A Risk Model of Admitting Patients With Silent SARS-CoV-2 Infection to Surgery and Development of Severe Postoperative Outcomes and Death

Projections Over 24 Months for 5 Geographical Regions

Kjetil Soreide, MD, PhD, FRCS, FACS,[*†✉] *Sheraz Yaqub, MD, PhD, FEBS,*[‡] *Julie Hallet, MD, MSc,*[§¶] *Jan Terje Kvaløy, PhD,*[||**] *and Tore Selland Kleppe, PhD*[||]

Objective: To model the risk of admitting silent COVID-19-infected patients to surgery with subsequent risk of severe pulmonary complications and mortality.

Summary Background Data: With millions of operations cancelled during the COVID-19 pandemic, pressure is mounting to reopen and increase surgical activity. The risk of admitting patients who have silent SARS-Cov-2 infection to surgery is not well investigated, but surgery on patients with COVID-19 is associated with poor outcomes. We aimed to model the risk of operating on nonsymptomatic infected individuals and associated risk of perioperative adverse outcomes and death.

Methods: We developed 2 sets of models to evaluate the risk of admitting silent COVID-19-infected patients to surgery. A static model let the underlying infection rate (R rate) and the gross population-rate of surgery vary. In a stochastic model, the dynamics of the COVID-19 prevalence and a fixed population-rate of surgery was considered. We generated uncertainty intervals (UIs) for our estimates by running low and high scenarios using the lower and upper 90% uncertainty limits. The modelling was applied for high-income regions (eg, United Kingdom (UK), USA (US) and European Union without UK (EU27), and for the World (WORLD) based on the WHO standard population.

Results: Both models provided concerning rates of perioperative risk over a 24-months period. For the US, the modelled rates were 92,000 (UI 68,000–124,000) pulmonary complications and almost 30,000 deaths (UI 22,000–40·000), respectively; for Europe, some 131,000 patients (UI 97,000–178,000) with pulmonary complications and close to 47,000 deaths (UI 34,000–63,000) were modelled. For the UK, the model suggested a median daily number of operations on silently infected ranging between 25 and 90, accumulating about 18,700 (UI 13,700–25,300) perioperative pulmonary complications and 6400 (UI 4600–8600) deaths. In high-income regions combined, we estimated around 259,000 (UI 191,000–351,000) pulmonary complications and 89,000 deaths (UI 65,000–120,000). For the WORLD, even low surgery rates estimated a global number of 1.2 million pulmonary complications and 350,000 deaths.

Conclusions: The model highlights a considerable risk of admitting patients with silent COVID-19 to surgery with an associated risk for adverse perioperative outcomes and deaths. Strategies to avoid excessive complications and deaths after surgery during the pandemic are needed.

Keywords: COVID-19, mortality, perioperative death, presymptomatic, pulmonary complications, risk, SARS-CoV-2, silent disease, surgery

(*Ann Surg* 2021;273:208–216)

In the ongoing pandemic, an unprecedented number of nonessential elective surgery have been postponed or cancelled resulting in a huge back-log of operations, estimated at 28 million cancelled operations globally over a peak period.[1] Real pressures now exist to reopen surgical elective activity, but with concerns of risk of second waves of pandemic outbursts and potentially introducing spread by reopening activities.

As the worst peak of hospital admissions fade and the effects of societal lock-down set in, there is a mounting pressure to restart surgical activity, catch up with the mounting back-log of surgical operations and restore economy. Of note, the primary focus of the pandemic has been on critical and emergency response with need for prioritizing essential surgical services,[2] but with very little focus on the postpandemic phase.[3] As society reopens, the control of ‘‘silent’’ COVID-19, for example, those without symptoms (asymptomatic or presymptomatic) will be a challenge.[4–6] Current tests have a low specificity for individuals without symptoms which makes screening unreliable, as the false negative rate is too high.[7,8]

From recent models, the SARS-CoV-2 virus is likely to circulate in the population for a considerable time.[9] Furthermore, even the highest endemic regions are nowhere close to herd immunity.[10,11] Available serological tests may not yet be universally available nor reliable.[12] The rate and re-emergence of peaks and further pandemic outbreaks depend on several factors. However, expected variation from modelled studies suggest a duration of at least another 2 years with ongoing viral concerns.[9]

Better understanding of the incidence and implications of perioperative COVID-19 infections is needed to plan the delivery of surgical services. Providing time-sensitive surgical care and catching up on the back-log of operations ought to be balanced against system and patient-level risks of perioperative COVID-19. Admitting patients with no symptoms who have silent COVID-19 to surgery is a real concern as pressure increases to restore surgical activities. A

From the *Department of Gastrointestinal Surgery, Stavanger University Hospital, Stavanger, Norway; †Department of Clinical Medicine, University of Bergen, Bergen, Norway; ‡Department of Hepato-Pancreato-Biliary Surgery, Oslo University Hospital, Oslo, Norway; §Department of Surgery, Sunnybrokk Health Science Center, Toronto, Ontario, Canada; ¶University of Toronto, Toronto, Ontario, Canada; ||Department of Mathematics and Physics, University of Stavanger, Stavanger, Norway; and **Department of Research, Stavanger University Hospital, Stavanger, Norway.

✉ksoreide@mac.com.

Contributors: KS conceived the research question. KS, SY, JH searched initial literature. KS, SY, TSK, JTK designed the study and analysis plan. TSK and JTK did the statistical analysis. KS drafted the initial version of the manuscript. TSK made the figures. All authors discussed and revised the manuscript in several rounds of revisions. All authors critically reviewed early and final versions of the manuscript and approved the final version for submission.

The authors report no conflicts of interest.

Raw data and codes are available in Supplementary information, Appendix F.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.annalsofsurgery.com).

Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0003-4932/20/27302-0208

DOI: 10.1097/SLA.0000000000004583

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

recent study found deaths occurred in 1 in 4 of all who underwent surgery, and pulmonary complications to occur in half of all who had or contracted SARS-Cov-2 in the perioperative period.[13] However, this study did not include the denominator of patients undergoing surgery during the same time period; the risk of perioperative COVID-19, either community or nosocomial acquired remains unknown.

The aim of this study was to project a temporal risk model of operating SARS-Cov-2 infected patients with no symptoms of COVID-19 and the estimated risk of perioperative adverse outcomes.

METHODS

The assumptions used are derived from available studies and models reported to the COVID-19 pandemic. The prevalence of silent COVID-19 disease is reported as those with no symptoms, either as asymptomatic (ie, those who never develop symptoms) and those that are presymptomatic (ie, have the disease but in incubation phase or before developing symptoms).[5] For ease of use due to overlap in definitions, we use silent, asymptomatic and presymptomtic COVID-19 to mean all individuals with no symptoms at time of presentation (eg, at admission to surgery). The ''silent'' or ''presymptomatic'' rate (or, asymptomatic or incubation phase)[5,14] was assumed to be between 45% and 55% of all with COVID-19 disease.[5,14–16]

This study includes 2 sets of models to evaluate the risk of surgery on silent COVID-19 infected patients, with a large degree of overlapping assumptions and use of available data for modelling. The former set of models involve static situations where we let the underlying infection rate and the gross amount of surgeries vary. The second set of models have fixed gross amount of operations, but we assume a stochastic model similar to that of Kissler et al[9] for the dynamics of the infection situation.

Static Model

The static model attempts to count the yearly number of operations performed on presymptomatic COVID-19-infected, divided into groups by age and sex, for a given population. Subsequently this information may be used in conjunction with data from the COVIDSurg Collaborative study[13] to infer the expected numbers of 30-day mortality and pulmonary complications.

The static models, for all outcomes of interest, take the form of

$$S \cdot r \cdot \beta \tag{1}$$

where S is the overall number of surgeries per 100,000 person-years, r is the instantaneous proportion of infected in the population and β represents the numbers ''at risk'' for the outcome of interest (measured in the unit 100,000 person-years). The coefficients β for different outcomes of interest are calculated, for a given population, based on:

- The relative rates of surgery for the different group, adapted from Omling et al,[17] which are scaled to absolute rates for the population when multiplied by S in Eq. (1) (Supplement, Appendix A, http://links.lww.com/SLA/C695).
- The demographics of the population in question, using 5-year age groups (Supplement, Appendix B, http://links.lww.com/SLA/C695).
- An infection loading function which, when multiplied by r in (1), results in higher than r proportions of infected in the middle age groups, while ensuring that the overall proportion of infected is still r.[15]
- The proportion of asymptomatic infected, set equal to 0.5 here, is based on Gudbjartsson et al.[15] Note that the asymptomatic rate scales each β linearly.

Further, the βs for pulmonary complications and 30-day mortality are obtained by appropriately scaling the age-group-wise expected numbers of *operations* on presymptomatic infected, using the probabilities from COVIDSurg Collaborative study data.[13]

The model was applied for Australia (AUS), Canada (CAN), United Kingdom (UK), European Union without UK (EU27), USA (US), and the World (WORLD), based on the WHO standard population scaled to 7594 million persons. Details of the calculations, including the demographic data and per-group surgery rates are provided in Supplementary Appendix A-C, http://links.lww.com/SLA/C695. The values of β for these populations and the different quantities of interest may be found in Table S3, http://links.lww.com/SLA/C695.

Stochastic Dynamic Model

Building on the static model, also a stochastic dynamic model is considered with the aim of accounting for uncertainty related both to daily variation in surgery demand, and more importantly, uncertainty in COVID-19 infection scenarios (Supplementary, Appendix D and E, http://links.lww.com/SLA/C695). The model is considered only for a selection of high-income countries/regions (AUS, CAN, EU27, UK, and US) as it relies on common infection dynamics for the whole population.

Conditionally on some infection trajectory $r(t)$ (in proportion of population) at day t, the surgery demand model is constructed so that the day t daily outcomes of interest are in expectation

$$S \cdot r(t) \cdot \frac{\beta(t)}{365} \tag{2}$$

Under this model the daily number of infected scheduled for surgery per group, the daily number of scheduled silent SARS-CoV-2 infected per group, the daily number of 30-day mortalities and the daily pulmonary complications are given nested stochastic models consistent with (2) in expectation. The exact specification of this stochastic model is given in Supplementary Appendix E, http://links.lww.com/SLA/C695.

Further, the uncertainty in COVID-19 infection scenarios $r(t)$ is generated using a stochastic version of the SEIR-type (Susceptible, Exposed, Infectious, and Recovered individuals) dynamic model, as considered in Kissler et al[9] (see Figs. 6 and S9 in Kissler et al).[9] Specifically, we let several of the parameters of the infection scenario model – for example, the effect of social distancing measures, and on-off triggers for social distancing measures – vary stochastically. The ranges of variation are consistent with Flaxman et al[18] with respect to the effect of social distancing, and otherwise with the parameter values used by Kissler.[9] Further, the silent/presymptomatic rate (or, aymptomatic or incubation phase) varies in the range of 45% to 55%, as reported previously.[5,14–16] More details regarding the stochastic infection scenario model are given in Supplementary Materials, Appendix D, http://links.lww.com/SLA/C695. Further, details on integration with the surgery demand model and Monte-Carlo simulations are given in Appendix E.

RESULTS

Static Model

Graphical representations of the output of the static model for the different populations is shown in Figure 1AB. For all populations scenarios up to 20,000 operations per 100,000 person years and infection rates up to 0.015 are considered, except for WORLD where rates are <5000 *operations* per 100,000 person years (see Supplementary info, http://links.lww.com/SLA/C695).

© 2020 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

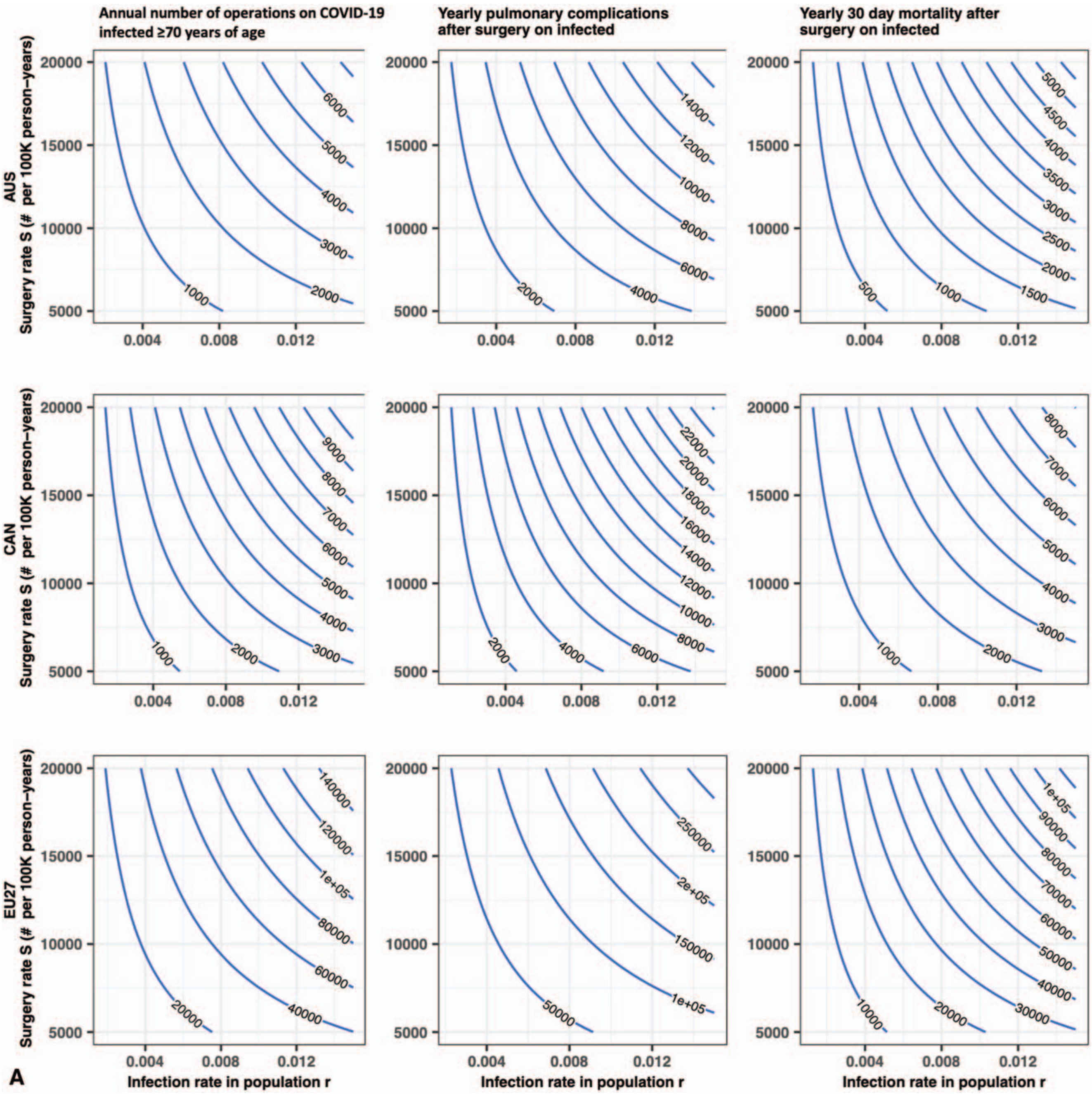

FIGURE 1. AB: Graphical representations (Contour plots) of the static model of risk. (A) for AUS, CAN, EU27 and (B) for UK, US and WORLD. *Left column*: the expected yearly number of *operations* on silent COVID-19 infected persons ≥70 years. *Middle column*: expected number of pulmonary complications due to *operations performed* on silent COVID-19 infected persons. *Right column*: expected yearly number of 30-day mortalities due to *operations performed on* silent COVID-19 infected persons. The plots give expectations for different combinations of overall surgery rates *S* (in number of *operations* per 100,000 person-years) and the proportion on the population with Covid-19 infection at any given time *r*. AUS: Australia (total population in 2016: 23.4 million). CAN: Canada (total population in 2016: 35.2 million). EU: EU27 (total population 445 million). UK: United Kingdom (total population in 2011: 63.2 million), US: United States (total population in 2010: 309 million), WORLD: World standard population with total population 7594 million. Notice the lower values of *S* considered in the World scenario, as the total number of *operations* per 100,000 person years has been estimated to be around 3400.

© 2020 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

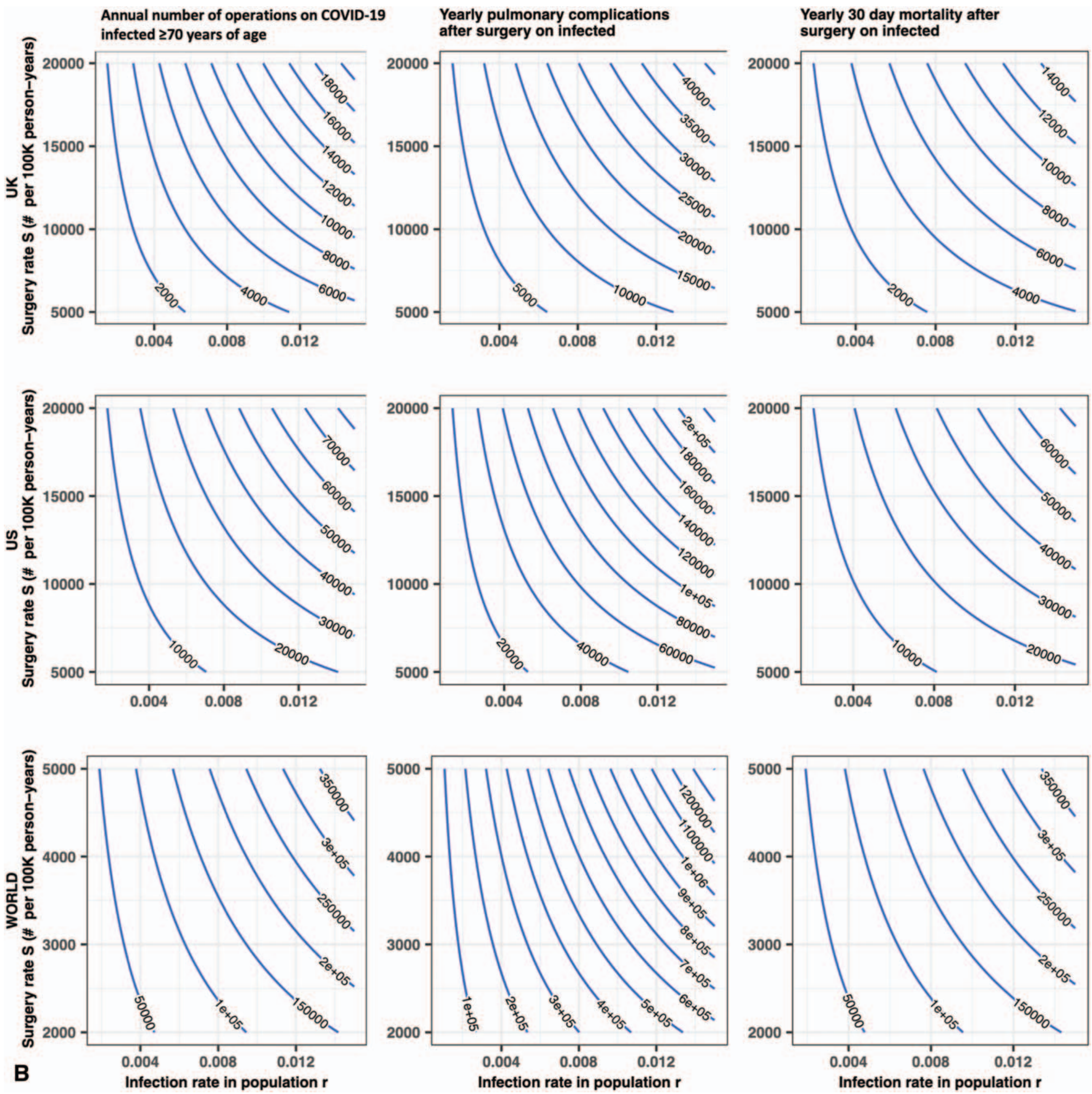

FIGURE 1. (Continued).

Stochastic Dynamic Model

Selected output from the stochastic dynamic model is applied to the US in Figure 2. The figure gives indications on magnitudes and ranges of variation over time.

The estimated number of adverse events is presented in Table 1, with uncertainty interval (UI) for ‘‘best case scenario’’ (5% quantile) and ‘‘worst case scenario’’ (95% quantile) for each region and for the 5 high-income regions combined. Figure 2A shows daily quantiles of the infection trajectories *r(t)* from the stochastic SEIR model, in median consistent with on the order of 0.25% to 0.5% of the population is potentially silent carriers at any given time. Panel 2B shows the daily cases of *operations* on silently infected COVID-19, which in mean are scaled with infection trajectories *r(t)* and thus resembles the pattern of Figure 2A.

At the population size of the US, and the assumed *S* the model implies median daily numbers of *operations* on silent SARS-CoV-2 carriers ranging somewhere between 150 and up to 500 cases (Fig. 2B). Figure 2C and D give the corresponding daily, and cumulative cases of pulmonary complications due *to operations* on silent cases, respectively. The model-implied median of daily new cases ranges between approximately 12 and 45 per day. Figure 2E and F are similar to C and D but for 30-day mortality

© 2020 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

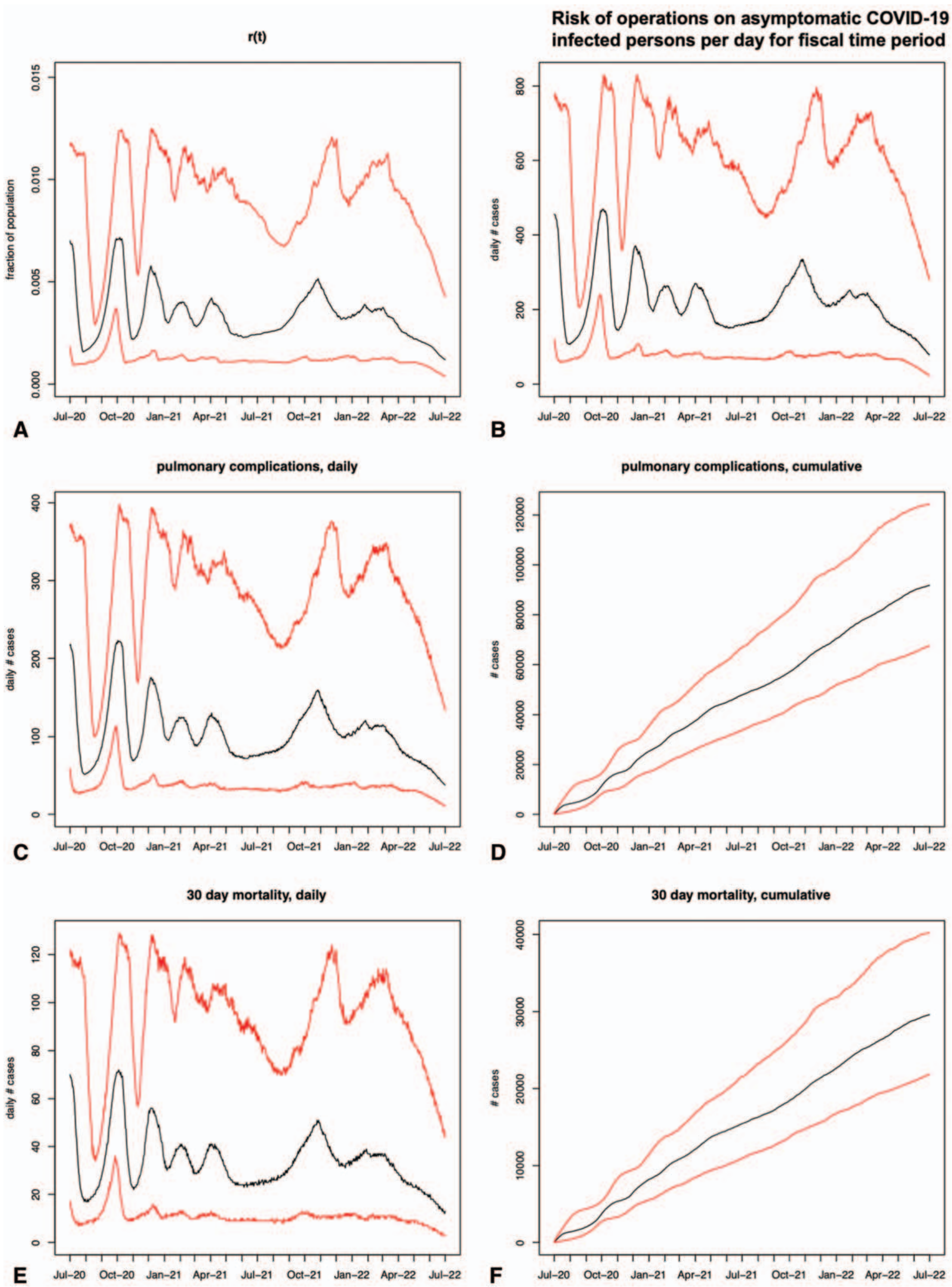

FIGURE 2. A–F: The stochastic dynamic risk model applied to the US population. Selected output of the stochastic dynamic model applied to the US population assuming $S = 15{,}000$ *operations* per 100,000 person years. Throughout black lines are the daily median and the red lines are the corresponding 5% and 95% quantiles. A: Proportion of population being infected and potentially silent carriers *of COVID-19*. B: Daily number of *operations on* silent COVID-19 infected *patients*. C: Daily 30-day mortalities following *surgery* on presymptomatic infected. D: Cumulative 30-day mortalities following surgery on presymptomatic infected since July 1, 2020. E: Daily cases of pulmonary complications following *operations* on silent COVID-19 infected *patients*. F: Cumulative cases of pulmonary complications following surgery on presymptomatic infected *patients*.

© 2020 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

TABLE 1. Estimated Number of Pulmonary Complications and 30-day Mortality Modelled Over a 12- and 24-Months Period

Periods	12-months period**			24-months period***		
UI*	5%	50%	95%	5%	50%	95%
Pulmonary complications						
AUS	2·556	3·608	5·052	5·055	6·941	9·474
CAN	3·864	5·473	7·654	7·645	10·499	14·244
EU27	48·565	68·742	95·917	96·577	131·505	178·482
UK	6·870	9·737	13·627	13·685	18·718	25·282
US	33·785	47·962	66·898	67·538	91·795	124·276
Combined	***95·789***	***135·357***	***188·979***	***190·683***	***259·248***	***351·552***
30-day mortality						
AUS	850	1·210	1·704	1·693	2·323	3·164
CAN	1·322	1·889	2·635	2·634	3·614	4·928
EU27	17·197	24·421	33·986	34·337	46·761	63·262
UK	2·342	3·312	4·621	4·630	6·357	8·612
US	10·936	15·438	21·582	21·817	29·601	40·192
Combined	***32·587***	***46·265***	***64·724***	***65·032***	***88·583***	***120·077***

Legend: from the stochastic dynamic model with S = 15.000 surgeries per 100·000 person-years.
*UI: uncertainty interval for estimates by running low and high scenarios using the lower and upper 90% confidence limits.
**July 1st 2020 to July 1st 2021
***July 1st 2020 to July 1st 2022
The "Combined" rows are the total over the five countries/regions.

and, show 12-months accumulated numbers of such cases roughly ranges between 2000 and 4500.

The US projections in Figure 2 for the other regions (data not shown) is similar up to a scaling factor equal to the population size of the remaining countries relative to that of the US (modulus minor corrections due to different age and sex compositions relative to US). Also choosing different surgery rates S scales the results linearly, as can be seen from the equation in (2).

Figure 3 shows cumulative cases of pulmonary complications (left, Fig. 3A) and 30-day mortality (right, Fig. 3B) for all of the high-income regions considered (similar to Fig. 2D and 2F). Again $S = 15{,}000$ *operations* per 100,000 person-years is assumed.

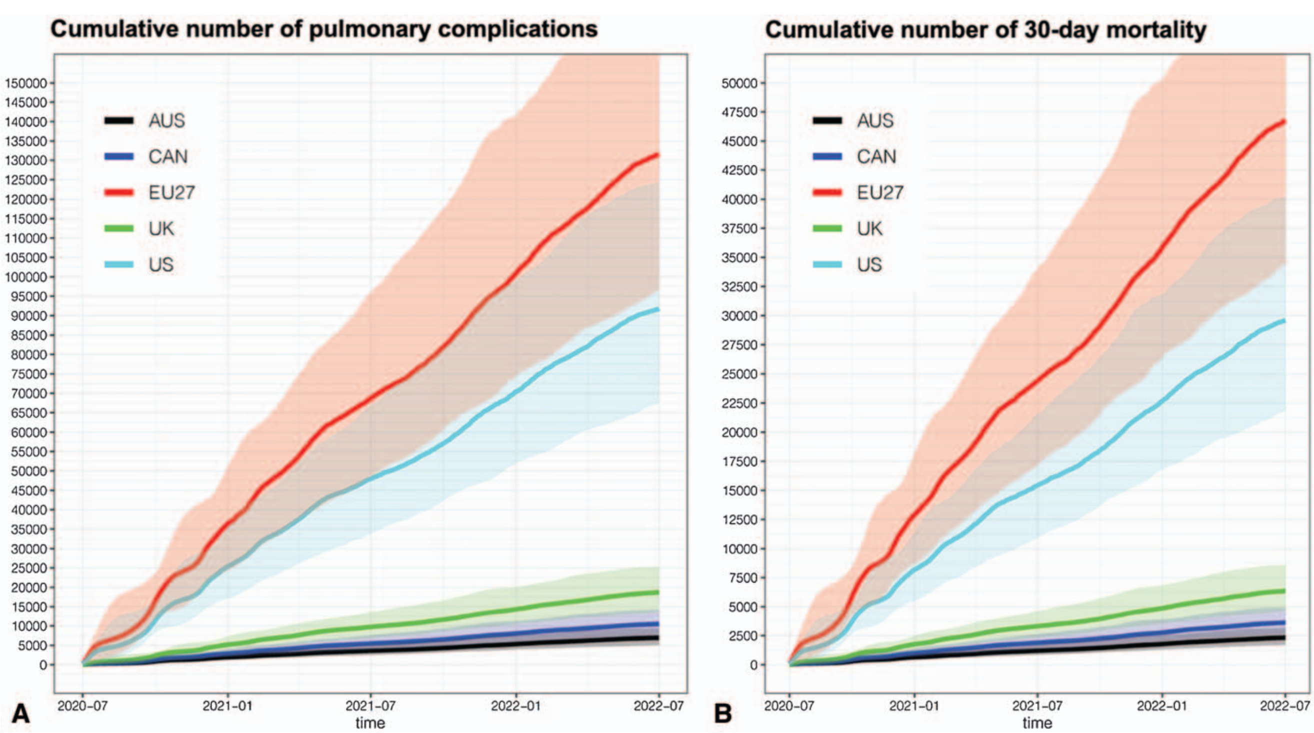

FIGURE 3. AB: Cumulative cases of (A) pulmonary complications and (B) 30-day mortality. Cumulative cases of pulmonary complications (left) and 30-day mortalities (right) since July 1, 2020 for the different high-income countries/regions considered, assuming $S = 15{,}000$ *operations* per 100,000 person years. Solid lines correspond to median, and the shaded regions give 90% model implied confidence intervals (5% and 95% quantiles) for best-case and worst-case estimates. plots have same interpretation as panels D and F of Figure 2, but show further countries/regions.

© 2020 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

DISCUSSION

This study models a temporal and regional risk for perioperative pulmonary complications and deaths from performing surgery on silent SARS-CoV-2 carriers over a 2-year period. The high numbers are of concern as they are based on conservative estimates, and real numbers may even exceed these figures. The data suggest an added burden for critical care resources and an excessive number of deaths due to perioperative COVID-19 complications. Even modelling for low surgical rates – simulating constrained surgical activity in high-income countries or the existing situation in low- and middle income countries – the accumulated number of pulmonary complications and deaths is high and should be considered a public health concern when planning for reopening surgical services.[3] Further, the models anticipate an ongoing pandemic situation up to 24 months, which may be prolonged depending on several unknown factors – ranging from political, scientific and medical standpoints. Also, we have anticipated surgical activity depending on COVID-19 prevalence up to a given threshold of intensive care bed capacity, beyond which most surgical services would be deferred or even cancelled. Hence, we believe the model to project conservative numbers that in a worst-case setting may be exceeded. The data should be considered by stakeholders, policy makers, health care managers, and surgical societies when considering the type, nature, and extent of surgical activities to reopen or increase in the upcoming period. Maintaining surgical services during the pandemic is essential for patients. Economic pressures on health care systems and managers should carefully be balanced against the potential risk of unchecked admissions of silent SARS-Cov-2 carriers to surgical care.

Surgery is an essential part of health care service with about 330 million operations done globally each year.[19,20] Most of these procedures are done in high-income countries, as essential surgery is lacking in several low and middle-income countries.[17,20] Opting out of surgery may not be an alternative in several situations, such as oncological surgery or emergency conditions. Although lower surgery rates or, even cancellations of surgery, in the population will mitigate some of the postoperative adverse events modelled in this study, unsubstantiated delays or cancellations may deprive patients of time-essential procedures that may be life-saving or life-prolonging.[2] Also, the accumulated back-log of procedures in the COVID-19 pandemic[1] has forced several health care systems to look into strategies to build capacity above regular levels. Hence, the surgical rates in some regions may potentially become higher for some time period, further increasing the risk of SARS-Cov-2 exposure and adverse perioperative events. The population-based surgery rates are difficult to estimate across systems due to varying definitions and coding, but far exceeds >10,000 procedures per 100,000 inhabitants per year for most high-income regions,[20] with data from Sweden[17] suggesting even an excess of 25,000 procedures per 100,000 inhabitants per year for high-income regions. The high-income regions also bear the highest demographic burden of elderly with comorbidity and, hence, a higher risk of adverse events from COVID-19 in general,[21] this further substantiates the risk of surgery on silent SARS-CoV-2 carriers.

Although many low- and middle-income countries are struggling to deliver basic surgical care and have a low surgical rate to start with (eg, <5·000 *operations* per 100,000 person years).[20] A different demographic composition of populations, for example, in African countries (eg, a lower rate of elderly and comorbid populations) may also result in a somewhat lower rate of population at risk.[21,22] Nonetheless, the consequences of surgical risks should not be downplayed or minimized for these regions,[23] as depicted in the WORLD estimates in the current study even for low surgical rates.

As governments, health care systems, and jurisdictional regions are looking into reopening surgical activity after a period of cancellations, considering the risk to benefit is required. Reopening surgical activity safely obliges an understanding of the magnitude of the back-log and the subsequent surgical rate needed to catch up. Furthermore, the risk of presenting with silent COVID-19 or contracting SARS-CoV-2 in the perioperative period ought to be considered and varies with the prevalence in the population. The current risk models consider temporal changes for when societal lock downs may occur and, hence, surgical activity may periodically drop, only to experience a subsequent increase. We expect this to change over time until either herd immunity, medical prevention, or vaccines are available, as modelled within 2 years by Kissler.[9] Notably, we used adverse outcomes of perioperative COVID-19 infection based on initial cohort studies that may change with increased understanding of risk.[13,24] The models described herein fill a gap in knowledge to those planning and providing surgical care as the COVID-19 pandemic continues.

Silent carriers of COVID-19 poses a particular risk in the management of the pandemic.[5,25,26] Here we have modelled the risk of admitting such individuals to surgery, given that normal or, even excessive, surgical activity is restarted in the health care systems. The rate of surgery in any given population is difficult to accurately estimate as there is no universal definitions, coding or registries used across regions for accurate comparison.[20] Global surgical estimates are variable and difficult to estimate, but in excess of 300 million operations are performed annually.[19] The surgical rate is highest in high-income countries, and data provided by Omling et al[17] likely provides one of the most accurate accounts of both inpatient and outpatient surgery, including both elective and emergency surgery, and minor an major procedures. However, the risk may not be distributed equal across procedures types and urgencies.[13,24]

Some may argue that there is a ‘‘Fermi paradox’’ (derived from the field of astrobiology) to this model, as discussed for other models in health care.[27] This paradox points to a discrepancy between cases observed compared to the probability of events calculated. In other words, if risk of surgery on silent COVID-19 is real, where are all the observed cases? In the current model, one should keep in mind that the estimates involve accumulated numbers over time for large populations, hence the current signal may be weak and not observed in any given local hospital system. The signal may only become stronger if surgery is performed at normal frequencies (or, higher rates to catch up with back log), with persisting and ongoing spread in the community (below the capacity of intensive care bed use) and with little or few mitigation strategies in place.

Current mitigation of the risk may come from down-scaling or even cancelling of surgical activity across several regions. However, this is not sustainable in the long-run and will only increase a back log of operations needed to be rescheduled for the future. Testing of all comers have been suggested and even takes place in several regions already. However, the existing problems with testing includes the huge variation in available tests and the variation in test accuracy,[28,29] with sensitivity reported as low as 30% in the early phase of disease (hence, lower test accuracy for silent COVID-19). Added to this is the low-test sensitivity in those without symptoms – typically those who would be admitted for planned surgery if no symptoms to trigger testing. Further, even very low variance in specificity for a given test will cause large numbers of false negative test when applied to large populations.[7,30] Even if the US has the highest per capita testing in the world (and higher than that in Canada) the case-fatality rate is lower in Canada,[30] suggesting that testing or capacity for testing is not related to prevention of spread or the only mitigation strategy needed to avoid deaths.

Transmission patterns and spread is unpredictable, and several regions are now seeing a resurgence of cases after a period of low prevalence. So-called ‘‘second waves’’ after a period of lock down of

© 2020 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

society point to the risk of new widespread transmission when precautions and measures are not adhered to by the public. Super-spreaders may rapidly cause new outbreaks.[31] Data suggest that infection rates are underestimated in the US[32] and concerns about lasting immunity from other coronaviruses[33] may suggest that infection may persist in society for a considerable period still. Thus, the 24 months model of the current study may even become longer, given a number of assumptions ahead.

Of note, the mortality risk and risk for pulmonary complications used in the current model stems from one study.[13] Even though this is the largest data set available to date, the risk of bias and overestimation of risk is present and, must be considered for the presented prediction model. As further data are gathered, this may allow for adjustment of the current model for better prediction of risk.

Surgery is not without risk per se, and the European Surgical Outcome Study estimated 4% mortality before discharge from hospital and 8% admission to critical care services after noncardiac general surgery.[34] Notably, postoperative mortality is highly variable within and between regions,[34,35] and, related to a number of factors, including patients' age and sex, comorbidity, type and severity of underlying disease, and type of surgery. Almost three-quarter of adverse events in the COVIDSurg study was related to emergency surgery, but this may also reflect a high degree of cancelled elective surgery during the period.[13] Nonetheless, the available data from patients undergoing surgery with COVID-19 suggest an excessive risk of mortality.[13,24] Whether surgery contributes to, or even triggers, an exaggerated inflammatory response is currently not known. However, an exaggerated cytokine storm and dysregulation of the complement system is described in severe COVID-19.[36,37] *This* warrants further investigation related to the causes to the increased perioperative risk.

Of concern is the high estimated rate of pulmonary complications which, when added to an already considerable strain on intensive care resources may further put pressure on hospital systems in a pandemic setting. Also, pulmonary complications contributed to about 80% of all postoperative deaths from COVID-19 in a multicentre study.[13] Particular age-groups and comorbidities are at higher risk for adverse outcomes,[21,22] and this needs to be taken into account when scheduling surgery. The risk of disease deterioration, loss of life or loss of function from delaying or cancelling surgery needs to be balanced against the risk of perioperative adverse events.[2] Planning of surgical and health services should consider the estimated impact of complications during rebuilding of surgical activity but also as we face subsequent waves of the pandemic. We provide population-level estimates of the complications of perioperative COVID-19 that should be used to inform such planning across various jurisdictions.

Uncertainty is inherent in any modelling,[38] but the most recent datasets available are used for modelling estimates in the current study. SARS-CoV-2 viral spread and containment may be unpredictable and population prevalence influenced by serval factors (mitigation strategies, development of vaccines, medications, travel restrictions etc).[6,25] Also, the estimated surgical risk may be particularly associated with certain demographic and disease groups and certain procedure types and hence not apply universally to surgery as such. Still, the risk is not negligible for "minor" surgery and elective surgery, based on the COVIDSurg Collaborative data.[13] As further data are accrued, the risk modelling may become more precise and may potentially define areas of concern, where mitigation strategies and planning for surgery needs to be built into the pandemic setting by governments and health care systems. Further investigation into surgical areas of particular risk is warranted.

REFERENCES

1. Nepogodiev D, Bhangu A. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans. *Br J Surg*. 2020. doi:10.1002/bjs.11746. doi: 10.1002/bjs.11746.
2. Prachand VN, Milner R, Angelos P, et al. Medically-necessary, time-sensitive procedures: a scoring system to ethically and efficiently manage resource scarcity and provider risk during the COVID-19 pandemic. *J Am Coll Surg*. 2020;231:281–288.
3. Soreide K, Hallet J, Matthews JB, et al. Immediate and long-term impact of the COVID-19 pandemic on delivery of surgical services. *Br J Surg*. 2020. doi: 10.1002/bjs.11670.
4. Gandhi M, Yokoe DS, Havlir DV. Asymptomatic Transmission, the Achilles' Heel of Current Strategies to Control Covid-19. *N Engl J Med*. 2020;382:2158–2160.
5. Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection. *Ann Intern Med*. 2020;173:362–367.
6. Li R, Pei S, Chen B, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). *Science*. 2020;368:489–493.
7. Woloshin S, Patel N, Kesselheim AS. False negative tests for SARS-CoV-2 infection - challenges and implications. *N Engl J Med*. 2020;283:e38.
8. Watson J, Whiting PF, Brush JE. Interpreting a covid-19 test result. *BMJ*. 2020;369:m1808.
9. Kissler SM, Tedijanto C, Goldstein E, et al. Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. *Science*. 2020;368:860–868.
10. Stringhini S, Wisniak A, Piumatti G, et al. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study. *Lancet*. 2020;396:313–319.
11. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet*. 2020;396:535–544.
12. Caini S, Bellerba F, Corso F, et al. Meta-analysis of diagnostic performance of serological tests for SARS-CoV-2 antibodies up to 25 April 2020 and public health implications. *Euro Surveill*. 2020;25:2000980.
13. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet*. 2020;396:27–38.
14. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med*. 2020;26:672–675.
15. Gudbjartsson DF, Helgason A, Jonsson H, et al. Spread of SARS-CoV-2 in the Icelandic population. *N Engl J Med*. 2020;382:2302–2315.
16. Kimball A, Hatfield KM, Arons M, et al. Asymptomatic and presymptomatic SARS-CoV-2 infections in residents of a long-term care skilled nursing facility - King County, Washington, March 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:377–381.
17. Omling E, Jarnheimer A, Rose J, et al. Population-based incidence rate of inpatient and outpatient surgical procedures in a high-income country. *Br J Surg*. 2018;105:86–95.
18. Flaxman S, Mishra S, Gandy A, et al. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nature*. 2020;584:257–261.
19. Weiser TG, Haynes AB, Molina G, et al. Size and distribution of the global volume of surgery in. *Bull World Health Organ*. 2016;94:201–209f.
20. Holmer H, Bekele A, Hagander L, et al. Evaluating the collection, comparability and findings of six global surgery indicators. *Br J Surg*. 2019;106:e138–e150.
21. Clark A, Jit M, Warren-Gash C, et al. Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study. *Lancet Global Health*. 2020;8:E1003–E1017.
22. Dowd JB, Andriano L, Brazel DM, et al. Demographic science aids in understanding the spread and fatality rates of COVID-19. *Proc Natl Acad Sci U S A*. 2020;117:9696–9698.
23. Walker PGT, Whittaker C, Watson OJ, et al. The impact of COVID-19 and strategies for mitigation and suppression in low- and middle-income countries. *Science*. 2020;369:413–422.
24. Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *EClinicalMedicine*. 2020. doi: 10.1016/j.eclinm.2020.100331.
25. Gandhi M, Yokoe DS, Havlir DV. Asymptomatic transmission, the Achilles' heel of current strategies to control Covid-19. *N Engl J Med*. 2020;382:2158–2160.

© 2020 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

26. Graham LA, Maldonado YA, Tomkins LS, et al. Asymptomatic SARS-CoV-2 Transmission from Community Contacts in Healthcare Workers. *Ann Surg*. 2020. doi: 10.1097/SLA.0000000000003968. Online ahead of print.
27. Berwick DM. Elusive waste: the fermi paradox in US health care. *JAMA*. 2019. doi: 10.1001/jama.2019.14610. Online ahead of print.
28. Axell-House DB, Lavingia R, Rafferty M, et al. The estimation of diagnostic accuracy of tests for COVID-19: a scoping review. *J Infect*. 2020. S0163-4453(20)30577-6. doi: 10.1016/j.jinf.2020.08.043.
29. Deeks JJ, Dinnes J, Takwoingi Y, et al. Antibody tests for identification of current and past infection with SARS-CoV-2. *Cochrane Database Syst Rev*. 2020;6:Cd013652.
30. Pettengill MA, McAdam AJ. Can we test our way out of the COVID-19 pandemic? *J Clin Microbiol*. 2020. doi: 10.1128/JCM.02225-20.
31. Adam DC, Wu P, Wong JY, et al. Clustering and superspreading potential of SARS-CoV-2 infections in Hong Kong. *Nat Med*. 2020. doi: 10.1038/s41591-020-1092-0.
32. Wu SL, Mertens AN, Crider YS, et al. Substantial underestimation of SARS-CoV-2 infection in the United States. *Nat Commun*. 2020;11:4507.
33. Edridge AWD, Kaczorowska J, Hoste ACR, et al. Seasonal coronavirus protective immunity is short-lasting. *Nat Med*. 2020. doi: 10.1038/s41591-020-1083-1.
34. Pearse RM, Moreno RP, Bauer P, et al. Mortality after surgery in Europe: a 7 day cohort study. *Lancet*. 2012;380:1059–1065.
35. Mortality of emergency abdominal surgery in high-, middle- and low-income countries. *Br J Surg*. 2016;103:971–988.
36. Mangalmurti N, Hunter CA. Cytokine Storms: Understanding COVID-19. *Immunity*. 2020;53:19–25.
37. Holter JC, Pischke SE, de Boer E, et al. Systemic complement activation is associated with respiratory failure in COVID-19 hospitalized patients. *Proc Natl Acad Sci U S A*. 2020;117:25018–25025.
38. Holmdahl I, Buckee C. Wrong but useful - what Covid-19 epidemiologic models can and cannot tell Us. *N Engl J Med*. 2020;383:303–305.

© 2020 Wolters Kluwer Health, Inc. All rights reserved.

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.