

Elective Cancer Surgery in COVID-19–Free Surgical Pathways During the SARS-CoV-2 Pandemic: An International, Multicenter, Comparative Cohort Study

James C. Glasbey, MBBCh, BSc, MRCS, PGCert¹; Dmitri Nepogodiev, MBBCh¹, Joana F.F. Simoes, MD¹; Omar Omar, MSc¹; Elizabeth Li, MBBCh, MRCS²; Mary L. Venn, MBBCh, BSc, MRCS, PGDME³; Mohammad K. About Chaar, MD⁴; Vita Capizzi, MD⁵; Daoud Chaudhry, MBBCh²; Anant Desai, MA, MD, FRCS⁶; Jonathan G. Edwards, MBChB, PhD, FRCS(C/Th)⁷; Jonathan P. Evans, MBChB, PhD, FRCS⁸; Marco Fiore, MD, FACS⁵; Jose Flavio Videria, MD⁹; Samuel J. Ford, MBBCh, PhD, FRCS⁶; Ian Ganly, BSc, MBChB, PhD, MSc, FRCS, FRCS-ORL¹⁰; Ewen A. Griffiths, MBBCh, MD, FRCS¹¹; Rohan R. Gujjuri, MBBCh²; Angelos G. Koliaas, MD, MSc, PhD, FRCS (SN)¹²; Haytham M.A. Kaafarani, MD, MPH, FACS¹³; Ana Minaya-Bravo, MD¹⁴; Siobhan C. McKay, PhD, MBBS, BMedSci, FRCS, DipEd¹⁵; Helen M. Mohan, PhD, FRCS¹⁶; Keith J. Roberts, PhD, FRCS¹⁵; Carlos San Miguel-Méndez, MD, PhD¹⁴; Peter Pockney, BSc, MBBS, DM, FRCS, FRACS¹⁷; Richard Shaw, BDS, MBChB(Hons), MD, FDS(RCSEng), FRCS(OMFS)¹⁸; Neil J. Smart, MBBS (Hons), PhD, FRCSEd¹⁹; Grant D. Stewart, BSc, MBChB, PhD, MA(Cantab), FRCSEd(Urol)²⁰; Sudha Sundar, MRCOG, MPhil²¹; Raghavan Vidya, MS, MD, FRCS²²; Aneel A. Bhangu, MBBCh, PhD, FRCS²; on behalf of the COVIDSurg Collaborative

PURPOSE As cancer surgery restarts after the first COVID-19 wave, health care providers urgently require data to determine where elective surgery is best performed. This study aimed to determine whether COVID-19–free surgical pathways were associated with lower postoperative pulmonary complication rates compared with hospitals with no defined pathway.

PATIENTS AND METHODS This international, multicenter cohort study included patients who underwent elective surgery for 10 solid cancer types without preoperative suspicion of SARS-CoV-2. Participating hospitals included patients from local emergence of SARS-CoV-2 until April 19, 2020. At the time of surgery, hospitals were defined as having a COVID-19–free surgical pathway (complete segregation of the operating theater, critical care, and inpatient ward areas) or no defined pathway (incomplete or no segregation, areas shared with patients with COVID-19). The primary outcome was 30-day postoperative pulmonary complications (pneumonia, acute respiratory distress syndrome, unexpected ventilation).

RESULTS Of 9,171 patients from 447 hospitals in 55 countries, 2,481 were operated on in COVID-19–free surgical pathways. Patients who underwent surgery within COVID-19–free surgical pathways were younger with fewer comorbidities than those in hospitals with no defined pathway but with similar proportions of major surgery. After adjustment, pulmonary complication rates were lower with COVID-19–free surgical pathways (2.2% v 4.9%; adjusted odds ratio [aOR], 0.62; 95% CI, 0.44 to 0.86). This was consistent in sensitivity analyses for low-risk patients (American Society of Anesthesiologists grade 1/2), propensity score–matched models, and patients with negative SARS-CoV-2 preoperative tests. The postoperative SARS-CoV-2 infection rate was also lower in COVID-19–free surgical pathways (2.1% v 3.6%; aOR, 0.53; 95% CI, 0.36 to 0.76).

CONCLUSION Within available resources, dedicated COVID-19–free surgical pathways should be established to provide safe elective cancer surgery during current and before future SARS-CoV-2 outbreaks.

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INTRODUCTION

During the initial phases of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, an estimated 2.3 million cancer operations worldwide were postponed because of the risk of in-hospital transmission.¹ Perioperative SARS-CoV-2 is associated with a high risk of pulmonary complications and death.²⁻⁵ Elective surgical activity was reduced to

increase critical care capacity for patients with coronavirus disease 2019 (COVID-19) and to release surgical team members to support wider hospital responses.⁶⁻⁸ However, some elective surgery for time-sensitive conditions continued, with prioritization of patients with resectable cancers at risk for progression and patients for whom alternative treatment modalities would be ineffective.⁹⁻¹¹

ASSOCIATED CONTENT

Listen to the podcast by Dr Tanabe at jcopodcast.libsynpro.com

Appendix

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

Surgical providers have begun to create COVID-19–free surgical pathways in both separate elective hospitals and major acute hospitals in which elective operating room, critical care, and inpatient ward areas are not shared with patients with COVID-19. Major service redesign to provide these pathways is expensive and difficult; evidence is urgently needed to inform clinical practice.

Knowledge Generated

Our data demonstrated that pulmonary complication rates, SARS-CoV-2 infection rates, and mortality rates were consistently lower for patients within COVID-19–free surgical pathways. These findings persisted after risk adjustment, sensitivity analyses of low-risk patients and propensity score–matched groups, and patients who had a negative pre-operative SARS-CoV-2 test. Differences in outcomes were observed in both high and low SARS-CoV-2 incidence areas.

Relevance

As health providers restart elective cancer surgery, they should prevent harm by investing in dedicated COVID-19–free surgical pathways tailored to local resources available.

Before the pandemic, most cancer surgery was performed in hospitals that also supported acute medical services.¹²⁻¹⁴ Such hospitals have admitted patients with COVID-19 during the pandemic, increasing the risk of cross infection of elective surgery patients. To avoid this, some health care providers have established dedicated COVID-19–free surgical pathways, which deliver surgery, critical care, and inpatient ward care with no shared areas with patients with COVID-19.

Major reorganization of hospital services to provide COVID-19–free surgical pathways for elective cancer surgery needs to be justified because it will carry significant costs for providers and patients. Information is urgently required to determine whether these pathways reduce adverse postoperative outcomes. This study aimed to compare the rate of postoperative pulmonary complications after elective cancer operations in COVID-19–free surgical pathways and hospitals with no defined pathway.

PATIENTS AND METHODS

Study Design and Protocol

This was an international, multicenter cohort study of adults who underwent elective cancer surgery. Local principal investigators were responsible for obtaining clinical audit, institutional review board, or ethical approval in line with local and national regulations. For example, in the United Kingdom, the study was registered as a clinical audit at each participating hospital, whereas in other countries, such as Saudi Arabia, nationwide ethics approval was granted. Data were collected online and stored on a secure data server running the Research Electronic Data Capture web application.¹⁵

Centers and Settings

Hospitals that performed elective cancer surgery in areas affected by the COVID-19 pandemic were eligible to

participate. Enrollment of consecutive patients commenced from the date of admission of the first patient with SARS-CoV-2 to the participating hospital or, in the case of COVID-19–free surgical pathways in hospitals where no cases had been recorded, to the nearest hospital treating patients with COVID-19.

Each patient was classified as having undergone surgery within a COVID-19–free surgical pathway or with no defined pathway. To determine whether a COVID-19–free surgical pathway was used, an assessment was made of the operating room, critical care, and inpatient ward areas where each patient was treated. Patients were classified as being treated within a COVID-19–free pathway if there was a policy of complete segregation in all three areas away from patients with COVID-19. Patients were classified as being treated within no defined pathway if in any one of these areas was shared with patients with COVID-19. The classification was based on whether there was a policy of segregation in place rather than whether individual elective patients came into contact with patients with COVID-19 because asymptomatic SARS-CoV-2 infection is common, so contact with an infectious patient was possible even if this was not known at the time. COVID-19–free surgical pathways could be provided by hospitals that only provided elective care, including specialized units set up during the pandemic. Alternatively, they could be provided by acute hospitals that designated separate COVID-19–free areas and COVID-19 treatment areas to ensuring that there were no shared areas. In any particular hospital, it was possible that some patients were treated within a COVID-19–free surgical pathway, whereas others had no defined pathway (eg, where a COVID-19–free surgical pathway was introduced part way through the study inclusion period), and our patient-level classification captured this. [Figure 1](#) shows examples of COVID-19–free surgical pathways and no defined pathways.

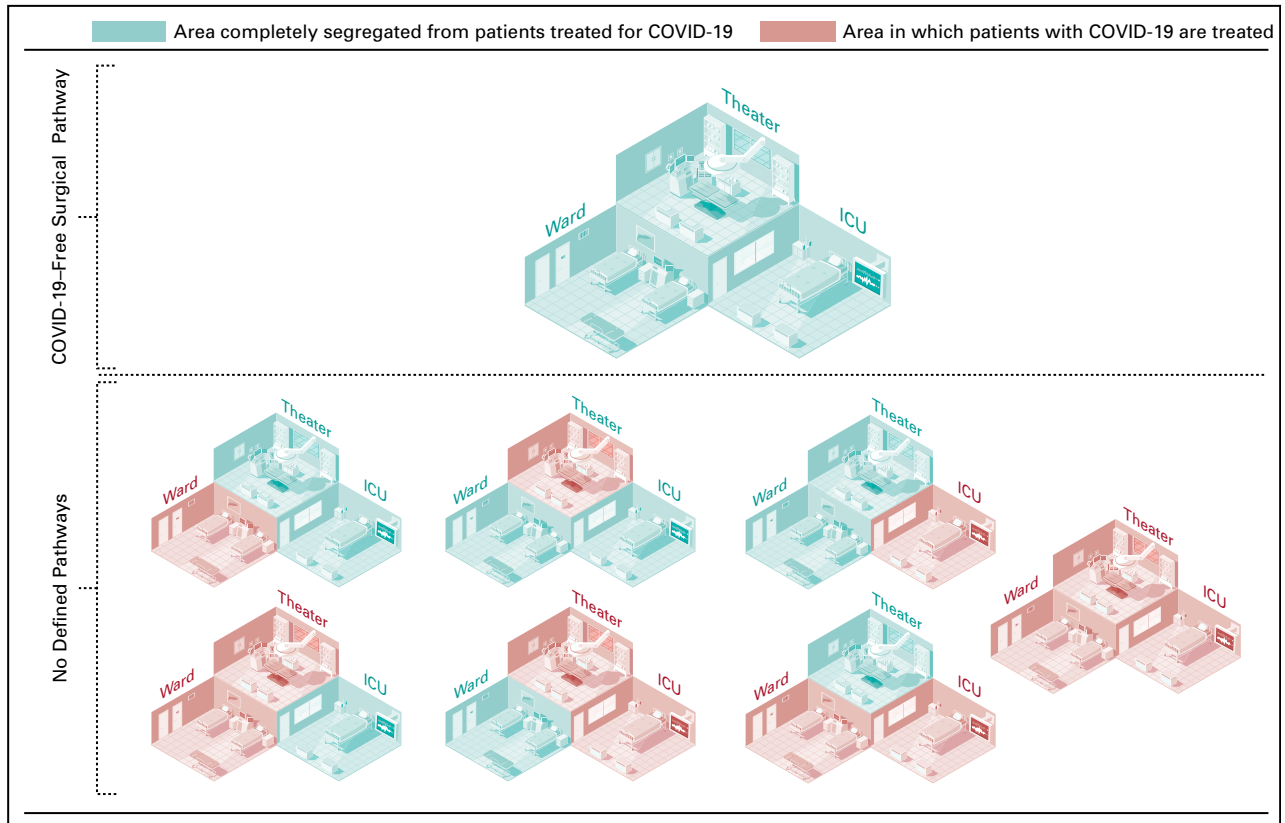


FIG 1. Differences between hospitals with a coronavirus disease 2019 (COVID-19)–free surgical pathway and hospitals with no defined pathway. COVID-19–free surgical pathways: complete segregation of operating room, critical care, and inpatient ward areas for elective cancer surgery away from patients being treated for COVID-19. No defined pathways: hospitals where there was mixing of patients who were undergoing treatment for COVID-19 and elective surgical patients in any operating room, critical care, or inpatient ward area. ICU, intensive care unit.

Surgical Pathway Components

To better understand health system responses to the COVID-19 pandemic, additional data points were introduced on April 2, 2020, to capture data on individual components of the surgical pathway (operating room, critical care, inpatient ward). These were completed for consecutive patients after this date.

Patients and Procedures

Adult patients (age ≥ 18 years) who underwent elective surgery with curative intent for a suspected cancer were included from emergence of COVID-19 up to April 19, 2020. Patients were identified preoperatively from multidisciplinary team (MDT) meeting (or tumor board) lists and the subsequent operation location identified by the operating surgeon. Patients were followed up to postoperative day 30, with the day of surgery being day 0. All consecutive patients who underwent eligible surgery were included (Data Supplement, online only). Eligible cancers included colorectal, esophagogastric, head and neck (oral, oropharyngeal, laryngeal, hypopharyngeal, salivary, thyroid, paranasal sinus, skin), thoracic (lung, pleural, mediastinal,

chest wall), hepatopancreatobiliary (liver, pancreatic), urologic (prostate, bladder, renal), gynecologic (uterine, ovarian, cervical, vulvar, vaginal), and breast as well as sarcoma (soft tissue, bony) and intracranial malignancies (Data Supplement). Participating centers could contribute data for either single or multiple cancers depending on local services and capacity.¹⁶ Patients who had clinical symptoms consistent with COVID-19 or who were confirmed to have SARS-CoV-2 infection (by quantitative reverse transcription polymerase chain reaction and/or positive thoracic computed tomography [CT] imaging performed within 72 hours before surgery) at the time of surgery were excluded.

Data Variables

To account for different tumor grading and staging systems across solid cancers, disease status was classified as early stage (organ confined, non-nodal, nonmetastatic, fully resectable) or advanced stage (growth beyond organ, nodal, metastatic operated with curative intent). Full definitions are provided in the Data Supplement. Grade of surgery was categorized on the basis of the Clinical Coding

& Schedule Development Group as either minor (minor/intermediate) or major (major/complex major).^{17,18} Preoperative testing was defined as a swab test and/or thoracic CT imaging performed in the 72 hours before surgery to confirm SARS-CoV-2 status.

Outcome Measures

The primary outcome measure was the rate of postoperative pulmonary complications within 30 days after surgery. This included pneumonia, acute respiratory distress syndrome, and/or unexpected postoperative ventilation (Data Supplement¹⁹). The secondary outcomes were postoperative SARS-CoV-2 infection and mortality within 30 days after surgery. Postoperative SARS-CoV-2 infection was defined as a positive swab, positive thoracic CT imaging, or a clinical diagnosis of symptomatic COVID-19 in patients for whom these tests were unavailable.

Community SARS-CoV-2 Incidence

The community SARS-CoV-2 incidence within each participating hospital's local community was extracted from WHO,²⁰ European Centre for Disease Prevention and Control,²¹ or US Centers for Disease Control and Prevention²² statistics. SARS-CoV-2 incidence was calculated for 2-week windows in March and April 2020 on the basis of the number of confirmed SARS-CoV-2 cases at the smallest available administrative level (city, region, or country).²³ Hospitals were classified as being in communities with either low (< 25 cases per 100,000 population) or high (\geq 25 cases per 100,000 population) SARS-CoV-2 incidence (Data Supplement).

Data Integrity

Previous international outcomes studies have achieved > 95% case ascertainment and > 98% data accuracy during external validation.²⁴ We identified low-volume centers (predefined as five or fewer patients per participating specialty) and asked local principal investigators to confirm case ascertainment against MDT records. If a specialty within a hospital was found to have incomplete case ascertainment, any data entered from this specialty were excluded from analysis.

Statistical Analysis

The study was conducted according to Strengthening of Reporting of Observational Studies in Epidemiology²⁵ and reported according to Statistical Analyses and Methods in the Published Literature.²⁶ Nonparametric data were summarized with medians and interquartile ranges, and differences between groups were tested using the Mann-Whitney *U* test. The χ^2 test was used for categorical data. Missing data were included in flowcharts and summary tables, which allowed denominators to remain consistent in calculations.

Bayesian univariable and multivariable mixed-effects logistic regression was used to calculate odds ratios (ORs) and 95% CIs. Clinically plausible patient-, disease-,

operation-, and location-specific factors were selected a priori for inclusion in adjusted analyses to identify independent predictors of postoperative pulmonary complications (primary outcome). Country was included as a random effect in both the unadjusted and the adjusted models. An exploratory analysis was conducted of the association between components of the COVID-19–free surgical pathway and the primary outcome measure. Analyses were carried out using R version 3.1.1 packages *finalfit*, *tidyverse*, and *BRMS*²⁷ (R Foundation for Statistical Computing, Vienna, Austria; Data Supplement).

Sensitivity Analyses

We anticipated a selection bias, with lower-risk patients being more likely to be treated within COVID-19–free surgical pathways. To account for this risk of bias, we explored differences in the postoperative pulmonary complications stratified by three common risk factors (age, sex, and American Society of Anesthesiologists [ASA] grade); performed a sensitivity analysis for pulmonary complications, including low-risk (ASA grade 1 or 2) patients only; and performed propensity score matching using a nearest neighbor method, including patients within COVID-19–free surgical pathways in a 1:1 ratio with those with no defined pathway (Data Supplement). To exclude a potential confounding effect of presymptomatic carriage of SARS-CoV-2 in the association between hospital type and the primary outcome, we performed a further sensitivity analysis that included only patients with a negative preoperative SARS-CoV-2 swab test.

RESULTS

Patients and Procedures

At the time of this analysis (June 15, 2020), a total 9,171 patients from 445 hospitals were included. These patients were from the United Kingdom (29.2%; 2,679 patients), Italy (17.3%; 1,583 patients), Spain (8.3%; 764 patients), United States (6.3%; 574 patients), and 50 other countries. Overall, 39.2% of patients (3,698) were male, 17.9% (1,644) were age < 50 years, and 8.3% (761) were age \geq 80 years. Complete baseline patient, disease, and operative characteristics are listed in [Table 1](#).

A total of 2,481 patients (27.1%) underwent surgery within COVID-19–free surgical pathways, and 6,689 (72.9%) underwent surgery within no defined pathway. Patients in COVID-19–free surgical pathways were younger, had fewer comorbidities, and had better performance scores. Major surgery accounted for 75.6% (1,866 of 2,481) of operations in COVID-19–free surgical pathways and 77.7% (5,179 of 6,689) where there was no defined pathway; a full list of operations performed is provided in the Data Supplement. The missing data rates were low (Data Supplement). Changes in local SARS-CoV-2 incidence over the study period are listed in the Data Supplement.

TABLE 1. Characteristics of Patients Treated Within COVID-19–Free Surgical Pathways and With No Defined Pathway

Characteristic	COVID-19–Free Surgical Pathway	No Defined Pathway	P
No. of patients	2,481	6,689	
Age, years			
< 50	558 (22.5%)	1,086 (16.2%)	< .001
50-59	576 (23.2%)	1,404 (21.0%)	
60-69	633 (25.5%)	1,911 (28.6%)	
70-79	552 (22.2%)	1,689 (25.3%)	
≥ 80	162 (6.5%)	599 (9.0%)	
Sex			
Female	1,743 (70.3%)	3,832 (57.3%)	< .001
Male	737 (29.7%)	2,856 (42.7%)	
Missing	1	1	
BMI			
Normal	996 (40.1%)	2,542 (38.0%)	.050
Overweight	796 (32.1%)	2,091 (31.3%)	
Obese	469 (18.9%)	1,443 (21.6%)	
Underweight	53 (2.1%)	164 (2.5%)	
Missing	167 (6.7%)	449 (6.7%)	
ASA grade			
1-2	1,959 (79.2%)	4,640 (69.7%)	< .001
3-5	515 (20.8%)	2,016 (30.3%)	
Missing	7	33	
RCRI			
0	949 (38.3%)	1,942 (29.0%)	< .001
1	1,181 (47.6%)	3,453 (51.6%)	
2	306 (12.3%)	1,023 (15.3%)	
≥ 3	45 (1.8%)	271 (4.1%)	
Respiratory comorbidity			
No	2,249 (90.6%)	5,929 (88.6%)	.007
Yes	232 (9.4%)	760 (11.4%)	
ECOG PS			
0	1,657 (67.1%)	4,087 (62.2%)	< .001
1-2	775 (31.4%)	2,367 (36.0%)	
3-4	36 (1.5%)	115 (1.8%)	
Missing	13	120	
Cancer type			
Colorectal	437 (17.6%)	1,873 (28.0%)	< .001
Breast	827 (33.3%)	1,313 (19.6%)	
Gynecologic	330 (13.3%)	772 (11.5%)	
Head or neck	253 (10.2%)	884 (13.2%)	
Hepatopancreatobiliary	161 (6.5%)	515 (7.7%)	
Intracranial	34 (1.4%)	130 (1.9%)	
Thoracic	172 (6.9%)	385 (5.8%)	
Esophagogastric	75 (3.0%)	312 (4.7%)	
Sarcoma	118 (4.8%)	143 (2.1%)	
Urologic	74 (3.0%)	362 (5.4%)	

(continued on following page)

TABLE 1. Characteristics of Patients Treated Within COVID-19–Free Surgical Pathways and With No Defined Pathway (continued)

Characteristic	COVID-19–Free Surgical Pathway	No Defined Pathway	P
Disease stage			
Early	1,822 (73.5%)	4,707 (70.4%)	.004
Advanced	657 (26.5%)	1,978 (29.6%)	
Missing	0.08	0.06	
Booking type			
Day case	206 (8.4%)	524 (7.9%)	.493
Inpatient	2,259 (91.6%)	6,117 (92.1%)	
Missing	0.6	0.08	
Anesthetic			
Regional/local	99 (4.0%)	388 (5.8%)	.001
General	2,382 (96.0%)	6,301 (94.2%)	
Operation grade			
Minor	601 (24.4%)	1,488 (22.3%)	.042
Major	1,866 (75.6%)	5,179 (77.7%)	
Missing	0.6	0.3	
Preoperative testing			
Not screened	1,511 (60.9%)	5,186 (77.5%)	< .001
Screened	970 (39.1%)	1,503 (22.5%)	
Community SARS-CoV-2 risk			
Low	1,948 (78.5%)	6,079 (90.9%)	< .001
High	533 (21.5%)	610 (9.1%)	

NOTE. See the Data Supplement for full definitions. Percentages calculated as a proportion of column total. *P* values calculated using χ^2 test.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; COVID-19, coronavirus disease 2019; ECOG PS, Eastern Cooperative Oncology Group performance status; RCRI, Revised Cardiac Risk Index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Preoperative Testing

Overall, 27.0% (2,473 of 9,409) of patients underwent preoperative SARS-CoV-2 testing; 75.9% (1,878 of 2,473) of these were performed using a swab test. The preoperative testing rate was higher in COVID-19–free surgical pathways versus no defined pathway (39.1% [970] *v* 22.5% [1,503]; *P* < .0001).

Postoperative Pulmonary Complications

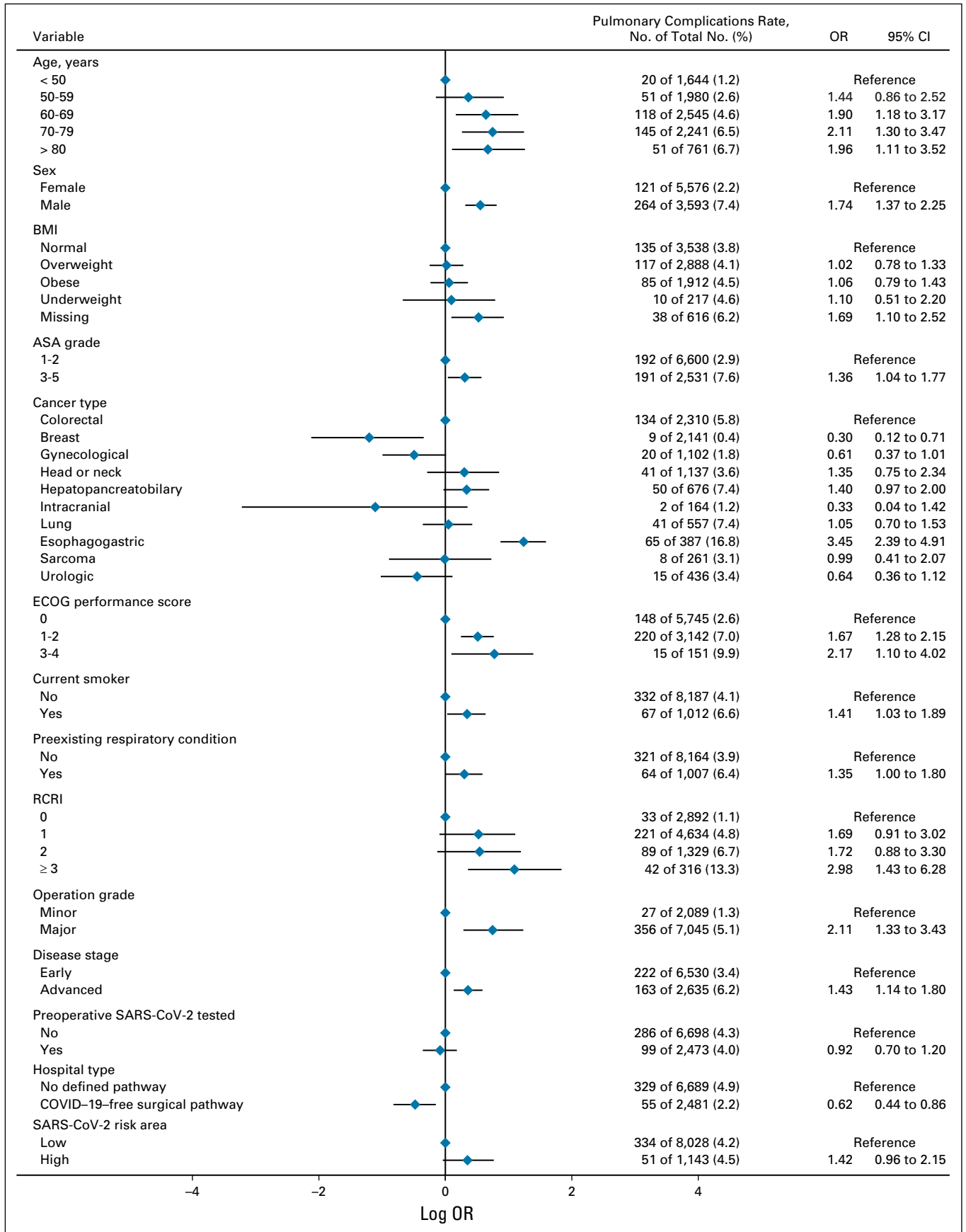
The overall 30-day pulmonary complication rate was 4.2% (385 of 9,171), which was lower for patients within a COVID-19–free surgical pathway than within no defined pathway (2.2% [55 of 2,481] *v* 4.9% [329 of 6,689]; unadjusted OR, 0.49; 95% CI, 0.36 to 0.66). After adjustment, surgery in a COVID-19–free surgical pathway remained associated with a lower postoperative pulmonary complication rate (adjusted OR [aOR], 0.62; 95% CI, 0.44 to 0.86). Older age, male sex, ASA grades 3-5, poorer performance status, higher cardiac risk, preexisting respiratory disease, advanced disease stage, major surgery, esophago-gastric surgery, and surgery in high SARS-CoV-2

incidence areas were also associated with a greater odds of pulmonary complications (Fig 2; Table 2; Data Supplement).

Sensitivity Analyses

Postoperative pulmonary complication rates stratified by age, sex, and ASA grade in hospitals with and without COVID-19–free surgical pathways are shown in the Data Supplement. In a sensitivity analysis including only low-risk patients (*n* = 6,489), COVID-19–free surgical pathways remained associated with a reduced odds of pulmonary complications (aOR, 0.58; 95% CI, 0.36 to 0.93; Data Supplement).

Propensity score matching created well-balanced groups (Data Supplement), with 2,449 patients within COVID-19–free surgical pathways matched to 2,449 with no defined pathway. After adjustment, surgery within a COVID-19–free surgical pathway was associated with a lower odds of pulmonary complications (aOR, 0.65; 95% CI, 0.44 to 0.96; Data Supplement). In a sensitivity analysis including only patients with a negative preoperative SARS-CoV-2 test (*n* = 2,447), again a COVID-19–free surgical pathway was



associated with lower pulmonary complication rates (aOR, 0.52; 95% CI, 0.29 to 0.91; Data Supplement).

Surgical Pathway Components

Consecutive data were available for 4,505 patients. Of these, 45.6% (2,053) were classified as having a COVID-19–free surgical pathway. Of 2,451 patients with no defined pathway, 86.5% (2,120) had an operating room, 21.5% (526) a critical care area, and 59.8% (1,466) had a ward space shared with patients with COVID-19. Treatment in both a COVID-19–free ward and a critical care area (aOR, 0.43; 95% CI, 0.24 to 0.77) or a complete COVID-19–free surgical pathway (aOR, 0.30; 95% CI, 0.17 to 0.54) was significantly associated with a lower odds of pulmonary complications versus treatment in shared operating room, critical care, and ward areas (Data Supplement).

Postoperative SARS-CoV-2 Infection

The overall rate of postoperative SARS-CoV-2 infection was 3.2% (291 of 9,171). A majority was confirmed with a swab test (85.6%; 249 of 291). The SARS-CoV-2 infection rate was lower in COVID-19–free surgical pathways (2.1%; 53 of 2,481) than with no defined pathway (3.6%; 238 of 6,820; aOR, 0.53; 95% CI, 0.36 to 0.76). This was consistent in a sensitivity analysis with swab testing only (aOR, 0.44; 95% CI, 0.28 to 0.68; Data Supplement) and was consistent across hospitals in high (3.9% v 8.2%) and low SARS-CoV-2 incidence areas (1.6% v 3.1%; Table 3). SARS-CoV-2 infection was associated with increased pulmonary complication rates compared with patients without infection (33.8% [130 of 385] v 1.8% [161 of 8,786]; OR, 29.78; 95% CI, 22.4 to 39.6).

Postoperative Mortality

The overall postoperative mortality rate was 1.5% (134 of 9,115). Mortality was higher in patients with pulmonary complications (OR, 25.64; 95% CI, 17.63 to 36.67) and in patients with SARS-CoV-2 infection (OR, 29.34; 95% CI, 20.13 to 43.04). It was lower in patients operated on in COVID-19–free surgical pathways (OR, 0.45; 95% CI, 0.25 to 0.78). Of the 30-day deaths, 49.3% (66 of 134) were associated with pulmonary complications, and 44.0% (59 of 134) were associated with SARS-CoV-2 infection (Fig 3). Mortality was higher after pulmonary complications in patients with SARS-CoV-2 (30.8%; 40 of 130) than in patients without infection with pulmonary complications (10.7%; 26 of 244).

DISCUSSION

This study identified that postoperative pulmonary complication rates were lower for patients in COVID-19–free surgical pathways during the SARS-CoV-2 pandemic. Despite a tendency for lower-risk surgeries to be performed in these pathways, effects persisted after risk adjustment, sensitivity analyses, and propensity score matching. The advantage of COVID-19–free pathways was also seen in patients with a negative SARS-CoV-2 test preoperatively. Older patients, males, and patients with cardiorespiratory comorbidities were consistently at greater risk of adverse outcomes. Mortality was primarily driven by pulmonary complications, which was low in COVID-19–free surgical pathways and high with postoperative SARS-CoV-2 infection. Overall, these data support major international redesign of surgical services, based on local available resources, to provide elective cancer surgery in COVID-19–free surgical pathways. While the greatest effect size was seen in areas of high SARS-CoV-2 incidence, there was also a significant difference in outcomes in low-incidence areas. Setup of COVID-19–free pathways is therefore likely to be justified during the end phases of current lockdowns in preparation for future wave.

It is likely that differences in SARS-CoV-2 transmission rates are responsible for differences in pulmonary complications between hospitals with COVID-19–free surgical pathways and those with no defined pathway. First, the rate of postoperative SARS-CoV-2 infection was consistently lower in COVID-19–free surgical pathways. Second, SARS-CoV-2 infection was associated with a very high rate of pulmonary complications. Third, the benefit of COVID-19–free pathways was greatest in high SARS-CoV-2 incidence areas. Finally, the effect size increased in proportion with the number of COVID-19–free components of the surgical pathway. The overall preoperative testing rate was low (27.0%), and testing was not associated with lower pulmonary complication rates in the main model. Furthermore, in a sensitivity analysis for patients with a negative preoperative swab test, the benefit of COVID-19–free pathways persisted.

Although we defined COVID-19–free pathways in the Protocol, the exact nature varied across this pragmatic study. For example, we did not include elective and emergency admission areas or the perioperative recovery room in the definition of center status. Patients with comorbidities and who are elderly will still need to undergo surgery in major acute hospitals because of resource availability (eg, critical care, interventional radiology, multispecialty operations), and these hospitals are likely to continue to admit patients with

FIG 2. Factors associated with postoperative pulmonary complications after elective cancer surgery, including data from 8,971 patients with complete data. See Data Supplement for the full model, details around missing data, and full definitions. ASA, American Society of Anesthesiologists; BMI, body mass index; COVID-19, coronavirus disease 2019; ECOG, Eastern Cooperative Oncology Group; OR, odds ratio; RCRI, Revised Cardiac Risk Index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

TABLE 2. Comparison of Patients With and Without Postoperative Pulmonary Complications

Factor	No Pulmonary Complications, No. (%)	Pulmonary Complications, No. (%)	P
No. of patients	8,786	385	
Age, years			
< 50	1,624 (18.5)	20 (5.2)	< .001
50-59	1,929 (22.0)	51 (13.2)	
60-69	2,427 (27.6)	118 (30.6)	
70-79	2,096 (23.9)	145 (37.7)	
≥ 80	710 (8.1)	51 (13.2)	
Sex			
Female	5,455 (62.1)	121 (31.4)	< .001
Male	3,329 (37.9)	264 (68.6)	
Missing	2	0	
BMI			
Normal	3,403 (38.7)	135 (35.1)	.100
Overweight	2,771 (31.5)	117 (30.4)	
Obese	1,827 (20.8)	85 (22.1)	
Underweight	207 (2.4)	10 (2.6)	
Missing	578 (6.6)	38 (9.9)	
ASA grade			
1-2	6,408 (73.3)	192 (50.1)	< .001
3-5	2,340 (26.7)	191 (49.9)	
Missing	38	2	
Current smoker			
No	7,843 (89.3)	321 (83.4)	< .001
Yes	943 (10.7)	64 (16.6)	
Preexisting respiratory condition			
No	7,873 (89.6)	306 (79.5)	< .001
Yes	913 (10.4)	79 (20.5)	
RCRI			
0	2,859 (32.5)	33 (8.6)	< .001
1	4,413 (50.2)	221 (57.4)	
2	1,240 (14.1)	89 (23.1)	
≥ 3	274 (3.1)	42 (10.9)	
ECOG PS			
0	5,597 (64.7)	148 (38.6)	< .001
1-2	2,922 (33.8)	220 (57.4)	
3-4	136 (1.6)	15 (3.9)	
Missing	131	2	
Cancer type			
Colorectal	2,176 (24.8)	134 (34.8)	< .001
Breast	2,132 (24.3)	9 (2.3)	
Gynecologic	1,082 (12.3)	20 (5.2)	
Head or neck	1,096 (12.5)	41 (10.6)	
Hepatopancreatobiliary	626 (7.1)	50 (13.0)	

(continued on following page)

TABLE 2. Comparison of Patients With and Without Postoperative Pulmonary Complications (continued)

Factor	No Pulmonary Complications, No. (%)	Pulmonary Complications, No. (%)	P
Intracranial	162 (1.8)	2 (0.5)	
Thoracic	516 (5.9)	41 (10.6)	
Esophagogastric	322 (3.7)	65 (16.9)	
Sarcoma	253 (2.9)	8 (2.1)	
Urologic	421 (4.8)	15 (3.9)	
Disease stage			
Early	6,308 (71.8)	222 (57.7)	< .001
Advanced	2,472 (28.2)	163 (42.3)	
Missing	6	0	
Booking type			
Day case	729 (8.4)	1 (0.3)	< .001
Inpatient	7,994 (91.6)	383 (99.7)	
Missing	63	1	
Anesthetic			
Regional/local	458 (5.2)	29 (7.5)	.061
General	8,328 (94.8)	356 (92.5)	
Operation grade			
Minor	2,062 (23.6)	27 (7.0)	< .001
Major	6,689 (76.4)	356 (93.0)	
Missing	35	2	
Preoperative testing			
Not screened	6,412 (73.0)	286 (74.3)	.612
Screened	2,374 (27.0)	99 (25.7)	
Hospital type			
COVID-19–free surgical pathway	2,426 (27.6)	55 (14.3)	< .001
No defined pathway	6,360 (72.4)	329 (85.7)	
Missing	0	1	
Community SARS-CoV-2 risk			
Low	7,694 (87.6)	334 (86.8)	.692
High	1,092 (12.4)	51 (13.2)	

NOTE. See the Data Supplement for full definitions. Percentages calculated as a proportion of column total. *P* values calculated using χ^2 test.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; COVID-19, coronavirus disease 2019; ECOG PS, Eastern Cooperative Oncology Group performance status; RCRI, Revised Cardiac Risk Index; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

COVID-19. COVID-19–free pathways must be robustly quality assured within these settings. Detailed evaluations of additional in-hospital measures to reduce SARS-CoV-2 exposure, including serial preoperative testing, personal protective equipment, drug prophylaxis, staff testing, and perioperative isolation, are still required.

The overall mortality rate with pulmonary complications (17.2%) is higher than would be expected compared with prepandemic rates.^{22-27,28} Data from elective and emergency surgical patients have shown high mortality associated with perioperative SARS-CoV-2 infection, which is consistent with

our series.⁵ This information should be used routinely as part of informed consent for elective surgery.

There were limitations to this study. First, the risk of selection bias in COVID-19–free surgical pathways was accounted for through risk adjustment and planned sensitivity analyses. Despite this, COVID-19–free pathways may have been better resourced, and there may have been residual bias. However, establishing COVID-19–free areas did not seem to be determined by resource availability alone; patients were operated on in these pathways in 27 of 37 countries in which five

TABLE 3. Clinical Outcomes for Patients Who Underwent Surgery in a COVID-19–Free Surgical Pathway Versus No Defined Pathway Split by Low Versus High Community SARS-CoV-2 Incidence

Community SARS-CoV-2 Incidence Area	COVID-19–Free Surgical Pathway (n = 2,481)		No Defined Pathway (n = 6,689)	
	% (95% CI)	No. of Total No.	% (95% CI)	No. of Total No.
Low				
Pulmonary complications	2.2 (1.6 to 3.0)	43 of 1,948	4.8 (4.2 to 5.3)	290 of 6,079
SARS-CoV-2 infection	1.6 (1.1 to 2.3)	32 of 1,948	3.1 (2.7 to 3.6)	188 of 6,079
30-day mortality	0.7 (0.4 to 1.2)	14 of 1,939	1.7 (1.4 to 2.1)	103 of 6,041
30-day mortality and SARS-CoV-2 infection	0.01 (0.001 to 0.04)	2 of 1,939	0.7 (0.5 to 1.0)	44 of 6,041
High				
Pulmonary complications	2.3 (1.2 to 3.9)	12 of 533	6.4 (4.6 to 8.6)	39 of 610
SARS-CoV-2 infection	3.9 (2.5 to 6.0)	21 of 533	8.2 (6.1 to 10.7)	50 of 610
30-day mortality	0.9 (0.3 to 2.2)	5 of 527	2.1 (1.1 to 3.6)	13 of 608
30-day mortality and SARS-CoV-2 infection	0.8 (0.2 to 1.9)	4 of 527	1.4 (0.7 to 2.8)	9 of 608

NOTE. Pulmonary complications were defined as pneumonia, acute respiratory distress syndrome, and/or unexpected postoperative ventilation. Areas defined as high (30-day cumulative notification rate of ≥ 25 cases per 100,000 population) or low (14-day cumulative notification rate of < 25 cases per 100,000 population) according to European Centre for Disease Control and Prevention reporting criteria during 2-week periods in March and April 2020. Proportions are presented as mean averages with 95% CIs calculated using the Pearson-Klopper exact method (R package binom.confint).

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

or more centers participated. Second, we included swab, CT, and clinical diagnoses of COVID-19 in the definition of postoperative SARS-CoV-2 infection to reflect variable access to testing during early phases of the pandemic.^{29,30} However, only 14.4% of patients infected had a CT or clinical diagnosis, which minimizes the risk of incorrect diagnosis. Third, borderline

operable cancers and high-risk patients may not have been offered surgery during the pandemic, so the potential benefits of COVID-19–free surgical pathways may be even greater for this group.^{31,32} Fourth, there is a possibility of incomplete case ascertainment, although we implemented a number of strategies to minimize this.

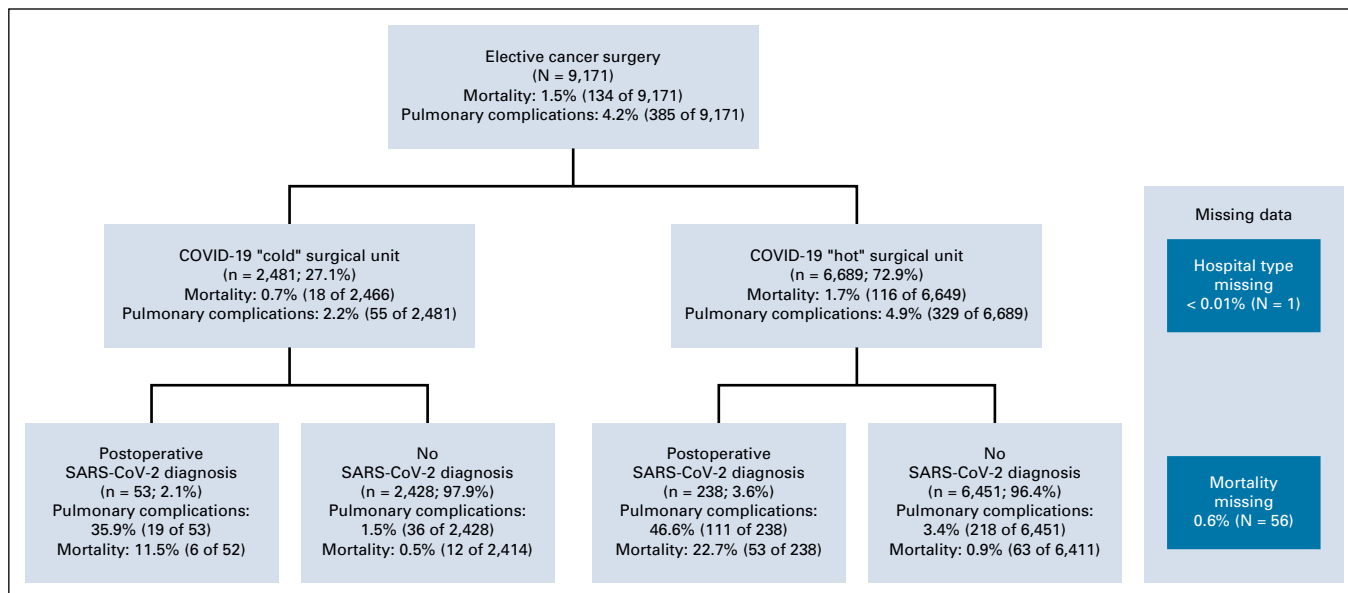


FIG 3. Rates of pulmonary complications, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and death in hospitals with coronavirus disease 2019 (COVID-19)–free surgical pathways v those with no defined pathway. Pulmonary complications were defined as pneumonia, acute respiratory distress syndrome, and/or unexpected postoperative ventilation.

COVID-19–free surgical pathways and entirely separate elective surgery hospitals may lead to unintended consequences that include reduction in

capacity for other health conditions. These consequences will need to be monitored at a whole-system level.

AFFILIATIONS

- ¹NIHR Global Health Research Unit on Global Surgery, University of Birmingham, Birmingham, United Kingdom
²University of Birmingham, Birmingham, United Kingdom
³Queen Mary University of London, London, United Kingdom
⁴King Hussein Cancer Foundation: King Hussein Cancer Center, Amman, Jordan
⁵Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy
⁶Midlands Abdominal and Retroperitoneal Sarcoma Unit, Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom
⁷Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom
⁸Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom
⁹Francisco Gentil Portuguese Institute for Oncology of Porto: Instituto Português de Oncologia do Porto Francisco Gentil EPE, Porto, Portugal
¹⁰Memorial Sloan Kettering Cancer Center, New York, NY
¹¹Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom
¹²Addenbrooke's Hospital, Cambridge University, Cambridge, United Kingdom
¹³Harvard Medical School, Centre for Outcomes & Patient Safety in Surgery, Boston, MA
¹⁴Henares University Hospital: Hospital Universitario del Henares, Madrid, Spain
¹⁵Liver Unit, Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom
¹⁶St. James Hospital, Dublin, Ireland
¹⁷University of Newcastle, NSW, Australia
¹⁸Liverpool Head and Neck Centre, University of Liverpool, Liverpool, United Kingdom
¹⁹Royal Devon and Exeter NHS Foundation Trust, Exeter, United Kingdom
²⁰University of Cambridge, Cambridge, United Kingdom
²¹Pan Birmingham Gynaecological Cancer Centre, City Hospital, Birmingham, United Kingdom
²²Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, United Kingdom

CORRESPONDING AUTHOR

Aneel Bhangu, MBChB, PhD, FRCS, NIHR, Global Health Research Unit on Global Surgery, Institute of Translation Medicine, University of Birmingham, B15 2TH, United Kingdom. email a.a.bhangu@bham.ac.uk.

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EQUAL CONTRIBUTION

J.C.G., D.N., J.F.F.S., O.O., E.L., and M.L.V. contributed equally to this manuscript as co-first authors.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

Conception and design: All authors
Administrative support: All authors
Provision of study materials or patients: All authors
Collection and assembly of data: All authors
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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9. NHS England and NHS Improvement: Advice to trusts on maintaining cancer treatment during the COVID-19 response, 2020 <https://www.england.nhs.uk/coronavirus/publication/advice-to-trusts-on-maintaining-cancer-treatment-during-the-covid-19-response>
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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Elective Cancer Surgery in COVID-19–Free Surgical Pathways During the SARS-CoV-2 Pandemic: An International, Multicenter, Comparative Cohort Study

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Jonathan Edwards

Consulting or Advisory Role: Stryker Leibinger GmbH, AstraZeneca

Speakers' Bureau: Zimmer Biomet

Carlos San Miguel-Méndez

Honoraria: W.L. Gore

Peter Pockney

Research Funding: Streck, Fisher and Paykel

Neil Smart

Speakers' Bureau: Medtronic

Speakers' Bureau: Gore

Grant Stewart

Honoraria: Pfizer, Merck, EUSA Pharma

Consulting or Advisory Role: CMR Surgical

Research Funding: Pfizer, AstraZeneca

Sudha Sundar

Honoraria: AstraZeneca

Consulting or Advisory Role: AstraZeneca

No other potential conflicts of interest were reported.

APPENDIX Author List (PubMed-citable)

Writing Group (*Denotes joint first author)

James C Glasbey* (UK), Dmitri Nepogodiev* (UK), Joana FF Simoes* (Portugal), Omar Omar* (UK), Elizabeth Li* (UK), Mary L Venn* (UK), Mohammad Abou Chaar (Jordan), Vita Capizzi (Italy), Daoud Chaudhry (UK), Anant Desai (UK), Jonathan G Edwards (UK), Jonathan P Evans (UK), Marco Fiore (Italy), Jose Flavio Videria (Portugal), Samuel J Ford (UK), Ian Ganyli (USA), Ewen A Griffiths (UK), Rohan R Gujjuri (UK), Angelos G Koliass (UK), Haytham MA Kaafarani (USA), Ana Minaya-Bravo (Spain), Siobhan C McKay (UK), Helen M Mohan (Ireland), Keith Roberts (UK), Carlos San Miguel-Méndez (Spain), Peter Pockney (Australia), Richard Shaw (UK), Neil J Smart (UK), Grant D Stewart (UK), Sudha Sundar (UK), Raghavan Vidya (UK), Aneel A Bhangu (UK, *overall guarantor*).

Statistical Analysis

James C Glasbey, Omar Omar (*Lead statistician*), Aneel A Bhangu

CovidSurg Operations Committee

Kwabena Siaw-Acheampong, Ruth A Benson, Edward Bywater, Daoud Chaudhry, Brett E Dawson, Jonathan P Evans, James C Glasbey, Rohan R Gujjuri, Emily Heritage, Conor S Jones, Sivesh K Kamarajah, Chetan Khatri, Rachel A Khaw, James M Keatley, Andrew Knight, Samuel Lawday, Elizabeth Li, Harvinder S Mann, Ella J Marson, Kenneth A McLean, Siobhan C McKay, Emily C Mills, Dmitri Nepogodiev, Gianluca Pellino, Maria Picciochi, Elliott H Taylor, Abhinav Tiwari, Joana FF Simoes, Isobel M Trout, Mary L Venn, Richard JW Wilkin, Aneel A Bhangu.

International Cancer Leads (*Denotes specialty Principal Investigators)

James C Glasbey (*Chair*); **Colorectal**: Neil J Smart*, Ana Minaya-Bravo*, Jonathan P Evans, Gaetano Gallo, Susan Moug, Francesco Pata, Peter Pockney, Salomone Di Saverio, Abigail Vallance, Dale Vimalchandran; **Oesophagogastric**: Ewen A Griffiths*, Sivesh K Kamarajah, Richard PT Evans, Philip Townend; **Hepatopancreatobiliary**: Keith Roberts*, Siobhan McKay*, John Isaac, Sohei Satoi; **Thoracic**: John Edwards*, Aman S Coonar, Adrian Marchbank, Edward J Caruana, Georgia R Layton, Akshay Patel, Alessandro Brunelli; **Sarcoma**: Samuel Ford*, Anant Desai*, Alessandro Gronchi*, Marco Fiore, Max Almond, Fabio Tirota, Sinziana Dumitru; **Neurosurgery**: Angelos Koliass*, Stephen J Price, Daniel M Fountain, Michael D Jenkinson, Peter Hutchinson, Hani J Marcus, Rory J Piper, Laura Lippa, Franco Servadei, Ignatius Esene, Christian Freyschlag, Iuri Neville, Gail Rosseau, Karl Schaller, Andreas K Demetriades, Faith Robertson, Alex Alamri; **Head and neck**: Richard Shaw*, Andrew G Schache, Stuart C Winter, Michael Ho, Paul Nankivell, Juan Rey Biel, Martin Batstone, Ian Ganly; **Breast**: Raghavan Vidya*, Alex Wilkins, Jagdeep K Singh, Dinesh Thekinkattil; **Gynaecology**: Sudha Sundar*, Christina Fotopoulou*, Elaine Leung, Tabassum Khan, Luis Chiva, Jalid Sehouli, Anna Fagotti, Paul Cohen, Murat Gutelkin, Rahel Ghebre, Thomas Konney, Rene Pareja, Rob Bristow, Sean Dowdy, TS Shylasree, R Kottayasamy Seenivasagam, Joe Ng, Keiji Fujiwara; **Urology**: Grant D Stewart*, Benjamin Lamb, Krishna Narahari, Alan McNeill, Alexandra Colquhoun, John McGrath, Steve Bromage, Ravi Barod, Veeru Kasivisvanathan, Tobias Klatte.

Dissemination Committee

Joana FF Simoes (*Chair*); Tom EF Abbott, Sadi Abukhalaf, Michel Adamina, Adesoji O Ademuyiwa, Arnab Agarwal, Murat Akkulak, Ehab Alameer, Derek Alderson, Felix Alakaloko, Markus Albertsmeiers, Osaid Alser, Muhammad Alshaar, Sattar Alshryda, Alexis P Arnaud, Knut Magne Augestad, Faris Ayasra, José Azevedo, Brittany K Bankhead-Kendall, Emma Barlow, David Beard, Ruth A Benson, Ruth Blanco-Colino, Amanpreet Brar, Ana Minaya-Bravo, Kerry A Breen, Chris Bretherton, Igor Lima Buarque, Joshua Burke, Edward J Caruana, Mohammad Chaar, Sohini Chakrabortee, Peter Christensen, Daniel Cox, Moises Cukier, Miguel F Cunha, Giana H Davidson, Anant Desai, Salomone Di Saverio, Thomas M Drake, John G Edwards, Muhammed Elhadi, Sameh Emile, Shebani Farik, Marco Fiore, J Edward Fitzgerald, Samuel Ford, Tatiana Garmanova, Gaetano Gallo,

Dhruv Ghosh, Gustavo Mendonça Ataíde Gomes, Gustavo Grecinos, Ewen A Griffiths, Madalegna Gründl, Constantine Halkias, Ewen M Harrison, Intisar Hisham, Peter J Hutchinson, Shelley Hwang, Arda Isik, Michael D Jenkinson, Pascal Jonker, Haytham MA Kaafarani, Debby Keller, Angelos Koliass, Schelto Kruijff, Ismail Lawani, Hans Lederhuber, Sezai Leventoglu, Andrey Litvin, Andrew Loehrer, Markus W Löffler, Maria Aguilera Lorena, Maria Marta Modolo, Piotr Major, Janet Martin, Hassan N Mashbari, Dennis Mazingi, Symeon Metallidis, Ana Minaya-Bravo, Helen M Mohan, Rachel Moore, David Moszkowicz, Susan Moug, Joshua S Ng-Kamstra, Mayaba Maimbo, Ionut Negoii, Milagros Niquen, Faustin Ntiringanya, Maricarmen Olivos, Kacimi Oussama, Oumaima Outani, Marie Dione Parreno-Sacalanm, Francesco Pata, Carlos Jose Perez Rivera, Thomas D Pinkney, Willemijn van der Plas, Peter Pockney, Ahmad Qureshi, Dejan Radenkovic, Antonio Ramos-De la Medina, Keith Roberts, April C Roslani, Martin Rutegård, Juan José Segura-Sampedro, Irène Santos, Sohei Satoi, Raza Sayyed, Andrew Schache, Andreas A Schnitzbauer, Justina O. Seyi-Olajide, Neil Sharma, Richard Shaw, Sebastian Shu, Kjetil Soreide, Antonino Spinelli, Grant D Stewart, Malin Sund, Sudha Sundar, Stephen Tabiri, Philip Townend, Georgios Tsoulfas, Gabrielle H van Ramshorst, Raghavan Vidya, Dale Vimalchandran, Oliver J Warren, Duane Wedderburn, Naomi Wright, EuroSurg, European Society of Coloproctology (ESCP), Global Initiative for Children's Surgery (GICS), GlobalSurg, GlobalPaedSurg, ItsURG, PTSurg, Spain-Surg, Italian Society of Colorectal Surgery (SICCR), Association of Surgeons in Training (ASiT), Irish Surgical Research Collaborative (ISRC), Transatlantic Australasian Retroperitoneal Sarcoma Working Group (TARPSWG), Italian Society of Surgical Oncology (SICO).

Collaborating Authors (*Denotes Site Principal Investigators)

Argentina: Allemand C, Boccalatte L*, Figari M, Lamm M, Larrañaga J, Marchitelli C, Noll F*, Odetto D, Perrotta M, Saadi J, Zamora L (*Hospital Italiano De Buenos Aires*); Alurralde C, Caram EL, Eskinazi D*, Mendoza JP, Usandivaras M (*Sanatorio 9 De Julio Sa*); Badra R, Esteban A, García JS, García PM, Gerchunoff JI, Lucchini SM*, Nlgra MA, Vargas L (*Sanatorio Allende*).

Armenia: Hovhannisyan T*, Stepanyan A* (*Nairi Medical Center*).

Australia: Gould T, Gourlay R*, Griffiths B (*Calvary Mater Newcastle*); Gananadha S*, McLaren M (*Canberra Hospital*); Cecire J, Joshi N, Salindera S*, Sutherland A (*Coffs Harbour Health Campus*); Ahn JH, Charlton G, Chen S, Gauri N, Hayhurst R, Jang S, Jia F, Mulligan C, Yang W, Ye G, Zhang H (*Concord Repatriation General Hospital*); Ballal M, Gibson D, Hayne D, Moss J*, Richards T, Viswambaram P, Vo UG* (*Fiona Stanley Hospital*); Bennetts J*, Bright T*, Brooke-Smith M*, Fong R, Gricks B, Lam YH, Ong BS, Szpytma M, Watson D (*Flinders Medical Centre*); Bagraith K, Caird S, Chan E, Dawson C, Ho D, Jeyarajan E, Jordan S, Lim A, Nolan GJ, Oar A, Parker D, Puhalla H, Quennell A, Rutherford L, Townend P*, Von Papen M, Wullschlegler M (*Gold Coast University Hospital*); Blatt A*, Cope D, Egoroff N, Fenton M, Gani J, Lott N, Pockney P*, Shugg N (*John Hunter Hospital*); Elliott M, Phung D (*Lifeshouse*); Phan D, Townend D* (*Lismore Base Hospital*); Bong C, Gundara J* (*Logan Hospital*); Frankel A* (*Princess Alexandra Hospital*); Bowman S*, Guerra GR (*Queen Elizabeth II Jubilee Hospital*); Bolt J, Buddingh K, Dudi-Venkata NN, Jog S, Kroon HM*, Sannour T, Smith R, Stranz C (*Royal Adelaide Hospital*); Batstone M*, Lah K*, McGahan W*, Mitchell D*, Morton A, Pearce A, Roberts M*, Sheahan G*, Swinson B (*Royal Brisbane And Women's Hospital*); Alam N, Banting S, Chong L, Choong P*, Clatworthy S, Foley D, Fox A, Hii MW, Knowles B, Mack J, Read M, Rowcroft A, Ward S*, Wright G* (*St Vincent's Hospital*).

Austria: Lanner M* (*Kardinal Schwarzenberg Klinikum*); Königsrainer I* (*Landeskrankenhaus Feldkirch*); Bauer M, Freyschlag C, Kafka M, Messner F, Öfner D*, Tschulak I (*Medical University Of Innsbruck*); Emmanuel K, Grechenig M, Gruber R, Harald M, Öhlberger L, Presl J*, Wimmer A (*Paracelsus Medical University Salzburg*).

Azerbaijan: Namazov İ, Samadov E (*Leyla Medical Center*).

Barbados: Barker D, Boyce R, Corbin S, Doyle A, Eastmond A, Gill R, Haynes A, Millar S, O'Shea M, Padmore G*, Paquette N, Phillips E, St. John S, Walkes K (*Queen Elizabeth Hospital*).

Belgium: Flamey N, Pattyn P* (*Az Delta*); Oosterlinck W*, Van den Eynde J, Van den Eynde R (*Uz Leuven*).

Brazil: Gatti A*, Nardi C, Oliva R (*Hospital Geral De Pirajussara*); De Cicco R* (*Instituto De Câncer Dr Arnaldo Vieira De Carvalho*); Cecconello I, Gregorio P, Pontual Lima L, Ribeiro Junior U, Takeda F*, Terra RM* (*Instituto Do Câncer De Estado De São Paulo*).

Bulgaria: Sokolov M* (*University Hospital Alexandrovska*).

Canada: Kidane B*, Srinathan S (*Health Sciences Centre*); Boutros M*, Caminsky N, Ghitulescu G, Jamjoum G, Moon J, Pelletier J, Vanounou T, Wong S (*Jewish General Hospital*); Boutros M*, Dumitra S, Kouyoumdjian A (*McGill University Health Center*); Johnston B*, Russell C (*Saint John Regional Hospital*); Boutros M*, Demyttenaere S*, Garfinkle R (*St. Mary's Hospital*); Abou-Khalil J, Nessim C*, Stevenson J (*The Ottawa Hospital*).

Chile: Heredia F* (*Clínica Universitaria De Concepción*).

Colombia: Almeciga A*, Fletcher A*, Merchan A* (*Centro De Investigaciones Oncológicas Clínica San Diego - Ciosad*); Puentes LO* (*Hospital San José*); Mendoza Quevedo J* (*Subred Sur Occidente De Kennedy (Hospital De Kennedy)*).

Croatia: Bačić G, Karlović D, Kršul D, Zelić M* (*University Hospital Center Rijeka*); Luksic I*, Mamic M (*University Hospital Dubrava*); Bakmaz B, Coza I, Dijan E, Katusic Z, Mihanovic J*, Rakvin I (*Zadar General Hospital*).

Cyprus: Frantzeskou K, Gouvas N*, Kokkinos G, Papatheodorou P, Pozotou I, Stavrinidou O, Yiallourou A* (*Nicosia General Hospital*).

Czechia: Martinek L, Skrovina M*, Szubota I (*Hospital & Oncological Centre Novy Jicin*); Zatecký J* (*Slezská Nemocnice V Opavě, P.o.*); Javurkova V, Klat J* (*University Hospital Ostrava*).

Denmark: Avlund T, Christensen P*, Harbjerg JL, Iversen LH, Kjaer DW, Kristensen HØ, Mekhael M (*Aarhus University Hospital*); Ebbenhøj AL, Krarup P, Schlesinger N, Smith H* (*Bispebjerg Hospital*).

Egypt: Abdelsamed A, Azzam AY*, Salem H*, Seleim A (*Al Azhar University Hospitals*); Abdelmajeed A, Abdou M, Abosamak NE, AL Sayed M, Ashoush F*, Atta R, Elazzazy E, Elhoseiny M, Elnemr M, Elqasabi MS, Elsayed Hewalla ME, Elsherbini I, Essam E, Eweda M, Ghallab I, Hassan E, Ibrahim M, Metwalli M, Mourad M, Qatora MS, Ragab M, Sabry A*, Saifeldin H, Saleh Mesbah Mohamed Elkaffas M, Samih A, Samir Abdelaal A, Shehata S*, Shenit K (*Alexandria Main University Hospital*); Attia D, Kamal N, Osman N* (*Alexandria Medical Research Institute*); Abbas AM*, Abd Elazeem HAS, Abdelkarem MM, Alaa S*, Ali AK, Ayman A, Azizeldine MG, Elkhatay H*, M. elghazaly S, Monib FA, Nageh MA, Saad MM*, Salah M, Shahine M*, Yousof EA, Youssef A (*Assiut University Hospital*); Eldaly A* (*El-Menshawey Hospital*); Elfiky M*, Nabil A (*Kasr Alainy Faculty Of Medicine, Cairo University*); Amira G, Sallam I*, Sherief M, Sherif A (*Misr Cancer Center*); Abdelrahman A, Aboukassam H, Ghaly G*, Hamdy R, Morsi A, Salem H*, Sherif G (*National Cancer Institute*); Abdeldayem H, Abdelkader Salama I*, Balabel M, Fayed Y, Sherif AE* (*National Liver Institute, Menoufia University*).

Ethiopia: Bekele D* (*Maddawalabu University Goba Referral Hospital*).

Finland: Kauppila J*, Sarjanoja E (*Länsi-Pohja Central Hospital*); Helminen O, Huhta H, Kauppila JH* (*Oulu University Hospital*).

France: Beyrne C, Jouffret L*, Lugans L, Marie-Macron L (*Centre Hospitalier Avignon*); Chouillard E*, De Simone B* (*Centre Hospitalier Intercommunal Poissy Saint Germain En Laye*); Bettoni J, Dakpé S, Devauchelle B, Lavagen N, Testelin S* (*Chu Amiens*); Boucher S*, Breheret R, Gueutier A, Kahn A, Kün-Darbois J (*Chu Angers*); Barrabe A, Lakkis Z*, Louvrier A, Manfredelli S, Mathieu P (*Chu Besançon*); Chebaro A*, Drubay V, El amrani M, Eveno C, Lecolle K, Legault G, Martin L, Piessen G*, Pruvot FR, Truant S, Zerbib P (*Chu Lille*); Ballouhey Q*, Barrat B, Laloze J, Salle H, Taibi A, Usseglio J (*Chu Limoges*); Bergeat D, Merdignac A (*Chu Rennes - General Surgery*); Le Roy B, Perotto LO, Scalabre A* (*Chu Saint Etienne*); Aimé A, Ezanno A*, Malgras B (*Hia Bégin*); Bouche P*, Tzedakis S* (*Hôpital Cochin - Aphp*); Cotte E, Glehen O, Kepenekian V, Lifante J, Passot G (*Hopital*

Lyon Sud); D'Urso A, Felli E, Mutter D, Pessaux P, Seeliger B* (*Hus, Pole Hépat-Digestif / Ihu-Strasbourg*); Bardet J, Berry R, Boddaert G, Bonnet S, Brian E, Denet C, Fuks D, Gossot D, Grigoriou M, Laforest A, Levy-Zauberman Y, Louis-Sylvestre C, Moumen A, Pourcher G, Seguin-givelet A*, Tribillon E (*Institut Mutualiste Montsouris*); Duchalais E*, Espitalier F, Ferron C, Malard O* (*Nantes University Hospital*).

Germany: Bork U*, Distler M, Fritzmann J, Kirchberg J, Praetorius C, Riediger C, Weitz J, Welsch T, Wimberger P* (*University Hospital Carl Gustav Carus, TU Dresden*); Beyer K, Kamphues C*, Lauscher J, Loch FN, Schineis C (*Charité University Medicine, Campus Benjamin Franklin*); Albertsmeier M*, Angele M, Kappenberger A, Niess H, Schiergens T, Werner J (*Department of General, Visceral and Transplantation Surgery, Ludwig-Maximilians-Universität Munich*); Becker R*, Jonescheit J (*Heilig-Geist Hospital Bensheim*); Pergolini I, Reim D* (*Klinikum Rechts Der Isar Tum School Of Medicine*); Boeker C, Hakami I*, Mall J* (*Krh Nordstadt-Siloah Hospitals*); Liokatis P*, Smolka W (*LMU Klinikum Campus Innenstadt*); Nowak K*, Reinhard T* (*Romed Klinikum Rosenheim*); Hölzle F, Modabber A*, Winnand P (*University Hospital Aachen*); Knitschke M* (*University Hospital Giessen And Marburg*); Kauffmann P, Wolfer S* (*University Hospital Goettingen / Universitätsmedizin Goettingen*); Kleeff J, Lorenz K, Michalski C, Ronellenfitsch U*, Schneider R (*University Hospital Halle (Saale)*); Bertolani E, Königsrainer A*, Löffler MW, Quante M*, Steidle C, Überrück L, Yurttas C (*University Hospital Tuebingen*); Betz CS, Bewarder J, Böttcher A, Burg S, Busch C, Gosau M*, Heuer A, Izbicki J, Klatté TO, Koenig D, Moeckelmann N, Nitschke C, Priemel M, Smeets R, Speth U, Thole S, Uzunoglu FG*, Vollkommer T, Zeller N (*University Medical Center Hamburg-Eppendorf*); Battista MJ*, Gillen K, Hasenburger A, Krajnak S, Linz V, Schwab R (*University Of Mainz, Department Of Gynaecology And Obstetrics*).

Greece: Angelou K, Haidopoulos D*, Rodolakis A (*Alexandra General Hospital*); Antonakis P, Bramis K, Chardalias L, Contis I, Dafnios N, Dellaportas D, Fragulidis G, Gklavas A, Konstadoulakis M, Memos N*, Papaconstantinou I*, Polydorou A, Theodosopoulos T, Vezakis A (*Aretaieion Hospital*); Antonopoulou MI, Manatakis DK*, Tasis N (*Athens Naval And Veterans Hospital*); Arkadopoulos N, Danias N, Economopoulou P, Kokoropoulos P, Larentzakis A, Michalopoulos N*, Selmani J, Sidiropoulos T, Tsaousis V, Vassiliu P (*Attikon University General Hospital*); Bouchagier K*, Klimopoulos S, Paspaliari D, Stylianidis G (*Evangelismos General Hospital*); Baxevanidou K, Bouliaris K, Chatzikomnitsa P, Efthimiou M, Giaglaras A, Kalfountzos C*, Koukoulis G, Ntziovara AM, Petropoulos K, Soulikia K, Tsiamalou I, Zervas K, Zourmtou S (*General Hospital Of Larissa "Koutlimpaneio And Triantafylleio"*); Baloyiannis I, Diamantis A, Gkrinia E, Hajioannou J*, Korais C, Koukoura O, Perivoliotis K, Saratziotis A, Skoulakis C, Symeonidis D, Tepetes K, Tzouvaras G*, Zacharoulis D (*General University Hospital Of Larissa*); Alexoudi V, Antoniadis K*, Astreidis I, Christidis P, Deligiannidis D, Grivas T, Ioannidis O*, Kalaitzidou I, Loutzidou L, Mantevras A, Michailidou D, Paraskevopoulos K, Politis S, Stavroglou A, Tatsis D, Tilaveridis I, Vahthevanos K, Venetis G (*George Papanikolaou General Hospital Of Thessaloniki*); Karaitianos I*, Tsirlis T (*Henry Dunant Hospital Center*); Charalabopoulos A, Liakakos T, Mpaili E, Schizas D*, Spartalis E, Syllaios A, Zografos C (*Laiko University Hospital*); Anthoulakis C, Christou C, Papadopoulos V, Tooulas A, Tsolakidis D*, Tsoulfas G*, Zouzoulas D (*Papageorgiou General Hospital*); Athanasakis E, Chrysos E, Tsiaoussis J, Xenaki S*, Xynos E* (*University Hospital Of Heraklion Crete And Interclinic Hospital Of Crete*).

Hong Kong: Futaba K*, Ho MF, Hon SF, Mak TWC, Ng SSM (*Prince of Wales Hospital*); Foo CC* (*Queen Mary Hospital*).

Hungary: Banky B*, Suszták N (*Szent Borbála Kórház*).

Ireland: Aremu M*, Canas-Martinez A, Cullivan O, Murphy C, Owens P, Pickett L (*Connolly Hospital Blanchardstown*); Akmenkalne L, Byrne J, Corrigan M*, Cullinane C, Daly A, Fleming C*, Jordan P, Killeen S, Lynch N, McCarthy A, Mustafa H, O'Brien S, O'Leary P, Syed WAS, Vernon L (*Cork University Hospital*); Callanan D, Huang L, Ionescu A, Sheahan P* (*South Infirmary Victoria University Hospital*); Balasubramanian I, Boland M, Conlon K, Evoy D, Fearon N, Gallagher T,

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Italy: Macina S* (*Asst Mantua*); Mariani NM*, Opocher E, Pisani Ceretti A (*Asst Santi Paolo E Carlo*); Ferrari F*, Odicino F, Sartori E* (*Asst Spedali Civili, Ospedale Di Brescia*); Cotsoglou C*, Granieri S (*Asst Vimercate*); Bianco F*, Camillo A, Colledan M*, Tornese S, Zambelli MF (*Asst-Papa Giovanni Xiii- Bergamo*); Bissolotti G, Fusetti S, Lemma F* (*Azienda Ospedaliera Di Padova*); Marino MV*, Mirabella A, Vaccarella G (*Azienda Ospedaliera Ospedali Riuniti Villa Sofia-Cervello, Palermo*); Agostini C, Alemanno G, Bartolini I, Bergamini C, Bruscano A, Checcucci C, De Vincenti R, Di Bella A, Fambrini M, Fortuna L, Maltinti G, Muesan P*, Petraglia F, Prospero P*, Ringressi MN, Risaliti M, Sorbi F*, Taddei A*, Tucci R (*Azienda Ospedaliera Universitaria Careggi*); Bassi C, Bortolasi L, Campagnaro T*, Casetti L, De Pastena M, Esposito A, Fontana M, Guglielmi A, Landoni L, Malleo G, Marchegiani G, Nobile S, Paiella S, Pedrazzani C, Rattizzato S, Ruzzenente A, Sallia R*, Turri G, Tuveri M (*Azienda Ospedaliera Universitaria Integrata Di Verona*); Bellora P, D'Aloisio G, Ferrari M, Francone E, Gentilli S*, Nikaj H (*Azienda Ospedaliera Universitaria Maggiore Della Carità*); Bianchini M, Chiarugi M, Coccolini F, Di Franco G, Furbetta N, Gianardi D, Guadagni S, Morelli L*, Palmeri M, Tartaglia D* (*Azienda Ospedaliera Universitaria Pisana*); Anania G*, Carcoforo P*, Chiozza M, De Troia A, Koleva Radica M, Portinari M, Sibilla MG, Urbani A (*Azienda Ospedaliera Universitaria Sant'anna*); Fabbri N, Feo CV*, Gennari S, Parini S, Righini E (*Azienda Unità Sanitaria Locale di Ferrara - University of Ferrara*); Ampollini L*, Bellanti L, Bergonzani M, Bertoli G, Bocchialini G, D'Angelo G*, Lanfranco D, Musini L, Poli T, Santoro GP, Varazzani A* (*Azienda Ospedaliera-Universitaria Di Parma*); Aguzzoli L, Borghonovo G, Castro Ruiz C, Coiro S, Falco G*, Mandato VD*, Mastrolillo P, Montella MT, Annessi V, Zizzo M* (*Azienda Unità Sanitaria Locale - Irccs Di Reggio Emilia*); Grossi U, Novello S, Romano M, Rossi S, Zanusi G* (*Ca' Foncello Treviso-DISCOG-Universit Di Padova*); Esposito G, Frongia F, Pisanu A, Podda M* (*Cagliari University Hospital*); Belluco C, Lauretta A*, Montori G, Moras L, Olivieri M (*Centro Di Riferimento Oncologico Di Aviano (Cro) Irccs*); Bussu F, Carta AG, Cossu ML, Cottu P, Fancellu A, Feo CF, Ginesu GC, Giuliani G, Madonia M, Perra T*, Piras A, Porcu A*, Rizzo D, Scanu AM, Tedde A, Tedde M (*Cliniche San Pietro, A.o.u. Sassari*); Delrio P*, Rega D* (*Colorectal Surgical Oncology Unit - Istituto Nazionale Tumori Fondazione, Pascale-I.r.c.c.s.*); Badalamenti G, Campisi G, Cordova A, Franza M, Maniaci G, Rinaldi G, Toia F* (*Department Of Surgical, Oncological And Oral Sciences. University Of Palermo*); Calabrò M*, Farnesi F, Lunghi EG, Muratore A*, Pipitone Federico NS (*Edoardo Agnelli*); Bãmbina F, D'Andrea G, Familiari P*, Picotti V (*Fabrizio Spaziani*); De Palma G, Luglio G*, Pagano G, Tropeano FP (*Federico II University Hospital*); Baldari L*, Beltramini GA, Boni L*, Cassinotti E*, Gianni A*, Pignataro L*, Torretta S (*Fondazione Irccs Ca' Granda - Ospedale Maggiore Policlinico*); Abatini C, Baia M, Bionani D, Bogani G, Cadenelli P, Capizzi V*, Cioffi SPB, Citterio D*, Comini LV, Cosimelli M, Fiore M*, Folli S, Gennaro M, Giannini L*, Gronchi A, Guaglio M*, Macchi A*, Martinelli F*, Mazzaferro V, Mosca A, Pasquali S, Piazza C, Raspagliesi F, Rolli L*, Salvioni R, Sarpietro G, Sarre C, Sorrentino L (*Fondazione Irccs Istituto Nazionale Dei Tumori, Milano*); Agnes A, Alfieri S, Belia F, Biondi A, Cozza V, D'Amore A, D'Ugo D, De Simone V, Fagotti A*, Gasparini G, Gordini L*, Litta F, Lombardi CP, Lorenzon L, Marra AA, Marzi F, Moro A, Parello A, Perrone E, Persiani R, Ratto C, Rosa F, Saponaro G,

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Graecia' Of Catanzaro); Balercia P, Catarzi L, Consorti G* (*University Hospital Umberto I Ancona*); Di Marzo F* (*Valtiberina*); Fontana T* (*Vittorio Emanuele*).

Japan: Daiko H*, Ishikawa M, Ishiyama K, Iwata S, Kanematsu K, Kanemitsu Y*, Kato T*, Kawai A*, Kobayashi E, Kobayashi Kato M, Moritani K, Nakatani F, Oguma J, Tanase Y, Uno M (*National Cancer Center Hospital*).

Jordan: Al Abdallah M*, Ayasra F, Ayasra Y, Qasem A (*Al-Basheer Hospital*); Abu Za'nouneh FJ, Fahmawee T, Hmedat A, Ibrahim A, Obeidat K* (*King Abdullah University Hospital*); Abdel Al S, Abdel Jalil R, Abou Charar MK, Al-Masri M*, Al-Najjar H, Alawneh F, Alsarairoh O, Elayyan M, Ghanem R, Lataifeh I (*King Hussein Cancer Center*).

Libya: Alkadeeki GZ*, Al Maadany FS (*Al-Jalaa Hospital*); Aldokali N, Senossi O, Subhi MT (*Alkhadra Hospital*); Burgan D*, Kamoka E, Kilani Al, Salamah A, Salem M, Shuwayyah A (*National Cancer Institute, Sabratha - Libya*); Abdulwahed E*, Alshareea E, Aribi N, Aribi S, Biala M, Ghamgh R, Morgom M (*Tripoli Central Hospital*); Aldayri Z, Ellojli I*, Kredan A (*Tripoli University Hospital*).

Lithuania: Bradulskis S, Dainius E, Kubiliute E, Kutkevicius J, Parse-liunas A, Subocius A, Venskutonis D* (*Lithuanian University Of Health Sciences Kaunas Clinical Hospital*).

Madagascar: Rasoaherinomenjanahary F*, Razafindrahita JB, Sami-son LH (*Joseph Ravoahangy Andrianavalona Hospital*).

Malaysia: Ong EC (*Bintulu*); Hamdan KH, Ibrahim MR, Tan JA, Thanapal MR* (*Hospital Kuala Lumpur*); Amin Sahid N, Hayati F*, Jayasilan J, Sriram RK*, Subramaniam S (*Queen Elizabeth Hospital & Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia*); Che Jusoh A, Hussain AH, Mohamed Sidek AS, Mohd Yunus MF, Soh JY, Wong MPK, Zakaria AD*, Zakaria Z (*School Of Medical Sciences & Hospital, Universiti Sains Malaysia*); Fadzli A*, Fathi NQ, Koh PS, Liew YT*, Roslani AC*, Tang CY, Teoh LY*, Wong WJ*, Yahaya AS (*University Malaya Medical Centre*).

Mexico: Alvarez MR, Arrangoiz R, Cordera F*, De la Rosa Abaroa MA, Gómez-Pedraza A, Hernandez R, Maffuz-Aziz A, Posada JA (*Abc Medical Center*); Becerra García FC* (*Hospital San Ángel Inn Chapultepec*); Alfaro-Goldaracena A, Buerba GA, Castillejos-Molina RA, Chan C, Dominguez-Rosado I, Medina-Franco H, Mercado MA*, Oropeza-Aguilar M, Peña Gómez Portugal E, Posadas-Trujillo OE, Rodriguez-Covarrubias F, Salgado-Nesme N, Sarre C, Vilatoba M (*Instituto Nacional De Ciencias Médicas Y Nutrición "Salvador Zubirán"*).

Morocco: Arkha Y, Bechri H, El Ouahabi A, Oudrhiri MY* (*Centre Hospitalier Universitaire Ibn Sina Raba*); Derkaoui hassani F*, El abbaoui N (*Cheikh Zaid International University Hospital*); Amrani L, Belkhadir ZH, Benkabbou A, Chakib O, El Ahmadi B, El Bouazizi Y, Essangri H, Ghannam A*, Majbar AM, Mohsine R, Souadka A* (*Institut National D'oncologie*).

Netherlands: Hompes R*, Meima-van Praag EM, Pronk AJM, Sharabiany S (*Amsterdam Umc, University Of Amsterdam*); Grotenhuis B*, Hartveld L, Reijers S, Van Houdt W* (*Antoni Van Leeuwenhoek Ziekenhuis*); Baaij J, Bolster-van Eenennaam M*, De Graaff M, Sloothaak D, Van Duijvendijk P* (*Gelre Ziekenhuis*); Posma-Bouman L* (*Slingeland Ziekenhuis*); Derksen T, Franken J, Oosterling S* (*Spaarne Gasthuis*); De Bree R* (*University Medical Center Utrecht*); Konsten J*, Van Heinsbergen M (*Viecuri Medisch Centrum*).

Nigeria: Fidelis L, Sholadoye TT*, Tolani MA* (*Ahmadu Bello University Teaching Hospital*); Olaogun J* (*Ekiti State University Teaching Hospital*); Egbuchulem IK*, Lawal TA*, Ogundoyin O*, Olulana DI (*University College Hospital*); Abdur-Rahman L*, Adeyeye A*, Aremu I, Bello J, Olasehinde O, Popoola A (*University Of Ilorin Teaching Hospital*).

Oman: Massoud J*, Massoud R, Sorour TM (*Khoulia Hospital*).

Pakistan: Jamal A, Kerawala AA* (*Cancer Foundation Hospital*); Memon AS*, Nafees Ahmed R, Rai L* (*Dr Ruth K.m. Pfau Civil Hospital*); Ayub B, Hassan N*, Martins RS, Ramesh P, Sayyed R* (*Patel Hospital*); Butt U*, Kashif M, Kashif M*, Khan WH*, Qureshi A*,

Umar M, Waris Farooka M*, Wasim T* (*Services Hospital Lahore*); Ayubi A, Rashid I, Waqar SH* (*The Pakistan Institute Of Medical Sciences*).

Peru: Falcon GM*, Robles R (*Instituto Regional De Enfermedades Neoplásicas Del Sur*).

Philippines: Jocson R, Teh C* (*National Kidney & Transplant Institute*).

Poland: Major P (*Jagiellonian University Medical College*); Bobiński M*, Kotarski J*, Rasoul-Pelińska K* (*Medical University Of Lublin, Chair And Department Of Gynaecological Oncology And Gynaecology*).

Portugal: Azevedo C, Machado D, Mendes F* (*Centro Hospitalar Cova Da Beira*); De Sousa X* (*Centro Hospitalar De Setúbal*); Fernandes U, Ferreira C*, Guidi G, Leal C, Marçal A, Marques R, Martins D, Melo A, Tenreiro N, Vaz Pereira R, Vieira B (*Centro Hospitalar De Trás-Os-Montes E Alto Douro, E.p.e.*); Almeida JI, Correia de Sá T, Costa MJMA, Fernandes V, Ferraz I, Gil CG, Lima da Silva C, Lopes L, Machado N, Marialva J, Nunes Coelho M, Pedro J, Pereira C, Reis R*, Ribeiro A, Santos R, Saraiva P, Silva R, Tavares F, Teixeira M (*Centro Hospitalar Do Tamega E Sousa*); Almeida AC, Amaral MJ, Andrade R, Athayde Nemésio R, Breda D, Camacho C, Canhoto C, Colino M, Correia S, Costa M, De Barros J, De Oliveira López AL, Duque M, Garrido S, Guerreiro P, Guimarães A, Lázaro A*, Lopes C, Martins R, Nogueira O, Oliveira A, Oliveira JM, Rodrigues M, Ruivo A, Santos E, Silva M, Simões J, Valente da Costa A (*Centro Hospitalar E Universitário De Coimbra*); Almeida A, Cavaleiro S, Devezes V, Faria CS, Jácome F, Magalhães Maia M, Nogueiro J, Pereira A, Pereira-Neves A, Pina-Vaz T, Santos-Sousa H*, Silveira H, Vaz S, Vieira P (*Centro Hospitalar E Universitário De São João*); Gomes da Costa A, Lobo Antunes I* (*Centro Hospitalar Lisboa Norte*); Pinto J, Tojal A* (*Centro Hospitalar Tondela-Viseu*); Cardoso N, Cardoso P*, Domingues JC, Henriques P, Manso MI, Martins dos Santos G, Martins R, Morais H*, Pereira R, Revez T, Ribeiro R, Ribeiro VI, Soares A, Sousa S, Teixeira J (*Centro Hospitalar Universitário Do Algarve - Unidade De Faro*); Amorim E, Baptista VH, Cunha MF*, Dias B, Fazenda A, Melo Neves JP, Policarpo F, Sampaio da Nóvoa Gomes Miguel II, Veiga D (*Centro Hospitalar Universitario Do Algarve - Unidade De Portimão*); Andrade AK, Bandoas JP, Borges N*, Branquinho A, Chumbinho B, Correia J, Fidalgo H, Figueiredo de Barros I, Frade S, Gomes J, Maciel J, Pina S, Rodrigues A, Silva N*, Silveira Nunes I, Sousa R (*Centro Hospitalar Universitário Lisboa Central*); Ascensão J, Azevedo P, Costeira B, Cunha C, Garrido R*, Gomes H, Lourenço I, Mendinhos G*, Miranda P, Nobre Pinto A, Peralta Ferreira M, Ribeiro J, Rio Rodrigues L, Sousa Fernandes M (*Hospital Beatriz Angelo*); Azevedo J* (*Hospital Da Horta, E.p.e.*); Galvão D, Soares AC, Vieira A*, Vieira B (*Hospital De Santo Espírito Da Ilha Terceira*); Patrício B, Santos PMDD*, Vieira Paiva Lopes AC (*Hospital De Torres Vedras - Centro Hospitalar Do Oeste*); Cunha R, Faustino A, Freitas A, Martins AB, Mendes JR*, Parreira R, Rosa J, Teves M (*Hospital Do Divino Espírito Santo*); Abreu da Silva A*, Claro M, Costa Santos D, Deus AC, Grilo JV (*Hospital Do Litoral Alentejano*); Borges F*, Corte Real J, Henriques S, Lima MJ, Matos Costa P (*Hospital Garcia De Orta*); Brito da Silva F, Caiado A*, Fonseca F (*Instituto Português De Oncologia De Lisboa Francisco Gentil*); Ângelo M, Baiao JM, Martins Jordão D*, Vieira Carçoço T (*Ipo Coimbra*); Messias J, Millan A, Salgado I, Santos P* (*Ipo Lisboa*); Baía C, Canotilho R, Correia AM, Ferreira Pinto AP, Peyroteo M, Videira JF* (*Ipo Porto*).

Puerto Rico: Escobar P*, Maldonado Santiago M (*Instituto Gineco Oncologico*).

Réunion: Kassir R*, Sauvat F (*Chu Reunion*).

Romania: Bezede C, Chitul A, Ciofic E, Cristian D, Grama F* (*Coltea Clinical Hospital*); Pirtea L*, Secosan C (*Emergency Clinical City Hospital*); Bonci E*, Gata V*, Titu S* (*Prof. Dr Ion Chiricuta Institute Of Oncology*); Ginghina O*, Iordache N, Iosifescu RV (*Saint John Emergency Hospital*).

Russia: Garmanova T, Kazachenko E, Markaryan D, Rodimov S, Tsarkov P*, Tulina I (*Clinic Of Coloproctology And Minimally Invasive Surgery, Sechenov Medical State University*); Litvina Y, Provozina A (*Immanuel Kant Baltic Federal University, Regional Clinical Hospital*);

Agapov M*, Galliamov E, Kakotkin V, Kubyskhin V, Камалов А (Moscow Research And Educational Center, Lomonosov Moscow State University).

Saudi Arabia: Alshahrani M*, Alsharif F, Eskander M (Aseer Central Hospital); Al Raddadi R, Majrashi S*, Mashat A (East Jeddah General Hospital); Akeel N, Alharthi M, Aljiffry M, Basendowah M, Farsi A, Ghunaim M, Khoja A, Maghrabi A, Malibary N*, Nassif M, Nawawi A, Saleem A, Samkari A, Trabulsi N* (King Abdulaziz University Hospital); Al Awwad S*, Alghamdi M*, Alnumani T*, Nasser M*, Said bayazeed A* (King Fahad General Hospital); Alhefthi A*, Almalik O, Alomair A, Alotaibi N, Alresaini F, Alsalamah R, Alsobhi S, Mahasin Z, Othman E, Velagapudi S (King Faisal Specialist Hospital); Ghedan S, Alharthi R, Awad S*, I Sharara M, Abdelrahman S, Althobaiti W (King Faisal Medical Complex); Al Habes H, Alamri A, Alkarak S, Alqannas M*, Alyami M*, Alzamanan M, Cortés Guiral D*, Elawad A (King Khalid Hospital); AlAamer O, Alriyees L, Alselaime N* (King Saud Bin Abdulaziz University For Health Sciences, King Abdullah International Medical Research Center, Ministry Of National Guard, Health Affairs, General Surgery Department.); Abdulkareem A, Ajan A, Akkour K, Al-Habib A, Al-Khayal K, Alatar A, Alburakan A, Alhalal H, Alhassan B, Alhassan N, Alobeed O, Alsaif A, Alsaif F, Alshammari S, Alshaygy I, Barry M, Bin Nasser A*, Bin Traiki T, Bokhari A, Elwatidy S, Helmi H, Madkhali A, Nough T*, Rabah PD, Zubaidi A (King Saud University).

Serbia: Paunovic I*, Slijepcevic N (Centre For Endocrine Surgery, Clinical Center Of Serbia); Aleksic L, Antic A, Barisic G*, Ceranic M, Galun D*, Grubač Ž, Jelenkovic J, Kecmanović D, Krmezić S, Knezevic D*, Krivokopic Z*, Latinčić S, Markovic V*, Matić S*, Miladinov M, Pavlov M*, Pejovic I, Radenkovic D*, Tadic B, Vasljević J, Velickovic D, Zivanovic M (Clinic For Digestive Surgery, Clinical Center Of Serbia); Perovic M, Srbinovic L (Clinic For Gynecology And Obstetrics Narodni Front); Andrijasevic S, Bozanovic T, Cerovic Popovic R, Dokic M, Janjic T, Jeremic K, Kadija S, Ladjevic Likić I, Mirkovic L, Pantovic S, Pilic I, Radojevic M, Stefanovic A*, Vidakovic S, Vilendecic Z (Clinic For Gynecology And Obstetrics, Clinical Center Of Serbia); Antic S, Dunderovic D, Jelovac D*, Jezdic Z, Konstantinovic V, Kotlar B, Kuzmanovic C, Lazić M, Petrovic M, Popovic F, Pucar A, Romic M, Sumrak S, Vujanac V (Clinic For Maxillofacial Surgery, School Of Dental Medicine, University Of Belgrade); Bascarevic V, Bogdanović I, Grujičić D*, Ilic R*, Miličević M, Milisavljević F, Miljković A, Paunovic A, Šćepanović V, Stanimirović A, Todorovic M (Clinic For Neurosurgery, Clinical Center Of Serbia); Jotic A, Milovanovic J*, Trivic A (Clinic For Otorhinolaryngology And Maxillofacial Surgery, Clinical Center Of Serbia); Bumbasirevic U*, Dzamic Z, Kajmaković B, Prijović N, Zivkovic M (Clinic Of Urology, Clinical Center Of Serbia); Buta M, Cvetkovic A, Djuricic I, Gacic S, Goran M, Inic Z, Jevtic N, Jevric M, Jokic V, Markovic I*, Milanović M, Nikolic S, Pejnovic L, Savković N, Spurnic I, Stevic D, Stojiljkovic D, Vucic N, Zegarac M (Institute For Oncology And Radiology Of Serbia); Karamarkovic A, Kenic M, Kovacevic B, Krdzic I*, Milutinović V (Zvezdara University Medical Center).

Singapore: Chan CW, Lieske B* (National University Hospital).

Slovakia: Gális B, Šimko K (University Hospital Bratislava).

South Africa: Almgla N*, Bernon M, Boutall A, Cairncross L*, Herman A, Hilton T, Jonas E, Kloppers C*, Malherbe F, Mugla W*, Nel D, Rayamajhi S, Van Wyngaard T, Vogel J (Groote Schuur Hospital).

Spain: Castaño-Leon AM*, Delgado Fernandez J, Eiriz Fernandez C, Espino Segura-Illa M, Esteban Sinovas O, Garcia Perez D, Gomez P, Jimenez-Roldan L, Lagares A, Moreno-Gomez L, Paredes I, Pérez Núñez A, Sánchez Aniceto G*, Santas M (12 De Octubre University Hospital); Fernández Rodríguez P, Paniagua García Señorans M*, Sanchez-Santos R, Vigorita V (Álvaro Cunqueiro Hospital); Acrich E, Baena Safelíu E, Barrios O, Gola T*, Santanach C, Serrano-Navidad M, Sorribas Grifell M, Vives RV (Bellvitge University Hospital); Escolà D, Jiménez A* (Comarcal Alt Penedés); Cayetano Paniagua L, Gómez Fernández L* (Consorci Sanitari De Terrassa); Artigues E, Bernal-Sprekelsen JC*, Catalá Bauset JC (Consorcio Hospital General Universitario); Collera P, Diaz Del Gobbo R, Farre Font R, Flores Clotet R, Gómez Díaz CJ*, Guàrdia N, Guariglia CA, Osorio A, Sanchez Jimenez R, Sanchon L, Soto Montesinos C (Fundació Althaia - Xarxa Assistencial

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Sri Lanka: Arulanantham A, Bandara GBK, Jayarajah U*, Ravindrakumar S, Rodrigo VS (*District General Hospital Chilaw*); Srishankar S* (*Teaching Hospital Anuradhapura*).

Sudan: Ali karar AA (*Al-Rajhi*).

Sweden: Elbe P*, Lindqvist EK* (*Karolinska University Hospital*); Taflin H* (*Sahlgrenska University Hospital*); Ålgå A*, Heinius G, Nordberg M, Pieniowski E (*South General Hospital*); Gkekas I, Löfgren N, Rutegård M*, Sund M* (*Umea University Hospital*).

Switzerland: Arigoni M, Bernasconi M, Christoforidis D*, Di Giuseppe M, La Regina D, Mongelli F (*Ente Ospedaliero Cantonale*); Chevally M, Dwidar O, Gialamas E, Sauvain M (*Hopital De Pourtales*); Klenke F, Kollár A*, Kurze C (*Inselspital, Bern University Hospital, University Of Bern*); Adamina M*, Bächler T, Crugnale AS, Giardini M, Guglielmetti L, Peros G, Solimene F (*Kantonsspital Winterthur*).

Turkey: Aghayeva A*, Hamzaoglu I, Sahin I (*Acibadem Altunizade Hospital*); Akaydin E, Aliyeva Z, Aytac E, Baca B, Dülgeroğlu O, Ozben V*, Ozmen BB, Uras C (*Acibadem Atakent Hospital*); Arikan AE*, Bilgin IA*, Bozkırlı B*, Ceyhan GO, Kara H, Karahasanoğlu T, Uras C (*Acibadem Maslak Hospital*); Celik H* (*Adana Baskent University*); Meydanlı MM* (*Ankara City Hospital*); Akilli H*, Ayhan A*, Kuscu E* (*Baskent University*); Onan MA* (*Gazi University Medical Faculty Hospital*); Akgör U*, Dincer HA, Erol T, Gultekin M*, Orhan N, Ozgul N*, Salman MC*, Soyak B* (*Hacettepe University Hospital*); Alhamed A, Ergün S*, Özcelik MF, Sanlı AN, Uludağ SS*, Velidedeoğlu M*, Zengin AK (*Istanbul University - Cerrahpaşa Medical Faculty*); Bozkurt MA, Kara Y*, Kocataş A (*Kanuni Sultan Suleyman Training And Research Hospital*); Cimenoglu B, Demirhan R, Saracoglu K* (*Kartal Dr Lutfi Kırdar Training And Research Hospital*); Azamat İF, Balık E*, Buğra D, Giray B, Kulle CB, Taskiran C*, Vatansever D (*Koç University Medical School*); Gözal K, Güler SA, Köken H, Tatar OC*, Utkan NZ,

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Uganda: Benson O*, Lule H* (*Kampala International University Teaching Hospital*).

United Kingdom: Agilinko J, Ahmeidat A, Barabasz M, Bekheit M*, Cheung LK, Colloc T, Cymes W, Elhusseini M, Gradinariu G, Hannah A, Kamera BS, Mignot G, Shaikh S*, Sharma P (*Aberdeen Royal Infirmary*); Abu-Nayla I, Agrawal A*, Al-Mohammad A, Ali S, Ashcroft J, Azizi A, Baker O, Balakrishnan A*, Byrne M, Colquhoun A, Cotter A, Coughlin P, Davies RJ*, Durrani A, Elshaer M, Fordington S, Forouhi P*, Georgiades F, Grimes H, Habeeb A, Hudson V, Hutchinson P*, Irune E, Jah A*, Khan DZ, Kolias A, Kyriacou H, Lamb B, Liau S*, Luke L, Mahmoud R, Mannion R, Masterson L*, Mitrofan CG, Mohan M, Morris A, Murphy S, O'Neill R*, Price S, Pushpa-rajah J, Raby-Smith W, Ramzi J, Rooney S, Santarius T, Singh A, Stewart GD*, Tan XS, Townson A, Tweedle E, Walker C, Waseem S, Yordanov S (*Addenbrooke's Hospital*); Jones T, Kattakayam A, Loh C, Lunevicius R, Pringle S, Schache A, Shaw R*, Sheel A (*Aintree University Hospital*); Rossborough C (*Altnagelvin Area Hospital*); Angelou D, Choynowski M, McAree B*, McCanny A, Neely D (*Antrim Area Hospital- Northern Health And Social Care Trust*); Tutoveanu G* (*Barnsley Hospital Nhs Foundation Trust*); Ahad S, De La Cruz Monroy MFI, Mosley F*, Oktseloglou V* (*Bradford Royal Infirmary*); Alanbuki A*, Patel M, Shabana A (*Brighton And Sussex Nhs Trust, Princess Royal Hospital*); Perera E, Raveendran D, Ravi-Shankar K, Thiruchelvam J* (*Broomfield Hospital*); Arrowsmith L*, Campbell W* (*Causeway Hospital*); Grove T, Kontovounisios C, Warren O* (*Chelsea And Westminster Hospital*); Rolland P* (*Cheltenham General Hospital*); Aggarwal A, Brown S, Jelley C, Neal N* (*Churchill Hospital*); Clifford R, Eardley N, Krishnan E, Manu N, Martin E, Roy Mahapatra S, Serevina OL, Smith C, Vimalachandran D* (*Countess Of Chester Hospital*); Bordenave M*, Houston R, Putnam G, Robson A*, Tustin H (*Cumberland Infirmary*); Emslie K*, Labib PL*, Marchbank A, Miller D, Minto G, Natale J, Nwinee H, Panahi P, Rogers L* (*Derrieff Hospital*); Abubakar A*, Akhter Rahman MM, Chan E, Ko KYK, O'Brien H, Sasapu K*, Woodun H (*Diana Princess Of Wales Hospital Grimsby*); Inglis R, Ng HJ* (*Dumfries And Galloway Royal Infirmary*); De Gea Rico A, Ghazali N*, Lambert J, Markose G, Math S, Sarantitis I, Shrestha D, Sultana A*, Taggarsi M, Timbrell S, Vaz OP, Vitone L* (*East Lancashire Hospitals Nhs Trust*); Day A*, Dent H, Fahim M, Waheed S* (*East Surrey Hospital*); Hunt A, Laskar N* (*East Sussex Healthcare (Conquest Hospital And Eastbourne District General Hospital)*); Gupta A*, Steinke J, Thrumurthy S (*Epsom & St Helier University Hospitals Nhs Trust*); Massie E, McGivern K, Rutherford D, Wilson M* (*Forth Valley Royal Hospital*); Hardie J, Kazzaz S* (*Frimley Health Nhs Ft - Frimley Park*); Handa S, Kaushal M, Kler A, Patel P*, Redfern J, Tezas S (*Furness General Hospital*); Aawsaj Y, Amonkar S, Barry C, Blackwell L, Blake D, Carter J, Emerson H, Fisher A*, Katory M, Korompelis P, McCormick W, Mustafa A, Pearce L, Ratnavel N*, Reehal R (*Gateshead Health Nhs Foundation Trust*); Kretzmer L*, Lalou L, Manku B, Parwaiz I, Stafford J (*George Eliot Hospital*); Abdelkarim M, Asqalan A, Gala T, Ibrahim S, Maw A*, Mithany R, Morgan R*, Sundaram Venkatesan G (*Glan Clwyd Hospital*); Ang K, Caruana EJ*, Chowdhry MF, Mohammad A, Nakas A, Rathinam S (*Glenfield Hospital*); Boal M*, Brown O, Dwerryhouse S*, Higgs S, Vallance A (*Gloucestershire Royal Hospital*); Boyd E, Irvine V, Kirk A* (*Golden Jubilee National Hospital*); Bakolas G, Boulton A, Chandock A*, Khan T, Kumar M* (*Good Hope Hospital*);

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Hospital Ayr); Chopra S, Egbeare D*, Thomas R (*University Hospital Llandough*); Combellack T*, Jones SEF*, Kornaszewska M, Mohammed M, Sharma A, Tahhan G, Valtzoglou V, Williams J (*University Hospital Of Wales*); Eskander P, Gash K*, Gourbault L, Hanna M, Maccabe T, Newton C*, Olivier J, Rozwadowski S, Teh E, West D* (*University Hospitals Bristol NHS Foundation Trust*); Al-omishy H, Baig M, Bates H, Di Taranto G, Dickson K, Dunne N, Gill C, Howe D*, Jeevan D*, Khajuria A, Martin-Ucar A*, McEvoy K, Naredla P, Ng V, Robertson S*, Sait M, Sarma DR, Shanbhag S*, Shortland T, Simmonds S, Skillman J, Tewari N*, Walton G (*University Hospitals Coventry And Warwickshire Nhs Trusts*); Akhtar MA*, Brunt A, McIntyre J, Milne K, Rashid MM, Sgrò A, Stewart KE, Turnbull A (*Victoria Hospital Kirkcaldy*); Aguilar Gonzalez M*, Talukder S* (*West Suffolk Hospital*); Boyle C, Fernando D, Gallagher K, Laird A*, Tham D (*Western General Hospital*); Bath M, Patki P*, Sohrabi C, Tanabalan C (*Whipps Cross University Hospital*); Arif T, Magee C*, Nambirajan T*, Powell S*, Vinayagam R* (*Wirral University Teaching Hospital*); Flindall I, Hanson A, Mahendran V (*Worcestershire Royal Hospital*); Green S, Lim M, MacDonald L, Miu V, Onos L, Sheridan K, Young R* (*York Teaching Hospitals Nhs Trust*); Alam F, Griffiths O, Houlden C, Jones R*, Kolli VS, Lala AK, Leeson S, Peevor R, Seymour Z* (*Ysbyty Gwynedd*).

United States of America: Chen L, Henderson E*, Loehrer A* (*Dartmouth-Hitchcock Medical Center*); Brown K*, Fleming D*, Haynes A*, Heron C, Hill C, Kay H, Leede E, McElhinney K, Olson K, Osterberg EC*, Riley C, Srikanth P, Thornhill M (*Dell Seton Medical Center At The University Of Texas*); Blazer D*, DiLalla G*, Hwang ES*, Lee W, Lidsky M*, Plichta J, Rosenberger L*, Scheri R, Shah K*, Turnage K, Visgauss J, Zani S (*Duke University Medical Center*); Farma J* (*Fox Chase*

Cancer Center); Clark J, Kwon D* (*Henry Ford Hospital*); Etchill E, Gabre-Kidan A*, Jenny HE, Kent A, Ladd M, Long C, Malapati H, Margalit A, Rapaport S, Rose J, Stevens K, Tsai L, Vervoort D, Yes-antharao P (*Johns Hopkins Hospital*); Dehal A* (*Kaiser Permanente Panorama City Medical Center*); Klaristenfeld D* (*Kaiser Permanente San Diego Medical Center*); Huynh K (*Kaiser Permanente West Los Angeles*); Brown L, Ganly I* (*Memorial Sloan Kettering Cancer Center*); Mullinax J* (*Moffitt Cancer Center*); Gusani N, Hazelton J*, Maines J, Oh JS, Ssentongo A, Ssentongo P (*Pennsylvania State University*); Azam M, Choudhry A*, Marx W (*Suny Upstate University Hospital*); Fleming J, Fuson A, Gigliotti J, Ovaitt A, Ying Y* (*University Of Alabama Birmingham*); Abel MK, Andaya V, Bigay K, Boeck MA, Chen L, Chern H, Corvera C, El-sayed I, Glencer A, Ha P, Hamilton BCS, Heaton C, Hirose K, Jablons DM, Kirkwood K, Kornblith LZ*, Kratz JR, Lee R, Miller PN, Nakakura E, Nunez-Garcia B, O'Donnell R, Ozgediz D, Park P, Robinson B, Sarin A, Sheu B, Varma M, Wai K, Wustrack R, Xu MJ (*University Of California, San Francisco (UCSF)*); Beswick D*, Goddard J, Manor J, Song J (*University Of Colorado Hospital/Memorial Hospital/ Medical Center Of The Rockies (All Within Uchealth System)*); Fullmer T, Gaskill C, Gross N*, Kiong K, Roland CL*, Zafar SN (*University Of Texas Md Anderson Cancer Center*); Abdallah M, Abouassi A, Almasri M, Kulkarni G, Marwan H*, Mehdi M (*University Of Texas Medical Branch*); Aoun S, Ban VS*, Batjer HH, Caruso J (*University Of Texas Southwestern*); Abbott D, Acher A, Aiken T, Barrett J, Foley E, Schwartz P, Zafar SN* (*University Of Wisconsin*); Hawkins A*, Maiga A (*Vanderbilt University Medical Center*).

Uruguay: Laufer J*, Scasso S* (*Hospital Pereira Rossell, Montevideo*).