



ScienceDirect

Contents lists available at sciencedirect.com
Journal homepage: www.elsevier.com/locate/jval

Themed Section: COVID-19

Minimizing Population Health Loss in Times of Scarce Surgical Capacity During the Coronavirus Disease 2019 Crisis and Beyond: A Modeling Study



Benjamin Gravesteyn, MSc,[†] Eline Krijkamp, MSc,[†] Jan Busschbach, PhD, Geert Geleijnse, MSc, Isabel Retel Helmrich, MSc, Sophie Bruinsma, PhD, Céline van Lint, PhD, Ernest van Veen, BSc, Ewout Steyerberg, PhD, Kees Verhoef, MD, PhD, Jan van Saase, MD, PhD, Hester Lingsma, PhD, Rob Baatenburg de Jong, MD, PhD, Value Based Operation Room Triage team collaborators*

ABSTRACT

Objectives: Coronavirus disease 2019 has put unprecedented pressure on healthcare systems worldwide, leading to a reduction of the available healthcare capacity. Our objective was to develop a decision model to estimate the impact of postponing semielective surgical procedures on health, to support prioritization of care from a utilitarian perspective.

Methods: A cohort state-transition model was developed and applied to 43 semielective nonpediatric surgical procedures commonly performed in academic hospitals. Scenarios of delaying surgery from 2 weeks were compared with delaying up to 1 year and no surgery at all. Model parameters were based on registries, scientific literature, and the World Health Organization Global Burden of Disease study. For each surgical procedure, the model estimated the average expected disability-adjusted life-years (DALYs) per month of delay.

Results: Given the best available evidence, the 2 surgical procedures associated with most DALYs owing to delay were bypass surgery for Fontaine III/IV peripheral arterial disease (0.23 DALY/month, 95% confidence interval [CI]: 0.13–0.36) and trans-aortic valve implantation (0.15 DALY/month, 95% CI: 0.09–0.24). The 2 surgical procedures with the least DALYs were placing a shunt for dialysis (0.01, 95% CI: 0.005–0.01) and thyroid carcinoma resection (0.01, 95% CI: 0.01–0.02).

Conclusion: Expected health loss owing to surgical delay can be objectively calculated with our decision model based on best available evidence, which can guide prioritization of surgical procedures to minimize population health loss in times of scarcity. The model results should be placed in the context of different ethical perspectives and combined with capacity management tools to facilitate large-scale implementation.

Keywords: healthcare planning, COVID-19, population health, prioritization, simulation model, surgery delay.

VALUE HEALTH. 2021; 24(5):648–657

Background

Coronavirus disease 2019 (COVID-19) has put unprecedented pressure on healthcare systems worldwide. The healthcare demand of this pandemic supersedes available healthcare capacity, far beyond the demand that was imposed by the 2017 influenza pandemic.^{1,2} The pressure on the available healthcare capacity affects the continuity of regular care. Among other reasons, this is because (1) wards and operating theaters are converted to COVID-19 care facilities,³ (2) physicians are deployed to care for patients with COVID-19,^{4,5} and (3) the fear of contagion with the severe acute respiratory syndrome coronavirus 2 virus (the virus that causes the COVID-19 disease) may leave susceptible patients reluctant to seek care,^{4,5} as was seen in similar health

crises like the severe acute respiratory syndrome epidemic in 2003.⁶

Delay in surgical care may dramatically affect healthcare quality and accessibility. In the first weeks of the COVID-19 crisis in The Netherlands, 75% to 90% fewer surgical procedures were performed compared with previous years.⁷ The delay in cancer surgery already has made a large impact in the life expectancy of oncological patients.⁸ Moreover, it may be impossible to treat the whole accumulating group of patients in the near future, as estimated for orthopedic and cardiothoracic surgery in the United States.^{9,10} Because of these problems, hospitals are facing a dilemma: Which patients should be prioritized?

As stated by Emanuel et al, “The question is not whether to set priorities, but how to do so ethically and consistently, rather than

*Value Based Operation Room Triage team collaborators: Chris Bangma, Ivo Beetz, Patrick Bindels, Alexandra Brandt-Kerkhof, Danielle van Diepen, Clemens Dirven, Tjebbe Galema, Jeanette Goudzwaard, Mieke Hazes, Sjoerd Lagarde, Harmke Polinder-Bos, Eva Maria Roes, Hanneke Takkenberg, Mark van Vledder.

[†]The first two authors contributed equally to this work.

basing decisions on individual institutions' approaches or a clinician's intuition in the heat of the moment."² In practice, individual surgical patients are most often triaged by experts from the respective surgical fields.¹¹ Unfortunately, the level of agreement on prioritization among experts is low.¹² Additionally, prioritization across disciplines is complicated by the high degree of specialization in modern medicine. Most importantly, this approach does not systematically optimize population health. The perspective of maximizing population health, a utilitarian ethical perspective that strives to achieve the greatest good for the greatest number,¹³ has been described to be most defensible in times of scarcity.^{2,14-18}

Therefore, to guide prioritization of semielective surgical procedures across disciplines from a utilitarian perspective, our study aims to develop a decision model to estimate the impact of postponing surgery on health.

Methods

Overview

This study focused on semielective surgical procedures (a semielective surgery is defined as a surgery that should ideally be performed within 3 days up to 3 weeks), because urgent procedures always have priority over other procedures, and elective procedures can, by definition, be delayed. The most frequently performed semielective surgical procedures in our institute were selected. Data about these surgical procedures were collected and used in a broadly applicable computer-based model to estimate the effect of surgical delay on life expectancy and health-related quality of life (QoL).

Patients and Setting

The evaluated surgical procedures in this study comprised nonpediatric and nonobstetric semielective surgical procedures at Erasmus University Medical Center, an academic tertiary referring hospital in The Netherlands. From the electronic patient registry (HiX, ChipSoft), the number of surgical procedures, surgery time, length of stay in an intensive care unit, and length of stay in a nonintensive care unit of all nonurgent surgical procedures were retrieved from July 2017 to December 2019. Next, 2 senior clinicians selected the semielective surgical procedures from this list. No objective criterion could be used, because the definition of semielective is subject to numerous aspects including environment, expert opinion, and alternative therapies. Finally, the Value Based Operation Room Triage team collaborators approved the selection. This team of collaborators was a diverse expert panel of 18 healthcare professionals from the Erasmus University Medical Center, including surgeons (eg, cardiothoracic surgeons, neurosurgeons, and gynecological surgeons) and generalists (eg, internists, geriatricians, and general practitioners) (see Appendix C in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>). Ultimately, 43 semielective surgical procedures were selected that were performed more than 80 times during the time window we used. Where relevant, mild and severe cases of patients undergoing the surgical procedure were distinguished based on clinical insight of our collaborators.

Model Input Parameters

The model required 7 input parameters: (1) survival rates presurgery, (2) survival rate postsurgery, (3) QoL presurgery, (4) QoL postsurgery, (5) mean age of patients undergoing the surgery,

(6) time until no effect of treatment can be expected on survival, or (7) time until no effect of treatment can be expected on QoL (see Appendix A in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>). The class of collected evidence was defined as class I (randomized controlled trials [RCT] or systematic reviews of RCTs), class IIa (prospective observational studies, before-after studies), class IIb (retrospective observational studies, expert panels for the disutility weights, national registries), or class III (expert opinion).

Survival Input

The survival rates postsurgery were obtained from national registries for oncological¹⁹ and cardiothoracic²⁰ surgical procedures. For the remaining surgical procedures, data were obtained from scientific literature. The survival data presurgery for all surgical procedures were based on data from published studies. If either survival with or without treatment was lacking, the reported treatment effect (preferably from an RCT) was used to calculate the missing survival parameter. The disease-specific mortality was added to the national overall age-specific mortality from the Central Bureau of Statistics in The Netherlands.²¹ The mean age of the patients was obtained from published studies. All survival data had to be converted to mortality risk per week and ultimately converted to probabilities to be used in the model (formulas presented in Appendix C in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>).²²

QoL Input

The disability weights from the Global Burden of Disease (GBD) Study 2016 from the World Health Organization (WHO) were used to value the QoL of our health states.²³ The GBD Study reports disability weights for nonfatal health conditions. These weights represent the magnitude of health loss associated with the conditions, where 0 represents no loss (full health) and 1 all lost (death). When these weights are multiplied by the duration lived in this conditions, one has calculated the weighted years lived with disability.²⁴ The years lived with disability summed with the years of life lost (YLLs) to premature death give the disability-adjusted life-years (DALY).²⁵ A full DALY can be thought of as losing 1 year in full health. In our analysis, the DALY is the difference in quality of life weighted life years with and without surgical delay.

Where possible, we based the disability weights of health conditions directly on the GBD study data. The remaining conditions were estimated using methods described by Stouthard et al. with the Value Based Operation Room Triage team collaborators.²⁶ We used a visual analog scale (VAS) calibrated with GBD 2016 QoL weights. Like in the study from Stouthard, we framed our VAS with 1 being the best imaginable health state and 0 the worst/dead. Therefore, we used the complement (1-x) of the disability weight from the GBD study to make our calibrated VAS. Stouthard et al. describe how experts can then place (map) the remaining health conditions on the VAS scale. Our protocol was slightly different from the protocol of Stouthard, in the way that we did not make use of the EQ-5D to classify all health conditions at hand. The health conditions were one by one valued by the experts from the Value Based Operation Room Triage team using the following procedure: first, the health condition was shortly introduced by an expert with the most clinical experience with this condition. The other experts were allowed to ask questions and discuss the QoL aspects of the condition. Subsequently, all experts wrote down their own QoL estimation of the health condition. Then, 2 to 3

other experts were invited to express their estimated QoL value for the health condition. Ultimately, the experts registered their own final values. In this way, the experts could use a maximum of information and opinions, but still express their own estimation. In addition, we could estimate the variance, the 95% confidence interval (95% CI), of the QoL values. The mean and 95% CI of the mapped QoL scores were used in the model. We used 2 sessions of 3 hours to collect QoL values. The preoperative and postoperative health states of 3 surgical procedures (one with a mild and severe subgroup) were estimated in both sessions, which effectively were 8 estimates of QoL. This allowed us to obtain an indication of the test-retest reliability (based on a *t* test) of the valuations. For the model, the first estimates obtained in the first session were used. More details about the methods used to collect all QoL data can be found in [Appendix C](https://doi.org/10.1016/j.jval.2020.12.010) in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>.

Time Until No Effect From Surgery

Because postponing surgery can have consequences on the effectiveness of the surgery, we included a model parameter that reflected the time until no effect can be expected of treatment on survival. In practice, this means that when this time has passed, we assumed that the surgery did no longer have an effect on the survival of the patient anymore. This time is often important in oncological surgical procedures, where after a specific time a tumor becomes inoperable or metastasizes. The effectiveness of nononcological surgery could be time dependent as well, for example, repairing an abdominal aneurysm of the aorta. The data for this parameter were obtained from the scientific literature (see [Appendix A](https://doi.org/10.1016/j.jval.2020.12.010) in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>). For most surgical procedures, only data about the minimal delay not associated with worse survival could be obtained from the scientific literature. For those surgical procedures, we assumed the upper limit of this parameter to be a year (the maximum delay we evaluated) and the mean of the lower and upper limit as average. The same was done for the time until no effect can be expected on QoL.

Markov Model

A 3-state cohort state-transition model, often called Markov model, was developed. This model simulates a hypothetical cohort of patients over a defined period in fixed time intervals, called cycles, to estimate the average time individuals spend in the various health conditions, called health states.^{22,27} Individuals could transition among a preoperative state, a postoperative state, and a dead state (Fig. 1). Based on the time spent in these states, health benefits, like life-years or years lived with disability are calculated.^{22,28,29} Since health benefits now are enjoyed more than in the distant future, it is recommended to perform discounting.^{30,31} A discount rate of 0.015 per year for health benefits was used, as this is common practice in The Netherlands.³¹

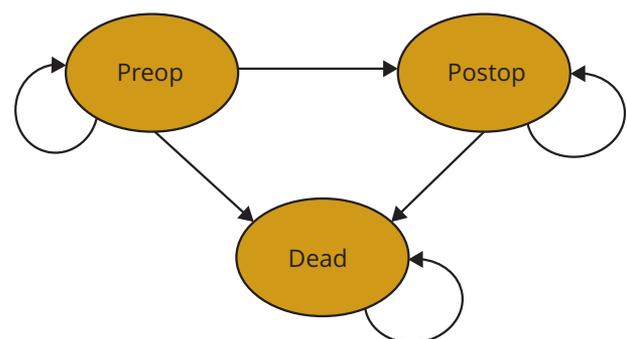
The entire cohort started in the preoperative state and was followed their remaining lifespan, until they were 100 years old, using weekly cycles. The transition from the preoperative state to the postoperative state was set to a specific week, depending on the scenario. Scenarios of surgical delay of 2 weeks were compared with surgical delay up to a year using intervals of 10 weeks. In addition, the scenario where patients never received treatment was evaluated: this was modeled by following patients their entire remaining lifespan in the preoperative health state. In all scenarios, the transitions from the pre- and postoperative states to the dead state were based on survival data. A description of the model assumptions can be found in [Appendix C](https://doi.org/10.1016/j.jval.2020.12.010) in

Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>.

Health Effects of Surgery

To be able to prioritize across disciplines, we chose to minimize health loss in YLL or QALY loss, which we define as DALY. Priority is given to the patients where surgery delay is associated with more health loss per unit of time. Therefore, the YLL and DALYs as a result of delays in surgery were evaluated. YLLs disregard QoL (QoL = 100%), whereas DALYs incorporate QoL and are therefore preferred. The expected health outcomes without surgery were compared to the expected health outcomes with surgery at 2 weeks to determine the overall health loss associated with not performing surgery. The expected health outcomes with surgery at 2 weeks were compared to the expected health outcomes at 52 weeks to determine the health lost per 50 weeks. This measure of urgency was converted to health lost per month delay and was used to rank the surgical procedures, where a high DALY/month or high YLL/month indicates an urgent surgery. DALYs are the difference in expected quality of life weighted life years, and YLLs the difference in expected life years.

Figure 1. State-transition diagram of the cohort model. The model is a state-transition cohort model with 3 health states, a preoperative health states (preop), a postoperative state (postop), and dead. All patients start in the preop health states. This is the health state where patient eligible for surgery start in our simulation. We follow these patients over time using fixed time intervals of 1 week; these fixed time intervals are called *cycles*. Every cycle, patients can transition to one of the other health states or they can remain in the health states they currently are. From the preop health state they either die (transition to dead health state) or continue to wait for their surgical procedure (stay in the preop health state, the arrow points back into the health state). At the time of surgical procedure, which is determined by the selected model scenario of surgical delay, all individuals still alive in the preop health state transition to the postop health state. The cohort is followed their remaining lifetime, defined as up to 100 years of age. While they are followed, they can die (transition from the postop state to dead state) or stay alive in the postop health state (transition back to the postop state). Finally, patients in the dead state remain dead, so every cycle they stay in the dead state.



Analysis

Probabilistic sensitivity analysis (PSA) was used to incorporate parameter uncertainty in the model outcome (see [Appendix A](#) for the parameter distributions and [Appendix C](#) for more details about the used PSA method in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>). Rankings based on health benefits or health loss per unit of time were compared using Spearman's rank correlation coefficient.

The model was built with R software³² and adapted from previously published code.^{33,34} The full model code is available on GitHub via the following link: <https://github.com/bgravesteijn/Utilitarian-distribution-of-OR-capacity-during-COVID-19>. The model results are described in the next section and can also be viewed in an online accessible tool where users can interactively select the surgical procedures of interest via the following link: <https://tinyurl.com/y2yzudgw>.

Results

Data Collection

In total, 12 cardiothoracic surgical procedures were evaluated, along with 23 oncological surgical procedures, 2 transplantations (liver and living donor kidney), 5 vascular surgical procedures, and 1 other type of surgical procedure (creation of a shunt to facilitate hemodialysis). These 43 evaluated surgical procedures comprised 69% of the total number of semielective surgical procedures in our hospital.

Survival with treatment was mostly based on national registries (31/43, [Table 1](#)). Survival without treatment was mostly based on data from (inter)national registries (12 of 43 surgical procedures, 6 calculated through the treatment effect), but also frequently from RCTs (10 of 43 surgical procedures, 7 calculated through the treatment effect) and observational studies (9 of 43 surgical procedures, 3 calculated through the treatment effect).

For 14 of 43 surgical procedures, QoL was available through the WHO GBD study.³⁵ For the remaining 29 surgical procedures, the QoL of the pre- and postoperative health state was estimated by the expert panel as described in the methods section. Test-retest validation analysis showed that the gain in QoL owing to surgical procedure was consistent in the 2 separate expert panel sessions (standardized mean difference 0.025, 95% CI: -0.11 to 0.16; [Appendix C: Table 1](#) and [Fig. 1](#) in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>).

For 6 of 43 surgical procedures, a time to no effect on QoL within 1 year, our maximum period of delaying surgery, was found in the literature. For 23 surgical procedures, a time to no effect of treatment on survival was assumed based on qualitative assessment of the literature. Most of these surgical procedures were oncological surgical procedures (20 of 23). The estimates for the time until surgical procedure becomes ineffective was mostly based on class IIb evidence (retrospective and prospective observational studies, [Table 1](#)).

Overall, input parameters varied widely among surgical procedures ([Fig. 2](#)). [Appendix A](#) presents all input parameters, their sources,^{19,20,35-89} and the corresponding model output (see [Appendix A](#) in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>).

Urgency

The delay of most surgical procedures resulted in a linear increase in DALYs per delay, except surgical procedures where a time until no effect of treatment on survival was included in the model ([Figure 1](#) in [Appendix B](#) in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>).

The DALYs associated with delay of the surgical procedures ranged from 0.01 DALY/month (95% CI: 0.00-0.01) for placing a shunt for dialysis to 0.23 DALY/month (0.13-0.36) for a bypass surgery for Fontaine III/IV peripheral arterial disease ([Fig. 3](#) and [Appendix B Table 1](#) in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>). If the latter would be

Table 1. Class and type of evidence underlying the model parameter inputs.

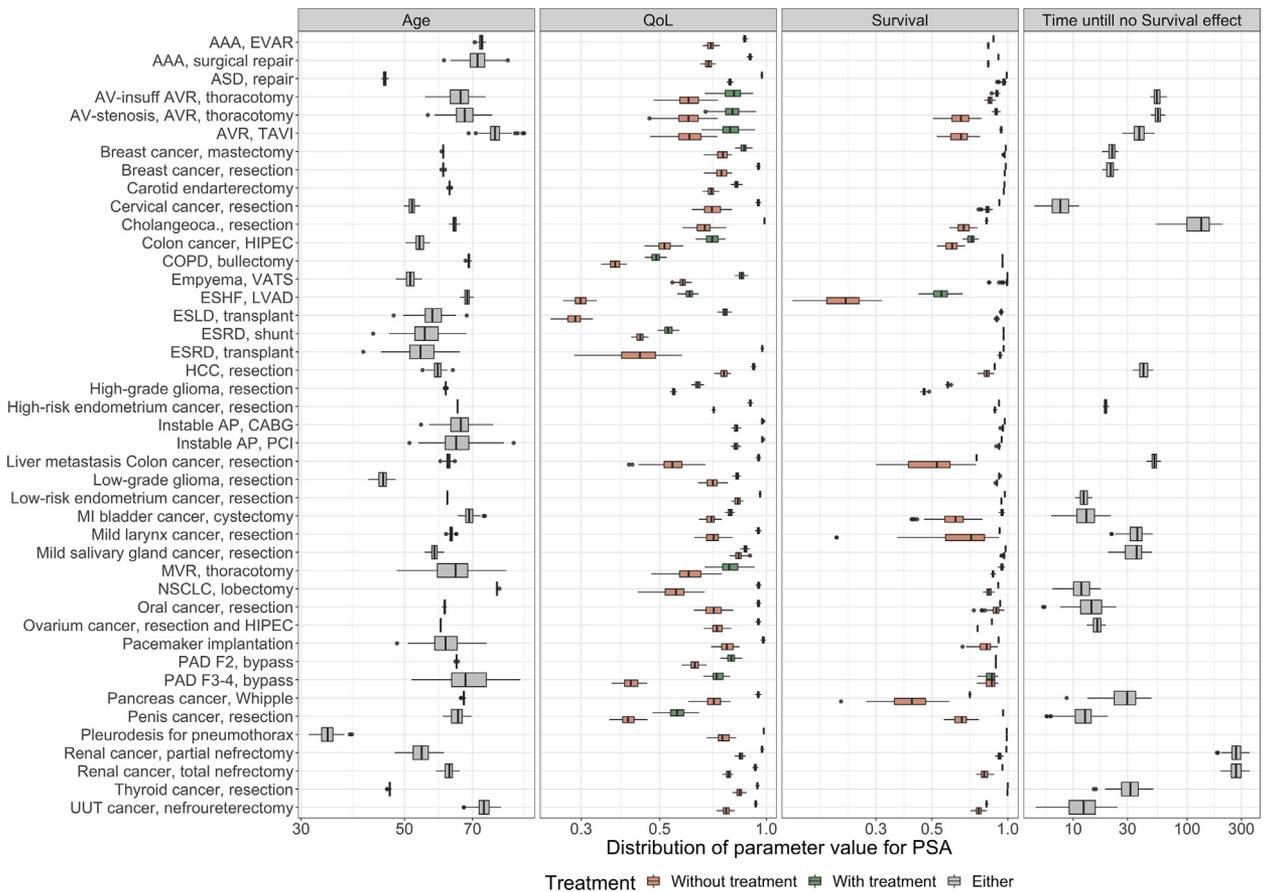
n	Age	Quality of life: preop	Quality of life: postop	Survival: preop	Survival: postop	Time no eff QoL	Time no eff survival	Treatment effect
43	43	43	43	43	43	6	23	22
Type of evidence (%)								
Before-after study	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)
Expert opinion	2 (4.7)	0 (0.0)	0 (0.0)	8 (18.6)	2 (4.7)	5 (83.3)	4 (17.4)	4 (18.2)
Expert panel*	0 (0.0)	29 (67.4)	29 (67.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
WHO GBD study	0 (0.0)	14 (32.6)	14 (32.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
National registry	21 (48.8)	0 (0.0)	0 (0.0)	12 (27.9)	31 (72.1)	0 (0.0)	9 (39.1)	6 (27.3)
Observational, Prospective	5 (11.6)	0 (0.0)	0 (0.0)	4 (9.3)	3 (7.0)	0 (0.0)	3 (13.0)	1 (4.5)
Observational, Retrospective	10 (23.3)	0 (0.0)	0 (0.0)	9 (20.9)	4 (9.3)	0 (0.0)	7 (30.4)	3 (13.6)
RCT	5 (11.6)	0 (0.0)	0 (0.0)	10 (23.3)	3 (7.0)	1 (16.7)	0 (0.0)	7 (31.8)
Class of evidence (%)								
I	5 (11.6)	0 (0.0)	0 (0.0)	10 (23.3)	3 (7.0)	1 (16.7)	0 (0.0)	7 (31.8)
Ila	5 (11.6)	0 (0.0)	0 (0.0)	4 (9.3)	3 (7.0)	0 (0.0)	3 (13.0)	2 (9.1)
IIb	31 (72.1)	43 (100.0)	43 (100.0)	21 (48.8)	35 (81.4)	0 (0.0)	16 (69.6)	9 (40.9)
III	2 (4.7)	0 (0.0)	0 (0.0)	8 (18.6)	2 (4.7)	5 (83.3)	4 (17.4)	4 (18.2)

Note. Class definitions: I = RCT or systematic reviews of RCTs; Ila = prospective observational studies, before-after studies; IIb = retrospective observational studies, expert panels for the utilities, national registries; class III = expert opinion.

GBD indicates Global Burden of Disease; QoL, quality of life; preop, preoperative; postop, postoperative; RCT, randomized controlled trial; Time no eff, time until no effect on QoL/survival expected; WHO, World Health Organization.

*Expert panel refers to the Value Based Operation Room Triage team collaborators (see [Appendix C](#) in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010> for details of this panel).

Figure 2. This figure shows the distribution of the parameter values as used during the probabilistic sensitivity analysis (PSA). For each PSA iteration (100 iterations in total), a value for each parameter was sampled from the original source input as described in Appendix A (in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>). The distribution of the final values used in the model is shown here. The y-axis shows the names of the surgical procedures. In the column called survival the x-axis represents the weekly probability of surviving. In the column Time until no Survival effect the x-axis represents the days until treatment is not effective. (For a full list of input parameters per disease and source, see Appendix A in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>.)



AAA indicates aneurysm of the abdominal aorta; AP, angina pectoris; ASD, atrial septum defect; AV, aortic valve; AVR, aortic valve replacement; -ca., cancer; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; ESHF, end-stage heart failure; ESLD, end-stage liver disease; ESRD, end-stage renal disease; EVAR, endovascular aortic repair; HIPEC, hyperthermic intraperitoneal chemotherapy; HCC, hepatocellular cancer; LVAD, left ventricular assist device; MI, muscle invasive; MVR, mitral valve replacement; NSCLC, non-small cell lung cancer; PAD F2, peripheral arterial disease Fontaine classification 2; PAD F3-4, peripheral arterial disease Fontaine classification 3-4; PCI, percutaneous coronary intervention; TAVI, transaortic valve implantation; UUT, upper urinary track; VATS, video-assisted thoracoscopic surgery.

postponed by a month, patients lose approximately 84 days (0.23×365) spent in perfect health.

After bypass surgery for Fontaine III/IV peripheral arterial disease, the surgical procedure associated with most DALYs in case of delay was transaortic valve implantation (0.15 DALY/month, 95% CI: 0.09-0.24). Following placing a shunt for patients with end-stage renal disease, the surgery associated with the least DALYs was thyroid cancer (0.01 DALY/month, 95% CI: 0.01-0.02). Surgical procedures that were associated with a higher expected DALY if not performed were also associated with more DALYs per month delay: The Spearman correlation coefficient between the ranking of health benefit, in DALYs, and urgency, in DALY/month, was 0.32 ($p = 0.04$).

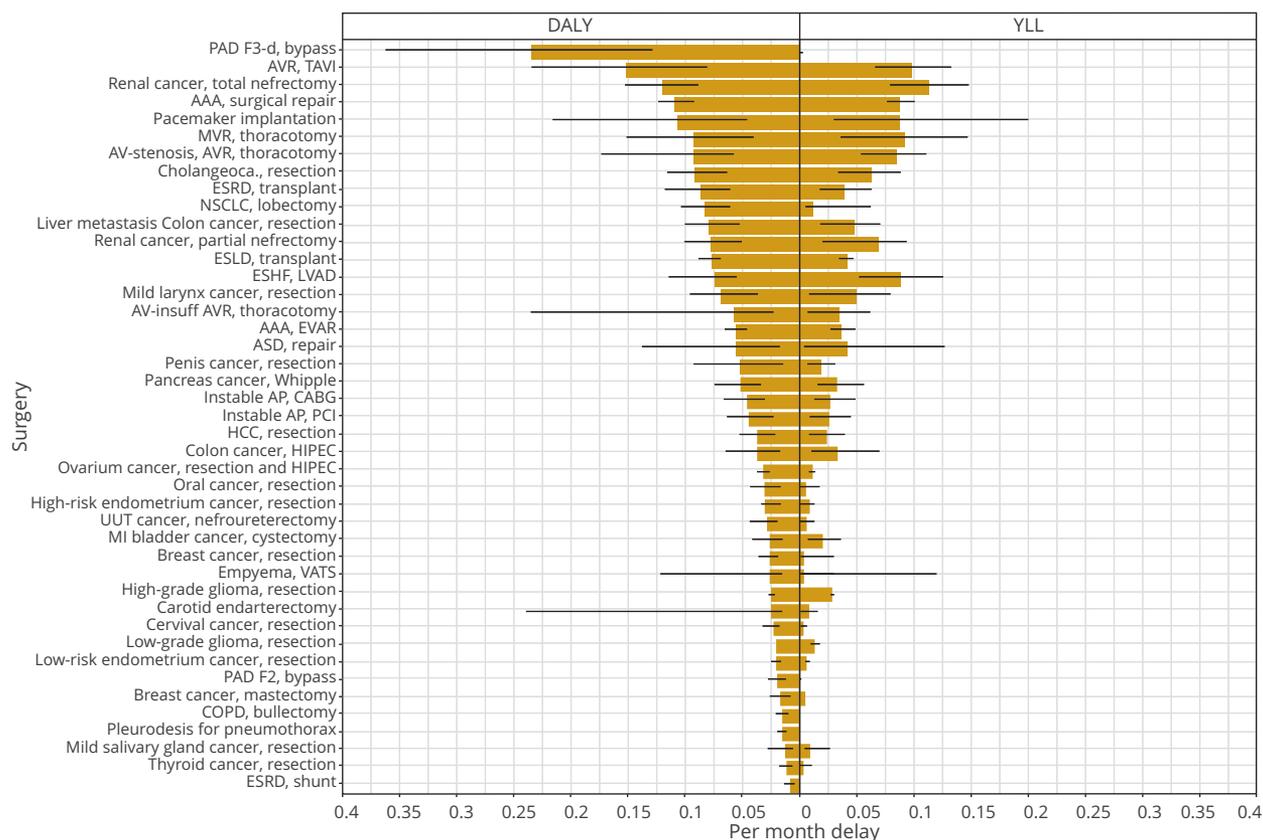
The DALYs were strongly correlated with the YLLs by not performing surgery: The Spearman rank correlation coefficient between the ranking of surgical procedures based on YLL/month and DALY/month was 0.79 ($p < 0.001$).

Discussion

Our proposed decision model is an attempt to systematically guide prioritization of surgical procedures from a utilitarian perspective. The decision model provides the expected health loss owing to surgical procedure delay, which can be interpreted as a measure of urgency. Our approach operationalizes ethical values that are the most appropriate in times of scarcity.² Available evidence suggests that semiselective surgical procedures can be ranked based on their urgency using a simple decision model. For survival after surgical procedure, most evidence was based on national registries, while treatment effects were mostly derived from RCTs. The time until no effect of treatment on survival or QoL was most often derived from retrospective observational studies and expert opinion, respectively class IIb/III evidence.

Among the 43 surgical procedures analyzed, bypass surgery for Fontaine III/IV peripheral arterial disease and transaortic valve

Figure 3. The average DALYs and YLLs per month of delay for the investigated surgical procedures based on the simulation of surgery delay of 52 weeks. The estimates (*gray bars*) and 95% confidence intervals (*black lines*) are shown. The actual data are presented in Appendix B in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>.



AAA indicates aneurysm of the abdominal aorta; AP, angina pectoris; ASD, atrial septum defect; AV, aortic valve; AVR, aortic valve replacement; -ca., cancer; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; DALY, disability-adjusted life-years; ESHF, end-stage heart failure; ESLD, end-stage liver disease; ESRD, end-stage renal disease; EVAR, endovascular aortic repair; HIPEC, hyperthermic intraperitoneal chemotherapy; HCC, hepatocellular carcinoma; LVAD, left ventricle assist device; MI, muscle invasive; MVR, mitral valve replacement; NSCLC, non-small cell lung carcinoma; PAD F2, peripheral arterial disease Fontaine classification 2; PAD F3-4, peripheral arterial disease Fontaine classification 3-4; PCI, percutaneous coronary intervention; TAVI, transaortic valve implantation; UUT, upper urinary track; VATS, video-assisted thoracoscopic surgery; YLL, years of life lost.

implantation appeared to be the most urgent surgical procedures, since delay was associated with most DALYs. Less urgent surgical procedures were placement of a shunt for dialysis and resection of thyroid cancer.

Interestingly, the ranking of health loss owing to delay is primarily driven by the YLL associated by not performing surgery. Surgical procedures that are associated with substantial YLL when not performed (eg, mitral valve replacement) also result in more DALY per month delay than surgical procedures that are associated with no YLL when not performed (eg, creation of a shunt for hemodialysis). The larger the total health benefit associated with surgery, the more health can potentially be lost by postponing surgery.

To make optimal use of operation room capacity, our metric for urgency could be used to fill operation room schedules. Hospital capacity, however, is a dynamic multidimensional concept, which includes, for example, staff, number of beds, number of operation theaters, and medical equipment. All these factors need to be sufficiently present, and bottlenecks in one of these factors can vary from week to week. Therefore, future research aims to model the dynamics of capacity, and use the predictions to optimally distribute capacity over most urgent procedures.

Although our modeling approach rationalizes and objectively quantifies urgency from a utilitarian perspective, it needs to be complemented by other perspectives to be used effectively in practice. First, a financial perspective might also be explored. This perspective might be less relevant in a crisis such as the COVID-19 pandemic, where the bottleneck mainly seems hospital capacity instead of costs. Moreover, in a high-income country such as The Netherlands, the bottleneck costs might be less relevant than in a low- or middle-income country. Even in our setting, the fairness of directing all resources to care for patients with COVID-19 is discussed as the crisis evolves. If this approach would be applied to the context of regular care, or in low- and middle-income countries, this perspective might be of increasing importance. A more traditional cost-effectiveness approach can be used to provide guidance on decision making in these settings. Second, other perspectives include the availability of alternative treatment strategies, for example, in cancer treatment, (chemo-)radiation or systematic therapy alone instead of surgery, and other ethical standpoints, for example, rule of rescue.¹³ By exploring all these perspectives, it can be established whether our approach is applicable to all surgical procedures.

There are practical advantages of comparing “average patients” on urgency, despite that there is no such thing as an average

patient: It prevents our approach from systematically discriminating against a specific group of patients. Our approach would only discriminate if specific socioeconomic groups would more frequently have diseases that are less urgent. It is known that lower socioeconomic groups are more prone to develop diseases that have clear association with unhealthy behavior, such as lung cancer.⁹⁰ Nevertheless, these diseases do not systematically rank low in our approach. Comparing the average patients across specialties on urgency may not seem to be a personalized approach, but it can be tailored to an individual's context by providing input for shared decision making. We believe that next to a quantitative estimation of urgency from a utilitarian perspective, individual patient's preferences, social contexts, and operability should also be included in the decision-making process.

Because all models are a simplification of reality, our model has several limitations. First, the survival data used were not all derived from high-quality evidence. Although survival with treatment might be validly estimated from national registries, the survival without treatment is harder to be unbiasedly estimated. The surgical procedures that were evaluated are often part of standard clinical practice. Therefore, data might be biased (eg, selection bias in the survival without treatment because patients opt for palliative care) or not available (it would be unethical now to perform RCTs evaluating surgery vs no surgery). Instead, best available evidence was used, which in part included evidence from more historical RCTs. As such, data might be biased, and as a result so might the estimates from our model. Because of this limitation, our approach is to aggregate transparently and systematically the best currently available evidence using a model. Nevertheless, we are convinced we used best available evidence.

Second, no extra harm due to surgical procedure was assumed. The current model does not simulate adverse events, like major bleedings or death owing to surgery. The estimates from comparison studies incorporate these harms of surgery, therefore the impact of this limitation on survival might be irrelevant. Nevertheless, the potential reduction of QoL owing to these adverse events was not incorporated, nor the QoL reduction of a temporary period of recovery after surgical procedure. Because of these assumptions, the overall DALYs associated with not performing a surgical procedure should not be interpreted as an absolute estimate. They are the maximum possible DALYs that can result from not performing the surgical procedure. Nevertheless, these assumptions were considered reasonable to achieve the main goal of this study: when surgical procedure without delay is compared to surgical procedure with delay, the harm in both scenarios is similar and therefore cancel out.

Third, because the health loss in 50 weeks was converted to loss per month, a linear approximation was effectively used to quantify urgency by delaying surgery up to a year. Nevertheless, some surgical procedures did show a slightly curved trend in the period up to 32 weeks delay (see Appendix B in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2020.12.010>). The data needed to validly model this decay in DALYs per unit of time for all surgical procedures likely does not exist: most of the estimates of time to no effect on survival were based on observational studies, which are likely biased. A more detailed approximation would be possible using a more individualized model that also models the natural growth of tumors, or aneurysms, and validly models the development of metastasis. It was not feasible to develop this for all evaluated surgical procedures. Instead, we opted for a more pragmatic approach.

Fourth, QoL weights were derived from expert opinion. In this approach, the patient is not involved. Instead, experts interpret the health states and give weights, thereby our approach takes a societal perspective. Besides being a relevant perspective, an

advantage of our approach is that it is a more distanced evaluation of health. Patient-reported evaluation of health might be less relevant in the prioritization of care owing to distortion by coping mechanisms. There are also multiple methodological, ethical, and contextual disadvantages of using DALYs, but most of those discussions are more about utilitarian principles.⁹¹

Fifth, the potential impact on QoL of delaying a semielective surgery was not included. This impact might differ across surgical procedures. Whereas literature on waiting lists for transplants indicates that especially the physical functioning part of QoL declines over time,^{92,93} longer waiting time for elective procedures such as repairing an inguinal hernia mostly affects the emotional well-being part of QoL.⁹⁴ Moreover, it might be hypothesized that surgical procedures performed after already a long disease history (eg, kidney transplant) might have less waiting time disutility than recently diagnosed diseases (eg, breast cancer).

Part of the input parameters were based on national registry data, but a substantial amount of the input originated from various international sources. Therefore, with some modifications, the model can easily be adapted to different contexts. Therefore, this study can be considered the first step towards a triaging strategy which optimizes surgical benefit in times of scarcity in surgical capacity, such as during the COVID-19 pandemic. To improve validity, it is however essential to periodically review the literature and update the model with higher quality evidence, much like a living systematic review.⁹⁵ If accepted, a wider range of surgical procedures should be considered, implementation strategies should be explored and evaluated, and the model should be applied to a variety of settings.

Conclusion

By transparently aggregating the best available evidence, our decision model supports prioritization of surgical care in times of scarce surgical capacity (eg, during pandemics) from a utilitarian perspective. Our approach quantifies the expected health loss owing to delay for semielective surgical procedures often performed in an academic hospital in The Netherlands. This approach can help to minimize health losses when trying to overcome delay in surgical procedures across disciplines. This approach is more transparent, more evidence-based, and more consistent than the alternative strategy of triaging based on expert opinion.

Evidence from well-controlled comparison studies is often lacking. Instead, adjusted estimates from observational studies are often the best available evidence for benefit of surgery and the effects of delay on survival. Therefore, model inputs should be periodically updated with newer, higher-quality evidence.

Finally, our approach should be placed in the context of other ethical perspectives and combined with capacity management tools. If accepted, we believe this modeling strategy should be implemented on a large scale, to minimize health loss of the accumulating group of patients awaiting surgery.

Supplemental Material

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.jval.2020.12.010>.

Article and Author Information

Accepted for Publication: December 13, 2020

Published Online: March 5, 2021

doi: <https://doi.org/10.1016/j.jval.2020.12.010>

Author Affiliations: Department of Otorhinolaryngology (ENT), Erasmus University Medical Center, Rotterdam, The Netherlands (Gravesteyn, Geleijnse); Department of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands (Gravesteyn, Helmrich, van Veen, Steyerberg, Lingsma, Baatenburg de Jong); Department of Epidemiology, Erasmus University Medical Center, Rotterdam, The Netherlands (Krijkamp); Department of Medical Psychology, Erasmus University Medical Center, Rotterdam, The Netherlands (Gravesteyn, Helmrich, van Veen, Steyerberg, Lingsma, Baatenburg de Jong); Department of Quality and Patient Care, Erasmus University Medical Center, Rotterdam, The Netherlands (Bruinsma, van Lint); Department of Intensive Care, Erasmus University Medical Center, Rotterdam, The Netherlands (van Veen); Department of Biostatistics, Leiden University Medical Center, Leiden, The Netherlands (Steyerberg); Department of Surgical Oncology and Gastrointestinal Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands (Verhoef); Department of Internal Medicine - Erasmus University Medical Center, Rotterdam, The Netherlands (van Saase).

Correspondence: Eline Krijkamp, Erasmus MC, Rotterdam, The Netherlands. Email: e.krijkamp@erasmusmc.nl

Author Contributions: *Concept and design:* Gravesteyn, Krijkamp, Busschbach, Geleijnse, Retel Helmrich, Steyerberg, Verhoef, van Saase, Lingsma, Baatenburg de Jong
Acquisition of data: Gravesteyn, Krijkamp, Busschbach, Geleijnse, Retel Helmrich, Bruinsma, van Lint, van Veen, Baatenburg de Jong
Analysis and interpretation of data: Gravesteyn, Krijkamp, Busschbach, Geleijnse
Drafting of the manuscript: Gravesteyn, Krijkamp, Busschbach, Geleijnse, Retel Helmrich, Bruinsma, van Lint, van Veen, Steyerberg, van Saase, Lingsma, Baatenburg de Jong
Critical revision of the manuscript for important intellectual content: Gravesteyn, Krijkamp, Busschbach, Geleijnse, Retel Helmrich, Bruinsma, van Lint, van Veen, Steyerberg, Verhoef, van Saase, Lingsma, Baatenburg de Jong
Statistical analysis: Gravesteyn, Krijkamp
Provision of study materials or patients: van Saase
Supervision: Busschbach, Geleijnse, Lingsma, Baatenburg de Jong
Other (validation): Steyerberg, Verhoef, van Saase, Baatenburg de Jong

Conflict of Interest Disclosures: Ms Helmrich reported receiving grants from the European Union's Seventh Framework Program, the Hannelore Kohl Stiftung (Germany), OneMind (USA), and Integra LifeSciences Corporation outside the submitted work. No other disclosures were reported.

Funding/Support: Eline Krijkamp was supported by the Society for Medical Decision Making fellowship through a grant (GBMF7853) by the Gordon and Betty Moore Foundation, Palo Alto, CA, United States. Support for this study was solely from institutional and/or departmental sources.

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Acknowledgment: We are grateful for Lisa Caulley for her suggestions to revise the final manuscript. We are grateful for H. Karreman and C. Van der Velden-van der Graaf for the work they have done for the quality-of-life data collection. Moreover, we want to thank Ruben Goedhart, Esther van Spronsen, and Linda van der Sluijs-van der Beek for extracting the data from the electronic patient registry. Finally, we also want to thank the anonymous reviewers of *Value in Health* for their valuable suggestions.

REFERENCES

- Office of the Assistant Secretary for Preparedness, US Department of Health and Human Services. *Pandemic influenza plan - update IV (December 2017)*. 2017.
- Emanuel EJ, Persad G, Upshur R, et al. Fair allocation of scarce medical resources in the time of Covid-19. *N Engl J Med*. 2020;382:1-7.
- D'Agostino A, Demartini B, Cavallotti S, Gambini O. Mental health services in Italy during the COVID-19 outbreak. *Lancet Psychiatry*. 2020;7:385-387.
- Lazzerini M, Barbi E, Apicella A, Marchetti F, Cardinale F, Trobia G. Delayed access or provision of care in Italy resulting from fear of COVID-19. *Lancet Child Adolesc Health*. 2020;4:e10-e11.
- Harahsheh AS, Dahdah N, Newburger JW, et al. Missed or delayed diagnosis of Kawasaki disease during the 2019 novel coronavirus disease (COVID-19) pandemic. *J Pediatr*. 2020;222:261-262.
- Chang H-J, Huang N, Lee C-H, Hsu Y-J, Hsieh C-J, Chou Y-J. The impact of the SARS epidemic on the utilization of medical services: SARS and the fear of SARS. *Am J Public Health*. 2004;94:562-564.
- NZA. Analyse van de gevolgen van de coronacrisis voor de reguliere zorg. https://zorgdomein.com/media/documents/NZA-analyse_van_de_gevolgen_van_de_coronacrisis_voor_de_reguliere_zorg_....pdf. Accessed May 17, 2020.
- Sud A, Jones M, Broggio J, et al. Collateral damage: the impact on outcomes from cancer surgery of the COVID-19 pandemic. *Ann Oncol*. 2020;31:1065-1074.
- Powell SN, Mullen T, Young L, Heald D, Iv ETP. SARS-CoV-2 impact on elective orthopaedic surgery: implications for post-pandemic recovery. *J Bone Jt Surg*. 2020;102:e68.
- Salenger R, Etchill EW, Ad N, et al. The surge after the surge: cardiac surgery post-COVID-19. *Ann Thorac Surg*. 2020;110:2020-2025.
- Qadan M, Hong TS, Tanabe KK, Ryan DP, Lillemoe KD. A multidisciplinary team approach for triage of elective cancer surgery at the Massachusetts General Hospital during the novel coronavirus COVID-19 outbreak. *Ann Surg*. 2020;272:e20-e21.
- MacCormick AD, Parry BR. Judgment analysis of surgeons' prioritization of patients for elective general surgery. *Med Decis Making*. 2006;26:255-264.
- Garner RT, Rosen B. *Moral Philosophy: A Systematic Introduction to Normative Ethics and Meta-Ethics*. New York: Macmillan; 1967.
- Vergano M, Bertolini G, Giannini A, et al. Clinical ethics recommendations for the allocation of intensive care treatments in exceptional, resource-limited circumstances [in Italian]. *Recenti Prog Med*. 2020;111:207-211.
- Daugherty Biddison L, Berkowitz KA, Courtney B, et al. Ethical considerations: care of the critically ill and injured during pandemics and disasters: CHEST consensus statement. *Chest*. 2014;146:e1455-e1555.
- Centers for Disease Control and Prevention. Ethical considerations for decision making regarding allocation of mechanical ventilators during a severe influenza pandemic or other public health emergency. https://www.cdc.gov/about/advisory/pdf/VentDocument_Release.pdf.
- New York State Department of Health. *Ventilator allocation guidelines*. New York State Task Force on Life and the Law. New York State Department of Health; 2015.
- Toner E, Waldhorn R. Responding to pandemic influenza - The ethical framework for policy and planning. *Health Service Journal*. <https://www.hsj.co.uk/swine-flu/responding-to-pandemic-influenza-the-ethical-framework-for-policy-and-planning/5005219.article>. Accessed May 17, 2020.
- Integrated Cancer Center Netherlands. *Cancers*. <https://ikn.nl/kanker-soorten>. Accessed May 19, 2020.
- Dutch Heart Registration. <https://nederlandsehartregistratie.nl/>. Accessed May 19, 2020.
- CBS. Mortality probabilities by age, gender, level of education. <https://www.cbs.nl/nl-nl/maatwerk/2017/23/sterftekansen-naar-leeftijd-geslacht-opleiding-gsniveau>. Accessed May 19, 2020.
- Hunink M, Weinstein MC, Wittenberg E, et al. *Decision Making in Health and Medicine: Integrating Evidence and Values*. 2nd ed. Cambridge: Cambridge University Press; 2003.
- Global Burden of Disease Collaborative Network. *Global Burden of Disease Study 2016 (GBD 2016) Disability Weights*. Seattle, WA: Institute for Health Metrics and Evaluation; 2017.
- General guidance for DALYs calculation. <https://montagu.vaccineimpact.org/contribution/resources/c978e5a1ac6fa502679c92200e78ef61.pdf>. Accessed May 19, 2020.
- World Health Organization. Disability-adjusted life years (DALYs). <https://www.who.int/data/gho/indicator-metadata-registry/imr-details/158>. Accessed May 19, 2020.
- Stouthard EA, Essink-Bot M-L, Bonsel GJ. Disability weights for diseases: a modified protocol and results for a Western European region. *Eur J Public Health*. 2000;10:24-30.
- Siebert U, Alagoz O, Bayoumi AM, et al. State-transition modeling: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-3. *Value Health*. 2012;15:812-820.
- Klarman H, Rosenthal GD. Cost effectiveness analysis applied to the treatment of chronic renal disease. *Med Care*. 1968;6(1):48-54.
- Sonnenberg FA, Beck JR. Markov models in medical decision making. *Med Decis Mak*. 1993;13:322-338.
- Torgerson DJ, Raftery J. Economic notes. Discounting. *BMJ*. 1999;319:914-915.
- Zorginstituut Nederland. Guideline for conducting economic evaluations in health care. <https://www.zorginstituutnederland.nl/publicaties/publicatie/2016/02/29/richtlijn-voor-het-uitvoeren-van-economische-evaluaties-in-de-zondheidszorg>.
- R Core Team. *R: a language and environment for statistical computing*. 2013.
- Alarid-Escudero F, Krijkamp EM, Enns EA, Hunink MGM, Pechlivanoglou P, Jalal H. Cohort state-transition models in R: from conceptualization to implementation. <http://arxiv.org/abs/2001.07824>. Accessed May 19, 2020.

34. Alarid-Escudero F, Krijkamp EM, Pechlivanoglou P, et al. A need for change! A coding framework for improving transparency in decision modeling. *Pharmacoeconomics*. 2019;37:1329–1339.
35. Salomon JA, Haagsma JA, Davis A, et al. Disability weights for the Global Burden of Disease 2013 study. *Lancet Glob Health*. 2015;3(11):e712–e723.
36. Shin DW, Cho J, Kim SY, et al. Delay to curative surgery greater than 12 weeks is associated with increased mortality in patients with colorectal and breast cancer but not lung or thyroid cancer. *Ann Surg Oncol*. 2013;20:2468–2476.
37. Chen EY, Mayo SC, Sutton T, et al. Effect of time to surgery of colorectal liver metastases on survival [e-pub ahead of print]. *J Gastrointest Cancer*. 2020 Feb 22. <https://doi.org/10.1007/s12029-020-00372-5>.
38. Yusuf S, Zucker D, Passamani E, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet*. 1994;344:563–570.
39. Noorbakhsh A, Tang JA, Marcus LP, et al. Gross-total resection outcomes in an elderly population with glioblastoma: a SEER-based analysis. Clinical article. *J Neurosurg*. 2014;120:31–39.
40. Nakano R, Ohira M, Kobayashi T, et al. Hepatectomy versus stereotactic body radiotherapy for primary early hepatocellular carcinoma: a propensity-matched analysis in a single institution. *Surgery*. 2018;164:219–226.
41. Lee JN, Kwon SY, Choi GS, et al. Impact of surgical wait time on oncologic outcomes in upper urinary tract urothelial carcinoma. *J Surg Oncol*. 2014;110:468–475.
42. Lim C, Bhangui P, Salloum C, et al. Impact of time to surgery in the outcome of patients with liver resection for BCLC 0-A stage hepatocellular carcinoma. *J Hepatol*. 2018;68:100–108.
43. Moss AJ, Jackson Hall W, Cannon DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. *N Engl J Med*. 1996;335:1933–1940.
44. Scott SWM, Batchelder AJ, Kirkbride D, Naylor AR, Thompson JP. Late survival in nonoperated patients with infrarenal abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg*. 2016;52:444–449.
45. Nyboe C, Karunanithi Z, Nielsen-Kudsk JE, Hjortdal VE. Long-term mortality in patients with atrial septal defect: a nationwide cohort-study.
46. Brewster DC, Jones JE, Chung TK, et al. Long-term outcomes after endovascular abdominal aortic aneurysm repair: the first decade. *Ann Surg*. 2006;244:426–436.
47. Brunner M, Olschewski M, Geibeli A, Bode C, Zehender M. Long-term survival after pacemaker implantation: prognostic importance of gender and baseline patient characteristics. *Eur Heart J*. 2004;25:88–95.
48. Rose EA, Gelijns AC, Moskowitz AJ, et al. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med*. 2001;345:1435–1443.
49. Mazzone E, Preisser F, Nazzani S, et al. More extensive lymph node dissection improves survival benefit of radical cystectomy in metastatic urothelial carcinoma of the bladder. *Clin Genitourin Cancer*. 2019;17:105–113.e2.
50. Kann BH, Verma V, Stahl JM, et al. Multi-institutional analysis of stereotactic body radiation therapy for operable early-stage non-small cell lung carcinoma. *Radiother Oncol*. 2019;134:44–49.
51. Huang CE, Yang YH, Chen WC, et al. Nephroureterectomy increase 5 year survival in patients on dialysis with upper urinary tract urothelial carcinoma. *Oncotarget*. 2017;8:79876–79883.
52. Shalowitz DI, Epstein AJ, Ko EM, Giuntoli RL. Non-surgical management of ovarian cancer: prevalence and implications. *Gynecol Oncol*. 2016;142:30–37.
53. Pedregal-Mallo D, Sánchez Canteli M, López F, Álvarez-Marcos C, Llorente JL, Rodrigo JP. Oncological and functional outcomes of transoral laser surgery for laryngeal carcinoma. *Eur Arch Otorhinolaryngol*. 2018;275:2071–2077.
54. Kim WR, Lake JR, Smith JM, et al. OPTN/SRTR 2016 Annual Data Report: liver. *Am J Transplant*. 2018;18:172–253.
55. Muluk SC, Muluk VS, Kelley ME, et al. Outcome events in patients with claudication: a 15-year study in 2777 patients. *J Vasc Surg*. 2001;33:251–258.
56. Wang J, Yan C, Fu A. A randomized clinical trial of comprehensive education and care program compared to basic care for reducing anxiety and depression and improving quality of life and survival in patients with hepatocellular carcinoma who underwent surgery. *Medicine (Baltimore)*. 2019;98:e17552.
57. Holtzman A, Morris CG, Amdur RJ, Dziegielewski PT, Boyce B, Mendenhall WM. Outcomes after primary or adjuvant radiotherapy for salivary gland carcinoma. *Acta Oncol*. 2017;56:484–489.
58. Murphy MM, Simons JP, Hill JS, et al. Pancreatic resection: a key component to reducing racial disparities in pancreatic adenocarcinoma. *Cancer*. 2009;115:3979–3990.
59. Mikkola R, Kelahaara J, Heikkinen J, Lahtinen J, Biancari F. Poor late survival after surgical treatment of pleural empyema. *World J Surg*. 2010;34:266–271.
60. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet*. 2003;361:13–20.
61. Piehler JM, Crichlow RW. Primary carcinoma of the gallbladder. *Arch Surg*. 1977;112:26–30.
62. Warner L, Chudasama J, Kelly CG, et al. Radiotherapy versus open surgery versus endolaryngeal surgery (with or without laser) for early laryngeal squamous cell cancer. *Cochrane Database Syst Rev*. 2014;2014:CD002027.
63. Warlow C, Farrell B, Fraser A, Sandercock P, Slattery J. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet*. 1998;351:1379–1387.
64. Soran A, Ozmen V, Ozbas S, et al. Randomized trial comparing resection of primary tumor with no surgery in stage IV breast cancer at presentation: protocol MF07-01. *Ann Surg Oncol*. 2018;25:3141–3149.
65. Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. *Ann Thorac Surg*. 1995;60:615–623.
66. Redden MD, Chin TY, van Driel ML. Surgical versus non-surgical management for pleural empyema. *Cochrane Database Syst Rev*. 2017;2017:CD010651.
67. Verwaal VJ, Bruin S, Boot H, Van Slooten G, Van Tinteren H. 8-year follow-up of randomized trial: cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy in patients with peritoneal carcinomatosis of colorectal cancer. *Ann Surg Oncol*. 2008;15:2426–2432.
68. Sørensen VR, Heaf J, Wehberg S, Sørensen SS. Survival benefit in renal transplantation despite high comorbidity. *Transplantation*. 2016;100:2160–2167.
69. Shalowitz DI, Epstein AJ, Buckingham L, Ko EM, Giuntoli RL. Survival implications of time to surgical treatment of endometrial cancers. *Am J Obstet Gynecol*. 2017;216:268.e1–268.e18.
70. van Harten M, de Ridder M, Hamming-Vrieze O, Smeele L, Balm A, van den Brekel M. The association of treatment delay and prognosis in head and neck squamous cell carcinoma (HNSCC) patients in a Dutch comprehensive cancer center. *Oral Oncol*. 2014;50:282–290.
71. Stewart JM, Tone AA, Jiang H, et al. The optimal time for surgery in women with serous ovarian cancer. *Can J Surg*. 2016;59:223–232.
72. Davies L, Welch G. Thyroid cancer survival in the United States: observational data from 1973 to 2005. *Arch Otolaryngol Head Neck Surg*. 2010;136:440–444.
73. Bleicher RJ, Ruth K, Sigurdson ER, et al. Time to surgery and breast cancer survival in the United States. *JAMA Oncol*. 2016;2:330–339.
74. Morse E, Fujiwara RJT, Judson B, Mehra S. Treatment times in salivary gland cancer: national patterns and association with survival. *Otolaryngol Head Neck Surg*. 2018;159:283–292.
75. United States Renal Data System. <https://www.usrds.org/2015/view/>. Accessed May 19, 2020.
76. Kirkegård J, Mortensen FV, Hansen CP, Mortensen MB, Sall M, Frstrup C. Waiting time to surgery and pancreatic cancer survival: a nationwide population-based cohort study. *Eur J Surg Oncol*. 2019;45:1901–1905.
77. Chung JH, Lee SH, Kim KT, Jung JS, Son HS, Sun K. Optimal timing of thoracoscopic drainage and decortication for empyema. *Ann Thorac Surg*. 2014;97:224–229.
78. Konstantinides S, Geibel A, Olschewski M, et al. A comparison of surgical and medical therapy for atrial septal defect in adults. *N Engl J Med*. 1995;333:469–473.
79. Organ Procurement and Transplantation Network. <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/>. Accessed May 19, 2020.
80. Howard DPJ, Banerjee A, Fairhead JF, Hands L, Silver LE, Rothwell PM. Population-based study of incidence, risk factors, outcome, and prognosis of ischemic peripheral arterial events: implications for prevention. *Circulation*. 2015;132:1805–1815.
81. Bonow RO, Greenland P. Population-wide trends in aortic stenosis incidence and outcomes. *Circulation*. 2015;131:969–971.
82. Badalato GM, Gaya JM, Hruby G, et al. Immediate radical cystectomy vs conservative management for high grade cT1 bladder cancer: is there a survival difference? *BJU Int*. 2012;110:1471–1477.
83. Lee CT, Madii R, Daignault S, et al. Cystectomy delay more than 3 months from initial bladder cancer diagnosis results in decreased disease specific and overall survival. *J Urol*. 2006;175:1262–1267.
84. Tan WS, Trinh QD, Hayn MH, et al. Delayed nephrectomy has comparable long-term overall survival to immediate nephrectomy for cT1a renal cell carcinoma: a population-based analysis. *Urol Oncol Semin Orig Invest*. 2020;38:74.e13–74.e20.
85. Janssen MWV, Linxweiler J, Terwey S, et al. Survival outcomes in patients with large (7cm) clear cell renal cell carcinomas treated with nephron-sparing surgery versus radical nephrectomy: results of a multicenter cohort with long-term follow-up. *PLoS One*. 2018;13:e0196427.
86. Fein DA, Mendenhall WM, Parsons JT, et al. Carcinoma of the oral tongue: a comparison of results and complications of treatment with radiotherapy and/or surgery. *Head Neck*. 1994;16:358–365.
87. Jakola AS, Myrmet KS, Kloster R, et al. Comparison of a strategy favoring early surgical resection vs a strategy favoring watchful waiting in low-grade gliomas. *JAMA*. 2012;308:1881–1888.
88. Haruna A, Muro S, Nakano Y, et al. CT scan findings of emphysema predict mortality in COPD. *Chest*. 2010;138:635–640.
89. Ruys AT, Heuts SG, Rauws EA, Busch ORC, Gouma DJ, Van Gulik TM. Delay in surgical treatment of patients with hilar cholangiocarcinoma: does time impact outcomes? *HPB (Oxford)*. 2014;16:469–474.
90. Ae LXC, Reichman ME, Ae BAM, et al. Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: National Longitudinal Mortality Study. *Cancer Causes Control*. 2009;20:417–435.
91. Pettitt D, Raza S, Naughton B, et al. The limitations of QALY: a literature review. *J Stem Cell Res Ther*. 2016;6.
92. Feltrim MIZ, Coelho AAC, Scatimburgo MM, Pereira GM, Pego-Fernandes P. Quality of life assessment in two consecutive years of patients in a waiting list for lung transplantation. *Transplant Proc*. 2014;46:3060–3063.

-
93. Auneau-Enjalbert L, Hardouin J-B, Blanchin M, et al. Comparison of longitudinal quality of life outcomes in preemptive and dialyzed patients on waiting list for kidney transplantation. *Qual Life Res.* 2020;29:959–970.
 94. Oudhoff JP, Timmermans D, Knol DL, Bijnen AB, Van Der Wal G. Waiting for elective general surgery: impact on health related quality of life and psychosocial consequences. *BMC Public Health.* 2007;7:164.
 95. Elliott JH, Synnot A, Turner T, et al. Living systematic review: 1. Introduction: the why, what, when, and how on behalf of the Living Systematic Review Network. *J Clin Epidemiol.* 2017;91:23–30.