,960
Fusion of joint of toe	Major Foot Procedures for Non-Trauma, 19 years and over, with CC Score 0-1	£4,975
Lower limb joint replacement	Complex, Hip or Knee Procedures for Non-Trauma, with CC Score 0-1	£9,775
Operations on bursa	Minor Knee Procedures for Non-Trauma, 19 years and over	£2,262
Other daycase orthopaedics	General orthopaedics (non-trauma)*	£3,960
Other daycase spinal surgery	Intermediate Extradural Spinal Procedures with CC Score 0-1	£4,884
Other inpatient orthopaedics	General orthopaedics (non-trauma)*	£3,960
Other inpatient spinal surgery	Major Extradural Spinal Procedures with CC Score 0-1	£5,667
Other reconstruction of joint	General orthopaedics (non-trauma)*	£3,960
Procedures on nail, nail bed	Soft Tissue Disorders with CC Score 0-2	£1,001
Procedures on peripheral nerves	Minor Hand Procedures for Non-Trauma, 19 years and over	£2,052
Reconstruction of foot	Major Foot Procedures for Trauma, 19 years and over, with CC Score 1	£4,877
Spinal fusion	Major Spinal Reconstructive Procedures with CC Score 0-1	£11,154
Surgery on ligament, tendon, muscle	Other Muscle, Tendon, Fascia or Ligament Procedures	£4,844
Upper limb joint replacement	Complex, Foot, Hand, Shoulder or Elbow Procedures for Non-Trauma, with CC Score 0-1	£7,942
Plastic surgery		
Excision of lesion of skin	Minor Skin Procedures, 19 years and over	£1,400
Other daycase plastic surgery	Intermediate Skin Procedures, 19 years and over	£2,157
Other inpatient plastic surgery	Major Skin Procedures	£7,680
Procedure on eyelid	Minor Oculoplastics Procedures, 19 years and over	£1,220
Procedure on lip	Minor, Mouth or Throat Procedures, 19 years and over	£2,063
Thoracic surgery		

Biopsy of lung	Minor Thoracic Procedures	£2,175
Bronchoscopy	Diagnostic Bronchoscopy, 19 years and over	£2,054
Lung resection	Major Thoracic Procedures, 19 years and over, with CC Score 0-2	£5,424
Other daycase thoracic surgery	Minor Thoracic Procedures	£2,175
Other inpatient thoracic surgery	Intermediate Thoracic Procedures, 19 years and over, with CC Score 0-2	£3,999
Urology		
Cystectomy	Cystectomy with Urinary Diversion and Reconstruction, with CC Score 0-2	£11,425
Extracorporeal fragmentation of calculus of kidney	Urinary Tract Stone Disease with Interventions, with CC Score 0-2	£3,836
Male sterilisation	Minor, Scrotum, Testis or Vas Deferens Procedures, 19 years and over	£2,368
Nephrectomy, uretectomy	Major Laparoscopic, Kidney or Ureter Procedures, 19 years and over, with CC Score 0-2	£6,902
Operations on bladder	Intermediate Open Bladder Procedures	£4,577
Other daycase urology	Ureteric or Bladder Disorders, with Interventions, with CC Score 0-3	£2,723
Other inpatient urology	Ureteric or Bladder Disorders, with Interventions, with CC Score 0-3	£2,723
Other interventional radiology	Unilateral, Percutaneous Insertion of, Ureteric Stent or Nephrostomy	£1,634
Percutaneous puncture of kidney	Other Percutaneous Therapeutic, Hepatobiliary or Pancreatic Procedures, with CC Score 0-2	£2,772
Prepuceplasty	Minor Penis Procedures, 19 years and over	£2,171
Prostatectomy	Transurethral Prostate Resection Procedures with CC Score 0-2	£3,420
Scrotal surgery	Scrotum, Testis or Vas Deferens Disorders, with Interventions, with CC Score 0-1	£6,474
Transplant surgery	Kidney Transplant, 19 years and over, from Live Donor	£12,840
Ureteric stent procedures	Unilateral, Percutaneous Insertion of, Ureteric Stent or Nephrostomy	£1,634
Ureteroscopy, cystoscopy & related procedures	Intermediate Endoscopic Ureter Procedures, 19 years and over	£2,115
Urethral surgery	Minor or Intermediate, Urethra Procedures, 19 years and over	£1,723
Vascular surgery		
Amputation of lower limb	Amputation of Single Limb with CC Score 0-9	£8,613
Amputation of upper limb	Amputation of Single Limb with CC Score 0-9	£8,613
Aortic surgery	Single Open Procedure, on Aorta or Abdominal Blood Vessel, with CC Score 0-3	£8,526
Arteriovenous shunt	Open Arteriovenous Fistula, Graft or Shunt Procedures	£3,261
Other daycase vascular surgery	Open Operations, on Other or Unspecified Blood Vessels, with CC Score 0-1	£3,780
Other inpatient vascular surgery	Open Operations, on Other or Unspecified Blood Vessels, with CC Score 0-1	£3,780
Surgery on arteries	Single Open Procedure on Blood Vessel of Lower Limb with CC Score 0-3	£6,968
Varicose vein surgery	Open Treatment of Primary Unilateral Varicose Veins	£2,669
Vascular interventional radiology	Percutaneous Transluminal Angioplasty of Single Blood Vessel with CC Score 0-2	£1,757

Costs are based on NHS reference costs for 2019-20

**Health Resource Group (HRG) categorisation is more granular than some of our orthopaedic procedure categories, making it difficult to match our procedures to a single HRG code. Therefore, for non-trauma procedures we took an average cost for the following HRG codes: Intermediate Hip Procedures for Non-Trauma, 19 years and over, with CC Score 1, Intermediate Knee Procedures for Non-Trauma, between 6 and 18 years, with CC Score 1+, Intermediate Foot Procedures for Non-Trauma, 19 years and over, with CC Score 0-1, Intermediate Hand Procedures for Non-Trauma, 19 years and over, with CC Score 0-1, Intermediate Shoulder Procedures for Non-Trauma, 19 years and over, with CC Score 0-1, Intermediate Elbow Procedures for Non-Trauma, 19 years and over, with CC Score 0-1, resulting in an estimated cost per procedure of £3,960. Equivalent trauma-related codes were used to calculate an average cost (£3,710) for trauma procedures.*