Minimizing Population Health Loss in Times of Scarce Surgical Capacity

Benjamin Gravesteijn\* (0000-0001-8096-5803)1,2, Eline Krijkamp\* (0000-0003-3970-2206)3,5, Jan Busschbach (0000-0002-8602-0381)4,5, Geert Geleijnse (0000-0002-4718-0032)1, Isabel Retel Helmrich (0000-0001-5257-395X)2, Sophie Bruinsma (0000-0003-3634-9899)6, Céline van Lint (0000-0002-7929-7622)6, Ernest van Veen (0000-0002-5495-3996)2,7, Ewout Steyerberg (0000-0002-7787-0122)8, Kees Verhoef (0000-0001-9980-8613)8, Jan van Saase (0000-0003-2874-6667)9, Hester Lingsma (0000-0003-2063-9533)2, Rob Baatenburg de Jong (0000-0001-7236-264X)1, and collaborators\*\*

\*Both authors contributed equally

Author affiliations - Request all authors to check the affiliation + ORCID ID

1) Department of Otorhinolaryngology (ENT); 2) Department of Public Health; 3) Department of Epidemiology; 4) Department of Medical Psychology; 5) Netherlands Institute for Health Sciences; 6) Department of Quality and Patient Care; 7) Department of Intensive Care; 9) Department of surgical oncology and gastrointestinal surgery; 10) Department of Internal Medicine - Erasmus University Medical Center, Rotterdam, the Netherlands.

\*\* 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

Intention to be submitted to:

1. NEJM (advice to try the COVID-19 special, because NEJM is not that into decision models - maybe for COVID they are) How about we also talk about “1. 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;1–7.” in the cover letter
2. Lancet
3. BMJ

Word count: <2700

# Abstract

## Background

COVID-19 has put unprecedented pressure on healthcare systems worldwide, leading to a reduction of the available healthcare capacity. Different ethical perspectives can be followed to prioritize patients waiting for surgery. Our objective was to develop a decision model that supports prioritization of care from a utilitarian perspective, which is to minimize population health loss.

Methods

A cohort state-transition model was developed and applied to 34 semi-elective surgeries for adults commonly performed in academic hospitals. We compared scenarios of delaying surgery from two weeks up to one year (with 10-week intervals) and no surgery at all. Model parameters were based on registries, scientific literature, and the World Health Organization global burden of disease study, with a focus on 2 effects: the benefit of surgery and the impact of delay. For each surgery, the urgency was estimated as the average expected loss of Quality-Adjusted Life-Years (QALYs) per month.

## Results

Class I evidence was not available for most surgeries. If best available evidence was used, the three most urgent surgeries were bypass surgery for Fontaine III/IV peripheral arterial disease (0.23 QALY loss/month 0.09 - 0.24), transaortic valve implantation (0.15 QALY loss/month, 95% CI: 0.09 - 0.24), and total nephrectomy for renal carcinoma (0.12 QALY loss/month, 95% CI: 0.09 - 0.15). The three least urgent surgeries were placing a shunt for dialysis (0.01, 95% CI: 0.005 - 0.01), thyroid carcinoma resection (0.01, 95% CI: 0.01 - 0.02), and mild salivary gland carcinoma resection (0.01, 95% CI: 0.01 - 0.03): these surgeries were associated with a limited amount of health lost on the waiting list.

## Conclusion

Expected health loss due to surgical delay can be objectively calculated with our decision model based on best available evidence, which can guide prioritization of surgeries to minimize population health loss in times of scarcity. Placing this tool in the context of different ethical perspectives and combining it with capacity management tools is key to facilitate large-scale implementation in hospitals, health insurance companies and health authorities.

## Background

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 impacts the continuity of regular care. First, because wards and operating theaters are converted to COVID-19 care facilities, fewer non-COVID-19 patients can undergo surgery.3 Second, because physicians are deployed to care for COVID-19 patients, they have less time to see non-COVID-19 patients.4,5Third, in the Netherlands, we observed a 90% decrease in referrals during the first weeks of the crisis and approximately 30% less cancer diagnoses compared to previous years.6,7 Finally, the fear of contagion with

SARS-CoV-2 may leave non-COVID patients reluctant to seek care 4,5, as was seen in similar health crises like the SARS epidemic.8

Delay in surgical care may dramatically impact health care quality and accessibility. In the first weeks of the COVID-19 crisis in the Netherlands, 75-90% fewer surgeries were performed compared to previous years.6 The delay in cancer surgery already has made a large impact in the life expectancy of oncological patients.9 Moreover, it may be impossible to treat the whole accumulating group of patients: it would take 7-16 months in the United States for the system of orthopedic surgery to recover to nearly full capacity if elective orthopedic surgeries would have been resumed in June 2020.10 Also, if regular cardiothoracic surgical care capacity does not increase, the backlog of these patients may never clear.11 Because of these problems, hospitals are facing a dilemma: Which patients should be prioritized?

Experts in the field of medical ethics recently proposed that the distribution of scarce (surgical) resources can be evaluated by the following four ethical values: 1) Scarce resources are used to maximize the benefits; 2) People are treated equally; 3) Instrumental value is promoted and rewarded; 4) People that are worst off (e.g., the sickest or youngest) are prioritized.2 In the context of a pandemic, it is justifiable to focus on maximizing benefits (ethical value 1).12–16 This is consistent with utilitarian ethical perspectives, which emphasize total population outcomes over individual outcomes when resources are scarce.17

As stated by Emanuel et al., “*The question is not whether to set priorities, but how to do so ethically and consistently, rather than basing decisions on individual institutions’ approaches or a clinician’s intuition in the heat of the moment*”.2 In reality, however, individual surgical patients are most often triaged by experts from the respective surgical fields.18 Unfortunately, it is known that the level of agreement on prioritization is low between experts.19 Additionally, prioritization across different disciplines is complicated by the high degree of specialization in modern medicine.

To guide prioritization of semi-elective surgeries 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

We selected 43 semi-elective surgeries (performed within three days up to three weeks) most frequently performed in our institute. We searched for input parameters for these surgeries. We applied these parameters in a broadly applicable state transition computer-based model to estimate the effect of surgical delay on survival and health related quality of life (QoL).

### Patients and setting

The evaluated surgeries in this study comprised of non-pediatric and non-obstetric, semi-elective surgeries in Erasmus University Medical Center, an academic tertiary referring hospital in the Netherlands. A semi-elective surgery should ideally be performed within three days up to three weeks. We retrieved the number of surgeries, surgery time, length of stay at an intensive care unit (ICU), and length of stay at a non-ICU of all non-urgent surgeries from July 2017 to December 2019 from the electronic patient registry (ChipSoft, HiX). The retrieved surgeries were classified as a semi-elective surgery by two senior clinicians. Finally, this selection was approved by the Value Based operation room (OR) team collaborators. Ultimately, 43 semi-elective surgeries were selected that were performed more than 80 times during the inclusion interval. Where relevant, we distinguished mild and severe cases undergoing the surgery based on clinical insight of our expert panel. We aimed to collect data of the patient populations with an indication of the 49 semi-elective non-pediatric and non-obstetric semi-elective surgery.

### Input parameters

The model required 7 input parameters: 1) survival rates pre-surgery, 2) survival rate post-surgery, 3) QoL pre-surgery, 4) QoL post-surgery, 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. An overview of all parameter values and their sources can be found in Appendix A, and a more description of the model parameters and assumptions can be found in Appendix C.

The class of evidence we collected was defined as class I (Randomized Controlled Trials or systematic reviews of Randomized Controlled Trials), class IIa (Prospective observational studies, before-after studies), class IIb (Retrospective observational studies, expert panels for the utilities, national registries), and class III (expert opinion).

### Markov model

For our aim, we developed a three-state cohort state-transition model. 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.23,28 Individuals could transition between a preoperative state, a postoperative state, and a dead state (Figure 1). Based on the time spent in these states, health benefits, like expected life years or QALYs are calculated.23,29,30 The entire cohort started in the preoperative state, and was followed their entire 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. We evaluated scenarios where patients were treated with a delay of two weeks up to a delay of a year using intervals of ten weeks. In addition, we evaluated the scenario where none of the patients ever received treatment: this was modeled by following patients their 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. If the delay was longer than the time until no effect of surgery on survival or QoL, the postoperative survival and QoL were set equal to the preoperative survival.

### Health Effects of Surgery

The effects of delays in surgery on survival and quality of life were evaluated. Survival and quality of life from no surgery was compared to survival and quality of life at 2 weeks and 52 weeks, to determine the survival and quality of life associated with surgery and survival and quality of life lost per 50 weeks, respectively. This measure of urgency was converted to loss per month and was used to rank the surgeries. Finally, the model results were compared visually to the capacity requirements in our hospital, obtained from the electronic patient registry.

### Analysis

Probabilistic sensitivity analysis was used to incorporate parameter uncertainty in the model outcome. In the probabilistic sensitivity analyses, the model was run 100 times, each taking random draws from prespecified uncertainty distributions of all inputs. We used triangle distributions for the survival probabilities, the time to no effect on survival or QoL, and QoL; we used lognormal distributions for relative treatment effects; and normal distributions for age. The 50th, 2.5th, and 97.5th percentile of these PSA estimates were calculated, which correspond to the main estimate and the lower and upper limit of the 95% confidence interval, respectively. To calculate QALY loss due to delay, the QALYs associated with delaying surgery for 52 weeks was subtracted from the QALYs associated with delaying the surgery for 2 weeks. This gives the QALY loss per 50 weeks, which in turn was converted to QALY loss per month. Rankings based on different absolute health benefits and loss per unit of time were compared using Spearman’s rank correlation coefficient.

This manuscript was reported in accordance with the CHEER guidelines for reporting health-economical evaluations.34 The model was built with R software35 and adapted from previously published code.36,37 The model code and input data are freely available via a GitHub repository: [ADD LINK IF JOURNAL AGREES].

# Results

## Data collection

We evaluated 12 cardiothoracic surgeries, 23 oncological surgeries, 2 transplantations (liver and living donor kidney), 5 vascular surgeries, and 1 other type of surgery (creation of a shunt to facilitate hemodialysis). These 43 evaluated surgeries comprised of 69% of the total semi-elective program in our hospital.

For all surgeries, survival with treatment could be obtained. Survival with treatment was mostly based on national registries (31/43; XX%). Survival without treatment could was mostly based on data from (inter)national registries (12 surgeries, 6 indirectly calculated through the treatment effect), but also frequently from RCT’s (10 surgeries, 7 indirectly calculated), and observational studies (9 surgeries, 3 indirectly calculated. For 14 surgeries, QoL was available through the WHO Global Burden of Disease study. For the remaining 29 surgeries, the QoL of the pre- and postoperative health state was estimated by the expert panel as described in the methods section. For 6 surgeries, a “time-to-no-effect-on-QoL” within one year, our maximum period of delaying surgery, was applicable. For 23 surgeries, we assumed a “time-to-no-effect-of-treatment-on-survival” based on qualitative assessment of the literature. Most of these surgeries were oncological surgeries (XX/XX%). The estimates for the time until surgery becomes ineffective was mostly based on class IIb evidence (retrospective and prospective observational studies, see table 1). Input parameters varied widely between surgeries (Figure 2). All input parameters, their sources20,21,38–92, and the corresponding model output for each semi-elective surgery are presented in Appendix A.

## Quality of Life

The preoperative and postoperative health state of 3 surgeries (one with a mild and severe subgroup) were estimated in both sessions, resulting in 8 double estimates of QoL. The gain in QoL due to surgery was not estimated different in the second session (the standardized mean difference was 0.025, 95% CI: -0.11 – 0.16, table 3 and figure 1 Appendix B).

The maximum expected benefit, i.e. in a scenario without delay, from the evaluated surgeries ranged from 0.48 QALYs (95% CI: 0.32 – 0.83) for resection of muscle invasive bladder cancer to 10.3 QALYs (95% CI: 8.7 – 11.9) for kidney transplantation (Figure 3). The ranking based on QALYs gained by surgery was correlated with the ranking based on life years gained by surgery:The Spearman rank correlation coefficient between the ranking of surgeries based on LYs and QALYs was 0.45 (p=0.003).

## Urgency

Most surgeries had a clear linear descend in terms of QALYs per delay, except for surgeries where a time until no effect of treatment on survival was assumed (figure 1, appendix B).

The urgency of the surgeries ranged from 0.01 QALY loss/month (95% CI: 0.00 - 0.01) for placing a shunt for dialysis, to 0.23 QALY loss/month (0.09 - 0.24) for a bypass surgery for Fontaine III/IV peripheral arterial disease (Figure 4, and table 1 Appendix B). This implies that if the latter would be postponed by a month, patients with this surgical indication lose approximately 84 days (0.23\*365) spent in perfect health of their remaining expected QALYs gained by surgery.

Surgeries that were associated with a higher expected QALY benefit, often lost more QALYs per month: The Spearman correlation coefficient between the ranking of health benefit, in terms of QALYs, and urgency, in terms of QALY loss per month, was 0.32 (p=0.04). The most urgent surgeries after bypass surgery for Fontaine III/IV peripheral arterial disease, were transaortic valve implantation (0.15 QALY loss/month, 95% CI: 0.09 - 0.24), and total nephrectomy for renal carcinoma (0.12 QALY loss/month, 95% CI: 0.09 - 0.15). After placing a shunt for patients with end-stage renal disease, the least urgent surgeries were resection of thyroid cancer (0.01 QALY loss/month, 95% CI:0.01 - 0.02) and the resection of mild salivary gland carcinoma (0.01 QALY loss/month, 95% CI: 0.01 - 0.03) (Appendix B). When ordering surgeries based on LYs lost per month instead of QALYs lost per month, bypass surgery for Fontaine III/IV peripheral arterial disease ranked substantially lower (from rank 1 to rank 39), while the resection of mild salivary gland carcinoma ranked substantially higher (from rank 41 to rank 28).

## Capacity

In order to optimize the available surgery resource, the surgery time is an important measure to relate to urgency. Surgeries that are ranked high in terms of urgency and had relative short surgery time compared to other surgeries include repair of atrial septum defects (surgery time: 74 min [IQR: 56-131], urgency: 0.06 QALY loss/month [95% CI: 0.02 – 0.14]), pacemaker implantations (115 min [82-154], 0.11 QALY loss/month [0.04 - 0.22]), resection of mild larynx carcinoma (70 min [38 – 109], 0.07 QALY loss/month[0.04 - 0.11]), and valve replacements (99 min [77 – 125]; mitral valve replacement: 0.09 QALY loss/month [0.04 - 0.15]; aortic valve replacement: 0.09 QALY loss/month [0.06 - 0.17]) (Figure 5). Liver transplant is relatively urgent but requires an exceptional amount of OR-time (875 min [797 - 957], 0.08 QALY loss/month [0.07 - 0.09]) (table 2 Appendix B).

# Discussion

The decision model proposed in our study is an attempt to systematically guide prioritization of surgeries from a utilitarian perspective. We quantified urgency based on the expected health loss due to surgery delay. Available evidence suggests that semi-elective surgeries can be ranked based on their urgency using a simple three-states cohort state transition model. For survival with treatment, most evidence was based on national registries, while treatment effects were mostly derived from randomized controlled trials. The time until no effect of treatment on survival or quality of life, however, was most often derived from class IIb/III evidence. Using this approach, we found that among the 43 surgeries we analyzed, bypass surgery for Fontaine III/IV peripheral arterial disease, transaortic valve implantation, and the resection renal carcinoma were the most urgent surgeries. Less urgent surgeries were installment of a shunt for dialysis, resection of thyroid cancer, and the resection of mild salivary gland carcinoma. Liver transplantation shows to be a relatively urgent surgery but requires an exceptionally long surgery time. In times of scarce OR-capacity, this surgery is less efficient in the prevention of QALY loss.

We propose to use the loss of QALY per unit time delay of surgery as a measure of urgency. This strategy in conjuction with the currently most employed approach: triaging by expert teams from the respective surgical fields.18 Since experts weigh each objective characteristic by their own personal values, the agreement in prioritization is low.19 ~~Moreover, prioritization across different disciplines is complicated by the high degree of specialization in modern medicine. Finally, this approach is not objective nor transparent, and conflicts of interests at the individual and departmental level may arise~~. Our approach operationalizes ethical values that are the most appropriate in times of scarcity.2

Interestingly, the ranking of urgency is primarily driven by the gain in life years associated with surgery rather than the anticipated impact of delay. Surgeries that are associated with substantial gain in life years (e.g. mitral valve replacement), also lose more QALYs per month delay than surgeries that are associated with no gain in life years (e.g. creation of a shunt for hemodialysis). The larger the total health benefit associated with surgery, the more health can potentially be lost by postponing the surgery.

Nevertheless for some surgeries, the health benefit when taking QoL into account sometimes differs substantially to the health benefit when QoL is disregarded. Bypass surgery for Fontaine III/IV peripheral arterial disease ranked substantially lower when QoL was not taken into account. This surgery’s aim is to prevent the loss of a limb due to ischemia, which would of course impact quality of life. However, the surgery does not directly increase life expectancy. Disregarding QoL therefore decreases the health benefit and urgency of this surgery. On the other hand, resection of mild salivary gland carcinoma ranked substantially higher (from rank 41 to rank 28). This surgery is mostly aimed at extending life, and is associated with only a minor increase in QoL. The burden of living with cancer is lifted postoperatively, increasing quality of life. However, a postoperative facial nerve paralysis is not uncommon, and was estimated to impact quality of life in general.93 Disregarding QoL therefore increases the health benefit and urgency of this surgery.

To optimize OR triage, our metric for urgency should be weighed against hospital capacity. This is effectively a cost-effectiveness analysis, where resource constraints represent costs. For the scenario where OR-capacity is the most scarce in terms of hospital capacity, urgency can be plotted against surgery time. This simple method revealed that pacemaker implantation, resection of mild larynx carcinoma, and repair of ASD are the most efficient surgeries in our hospital to perform in this context. However, there are contexts where other types of capacity (e.g. ICU beds, hospital beds) are scarcer, and therefore more relevant to be weighed against urgency. Scarcity might even vary per week, in different phases of a crisis situation such as the COVID-19 pandemic.

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, an important consideration from the medical perspective may be the availability of alternative treatment strategies. In cancer treatment, (chemo-)radiation or systematic therapy alone may be considered instead of surgery, even when the effectivity would be lower, since waiting lists may be shorter and no OR or ICU capacity is needed. Second, an important consideration from the logistical perspective might be the impact of surgeries on the hospital capacity, which can differ in different phases of crises (e.g. surgery time is scarce in one week, and ICU capacity in the other). Third, 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. If this approach would be applied to the context of regular care, this perspective might be of increasing importance. Finally, other ethical perspectives (e.g. rule of rescue17) might be explored to assess the viability of our approach, and we need to establish whether our approach is applicable to all surgical procedures.

There are practical advantages of comparing “average patients” on urgency, despite the fact 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 suffer more frequently from diseases that are less urgent. It is known that lower socioeconomic groups are more prone to develop cancers that have clear association with unhealthy behavior, such as lung cancer.94 However, these diseases do not systematically rank low in our approach. Comparing the average patients across specialties on urgency may not be a very personalized approach, but it can be tailored to an individual’s context by providing input for shared decision making: we feel 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 of prioritization.

Since all models are, by definition, a simplification of reality, our model has several limitations. First, the survival data used were not always 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 surgeries that we evaluate are often part of standard clinical practice. Therefore, data might be biased (e.g. selection bias in the survival without treatment because patients opt for palliative care), or not available (it would be unethical now to perform randomized controlled trials evaluating surgery versus no surgery). Instead, we often used best available evidence, which found adjusted estimates from observational studies. For some surgeries, however, we did have evidence from more historical randomized controlled trials. As such, data might be biased, and as a result, the estimates from our model might also be somewhat biased. Because of this limitation, our approach is simply to aggregate transparently and systematically the best currently available evidence using a model.

Second, we assume that all surgeries are successful. We do not simulate adverse events, like major bleedings or death due to surgery. We also did not incorporate the potential reduction of QoL due to these adverse events or QoL reduction of a temporary period of recovery after surgery. Because of these assumptions, the overall QALYs associated with the surgery should not be interpreted as an absolute estimate. They can be considered the maximum possible QALYs that can be acquired by performing the surgery. However, these assumptions were considered reasonable to achieve the main goal of this study: when surgery without delay is compared to surgery with delay, the harm in both scenarios is similar and therefore cancel out.

Third, we used a linear approximation to quantify urgency by delaying surgery up to a year. Some surgeries did show a slightly steeper decrease in the period up to 32 weeks delay. The data needed to validly model this decay in QALYs per unit of time for all surgeries likely don’t 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 which also models the natural grow of tumors, or aneurysms, and validly model the development of metastasis. It was not feasible to develop this for all evaluated surgeries. Instead, we opted for a more pragmatic approach.

Fourth, we relied on QoL weights derived from expert-opinion. In this approach the patient is not involved, as experts interpret the health states and give weights. ~~Patient involvement could be achieved by administering often used generic QoL questionnaires which had been valued by the general public, like the EQ-5D or AQoL~~~~95~~~~.~~ There are also multiple methodological, ethical, and contextual disadvantages of using QALYs reported, but it should be noted that most of those discussion are more about utilitarian principles, than discussion specific for QALY.96

Fifth, we did not include the potential impact on QoL of delaying a semi-elective surgery. This impact might differ across surgeries. It might be hypothesized that surgeries performed after already a long disease history (e.g. kidney transplant) might have less “waiting time disutility” than recently diagnosed diseases (e.g. mammacarcinoma).

Sixth, we found that absolute QoL was estimated higher in the second expert session. However, the relevant measure of QoL in our model is the difference between preoperative and postoperative QoL, which did not differ significantly between the two sessions. Although our estimates remain valid, it might be reasonable to validate our QoL estimates in a larger sample of experts.

The model was tailored to the context in the Netherlands by using the national registry data. However, a substantial amount of the input used in the model originated from various international sources. Therefore, with some modifications, and using international data, the model can easily be applied to different contexts. Moreover, the model could be further developed by also modeling complications, recovery periods and the effect of comorbidity on survival. 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 ensure validity, it is however essential to periodically review the literature to improve the model inputs with higher quality evidence, much like a living systematic review. 97 If successful, a wider range of surgeries 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 best available evidence, our decision model may support prioritization of surgical care in times of scarcity in surgical capacity (e.g. due to COVID-19) from a utilitarian perspective. Based on our approach, the expected health loss due to delay was quantified for semi-elective surgeries in an academic hospital in the Netherlands. This approach can help to minimize health losses when trying to overcome delay in surgeries across disciplines. This approach is more transparent, more evidence-based, and more consistent than the alternative strategy of triaging based on expert opinion.

It should be noted that 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, the model inputs should be periodically updated with newer, higher quality evidence.

Finally, this tool should be placed in the context of other ethical perspectives and combined with capacity management tools. If successful, we believe this tool should be implemented on a large scale, in order to minimize health loss of the accumulating group of patients waiting for surgery.



Figure 1, state-transition diagram of the cohort model. The model is a state transition model with three health states, a preoperatieve health states (Preop), a postoperatieve state (Postop) and Dead. All patients start in the Preop health states. This is the health states 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 state they either die (transition to dead state) or continue to wait for their surgery (stay in the Preop state, the arrow points back into the health state). At the time of surgery, which is determined by us, all individuals still alive in the Preop health state transition to the Postop health state. The remaining lifetime the cohort is 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.

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

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Age | Quality of life - Preop | Quality of life - Postop | Survival - Preop | Survival - Postop | Time no eff Survival | Time no eff QoL | Treatment effect |
| n | 43 | 43 | 43 | 43 | 43 | 43 | 6 | 23 |
| 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) | 0 ( 0.0) |
| Expert opinion | 3 ( 6.8) | 2 ( 4.7) | 0 ( 0.0) | 0 ( 0.0) | 8 (18.6) | 2 ( 4.7) | 5 (83.3) | 4 (17.4) |
| Expert panel | 0 ( 0.0) | 0 ( 0.0) | 29 ( 67.4) | 29 ( 67.4) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| Expert panel (WHO) | 0 ( 0.0) | 0 ( 0.0) | 14 ( 32.6) | 14 ( 32.6) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) | 0 ( 0.0) |
| National registry | 21 (47.7) | 21 (48.8) | 0 ( 0.0) | 0 ( 0.0) | 12 (27.9) | 31 (72.1) | 0 ( 0.0) | 9 (39.1) |
| Observational, prospective | 5 (11.4) | 5 (11.6) | 0 ( 0.0) | 0 ( 0.0) | 4 ( 9.3) | 3 ( 7.0) | 0 ( 0.0) | 3 (13.0) |
| Observational, retrospective | 10 (22.7) | 10 (23.3) | 0 ( 0.0) | 0 ( 0.0) | 9 (20.9) | 4 ( 9.3) | 0 ( 0.0) | 7 (30.4) |
| RCT | 5 (11.4) | 5 (11.6) | 0 ( 0.0) | 0 ( 0.0) | 10 (23.3) | 3 ( 7.0) | 1 (16.7) | 0 ( 0.0) |
| Class of evidence (%) | | | | | | | | |
| I | 5 (11.4) | 5 (11.6) | 0 ( 0.0) | 0 ( 0.0) | 10 (23.3) | 3 ( 7.0) | 1 (16.7) | 0 ( 0.0) |
| IIa | 5 (11.4) | 5 (11.6) | 0 ( 0.0) | 0 ( 0.0) | 4 ( 9.3) | 3 ( 7.0) | 0 ( 0.0) | 3 (13.0) |
| IIb | 31 (70.5) | 31 (72.1) | 43 (100.0) | 43 (100.0) | 21 (48.8) | 35 (81.4) | 0 ( 0.0) | 16 (69.6) |
| III | 3 ( 6.8) | 2 ( 4.7) | 0 ( 0.0) | 0 ( 0.0) | 8 (18.6) | 2 ( 4.7) | 5 (83.3) | 4 (17.4) |

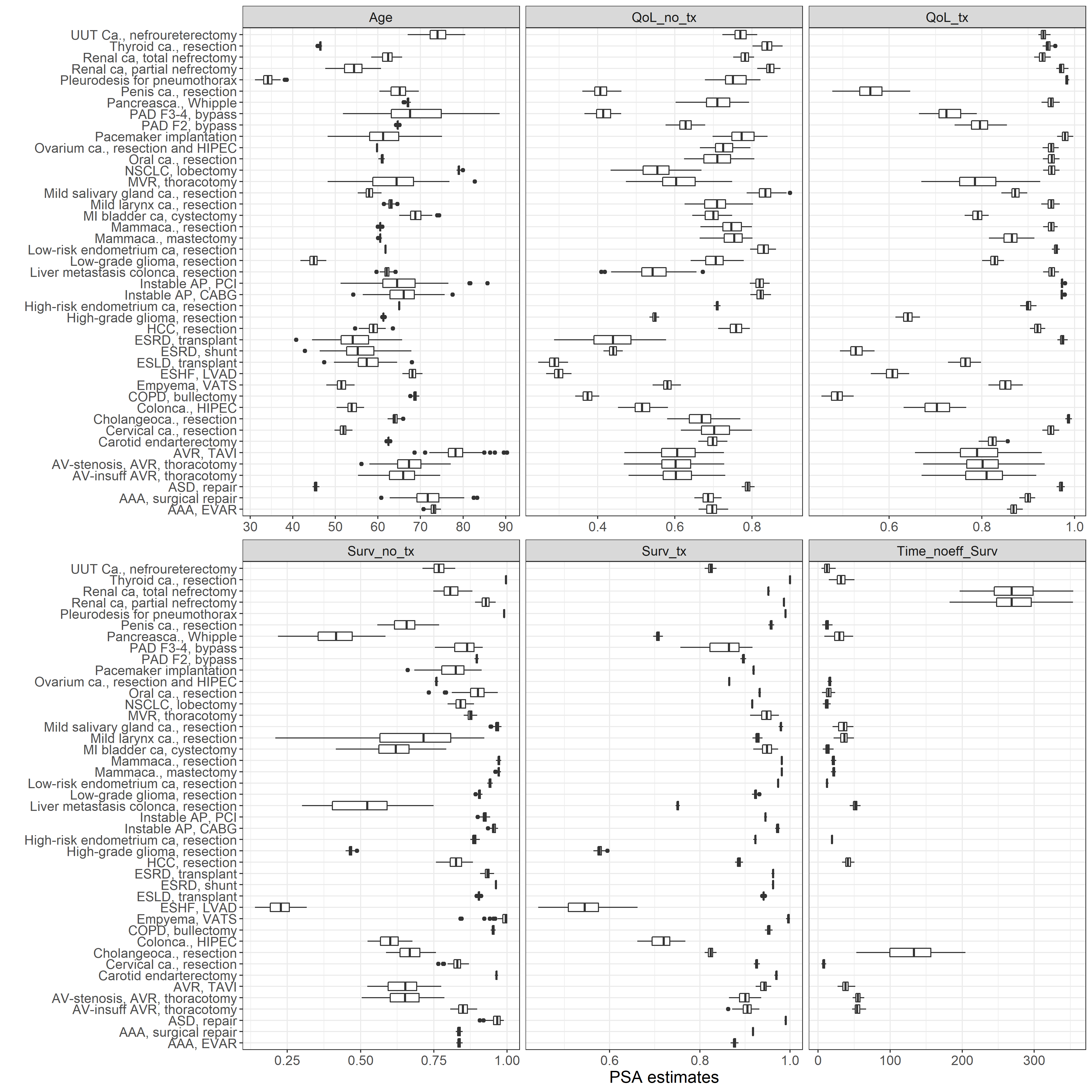


Figure 2, input parameters for the model. For a full list of input parameters per disease and source, see appendix A. **Abbreviations Figure titles**: Qol\_no\_tx: Quality of Life without treatment; QoL\_tx: quality of life with treatment; Surv\_no\_tx: 1-year survival probability without treatment; Surv\_tx: 1-year survival probability with treatment; Time\_noeff\_surv: days until no treatment is effective. **Abbreviations surgery/indications:** AAA: aneurysm of the abdominal aorta; AP: angina pectoris; ESRD: end-stage renal disease; ASD: atrial septum defect; ca.: carcinoma; CABG: coronary artery bypass graft; ESHF: end-stage heart failure; ESLD: end-stage liver disease; EVAR: endovascular aortic repair; HIPEC: hyperthermic intraperitoneal chemotherapy; HCC: hepatocellular carcinoma; NSCLC: non-small cell lung carcinoma; PAD: peripheral arterial disease; PCI: percutaneous coronary intervention; UUT: upper urinary track; VATS: video assisted thoracoscopic surgery

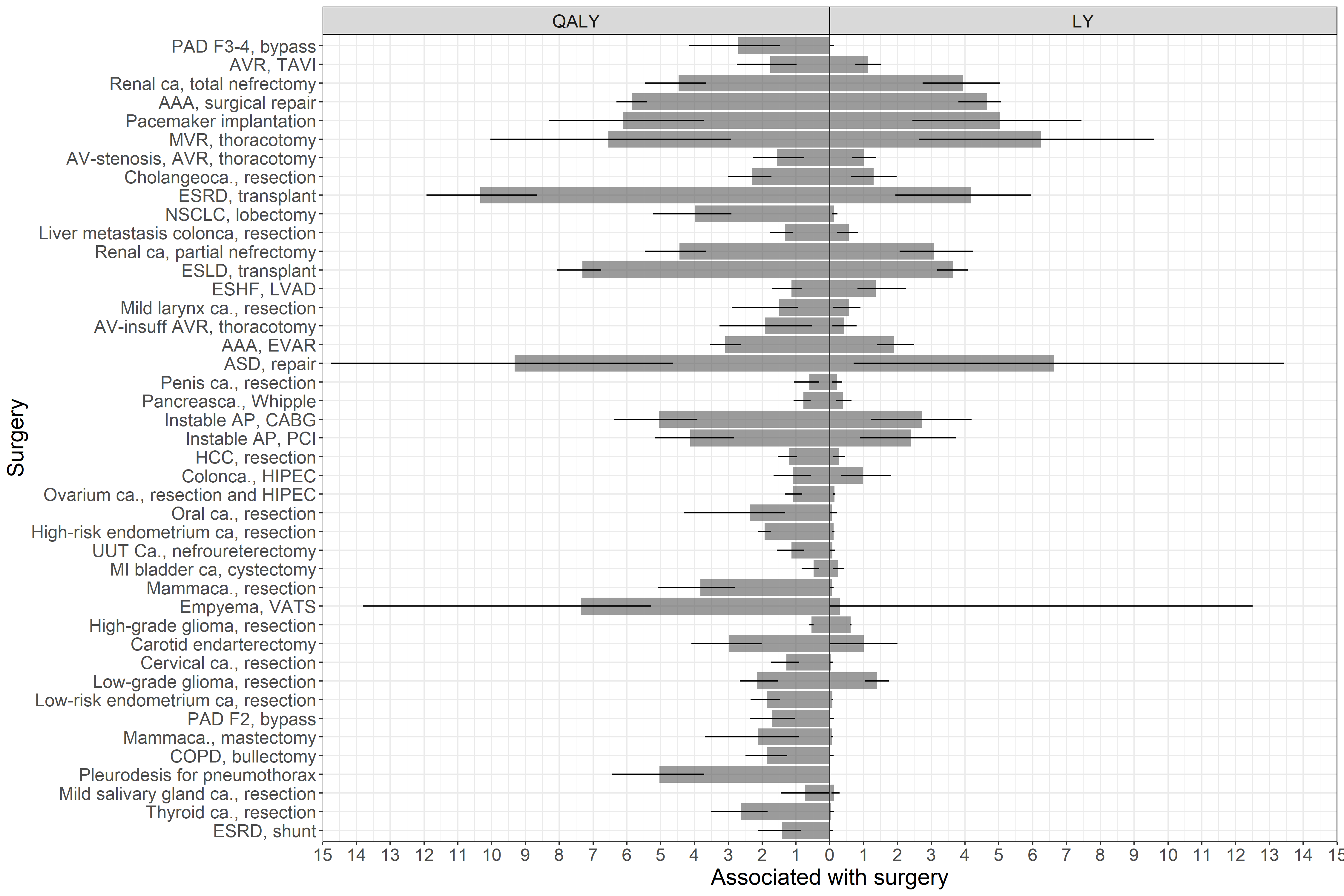


Figure 3, the maximum expected QALYs and LYs per surgery, in descending order of urgency (see figure 4). The estimates (gray bars) and 95% confidence intervals (black lines) are shown. The model output for no surgery was subtracted from the model output for a delay of 2 weeks. The actual data are presented in Appendix B. **Abbreviations Figure titles**: QALY: Quality of Life without treatment; LY: life years. **Abbreviations surgery/indication**: AAA: aneurysm of the abdominal aorta; AP: angina pectoris; ESRD: end-stage renal disease; ASD: atrial septum defect; ca.: carcinoma; CABG: coronary artery bypass graft; ESHF: end-stage heart failure; ESLD: end-stage liver disease; EVAR: endovascular aortic repair; HIPEC: hyperthermic intraperitoneal chemotherapy; HCC: hepatocellular carcinoma; NSCLC: non-small cell lung carcinoma; PAD: peripheral arterial disease; PCI: percutaneous coronary intervention; UUT: upper urinary track; VATS: video assisted thoracoscopic surgery; COPD: chronic obstructive pulmonary disease; PAD: peripheral arterial disease (F: Fontaine classification); AV: aortic valve; AVR: aortic valve replacement; MVR: mitral valve replacement; TAVI: transaortic valve implantation.

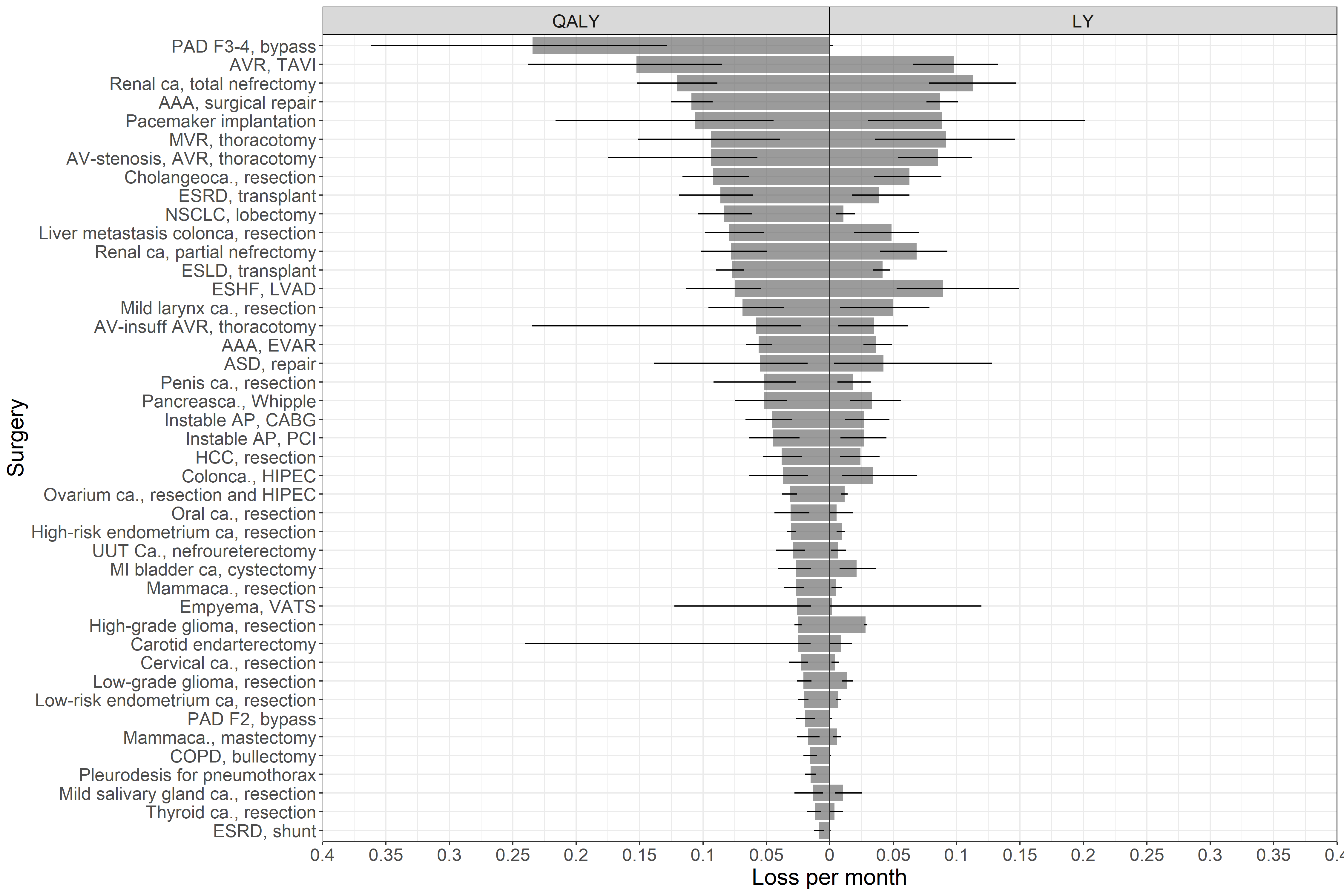


Figure 4, the average loss of QALYs and LYs per month of delay for the investigated surgeries based on the simulation of surgery delay of 52 weeks. The estimates (gray bars) and 95% confidence intervals (black lines) are shown. The actual data are presented in appendix B. **Abbreviations Figure titles**: QALY: Quality of Life without treatment; LY: life years **Disease abbreviations**: AAA: aneurysm of the abdominal aorta; AP: angina pectoris; ESRD: end-stage renal disease; ASD: atrial septum defect; ca.: carcinoma; CABG: coronary artery bypass graft; ESHF: end-stage heart failure; ESLD: end-stage liver disease; EVAR: endovascular aortic repair; HIPEC: hyperthermic intraperitoneal chemotherapy; HCC: hepatocellular carcinoma; NSCLC: non-small cell lung carcinoma; PAD: peripheral arterial disease; PCI: percutaneous coronary intervention; UUT: upper urinary track; VATS: video assisted thoracoscopic surgery; COPD: chronic obstructive pulmonary disease; PAD: peripheral arterial disease (F: Fontaine classification); AV: aortic valve; AVR: aortic valve replacement; MVR: mitral valve replacement; TAVI: transaortic valve implantation.

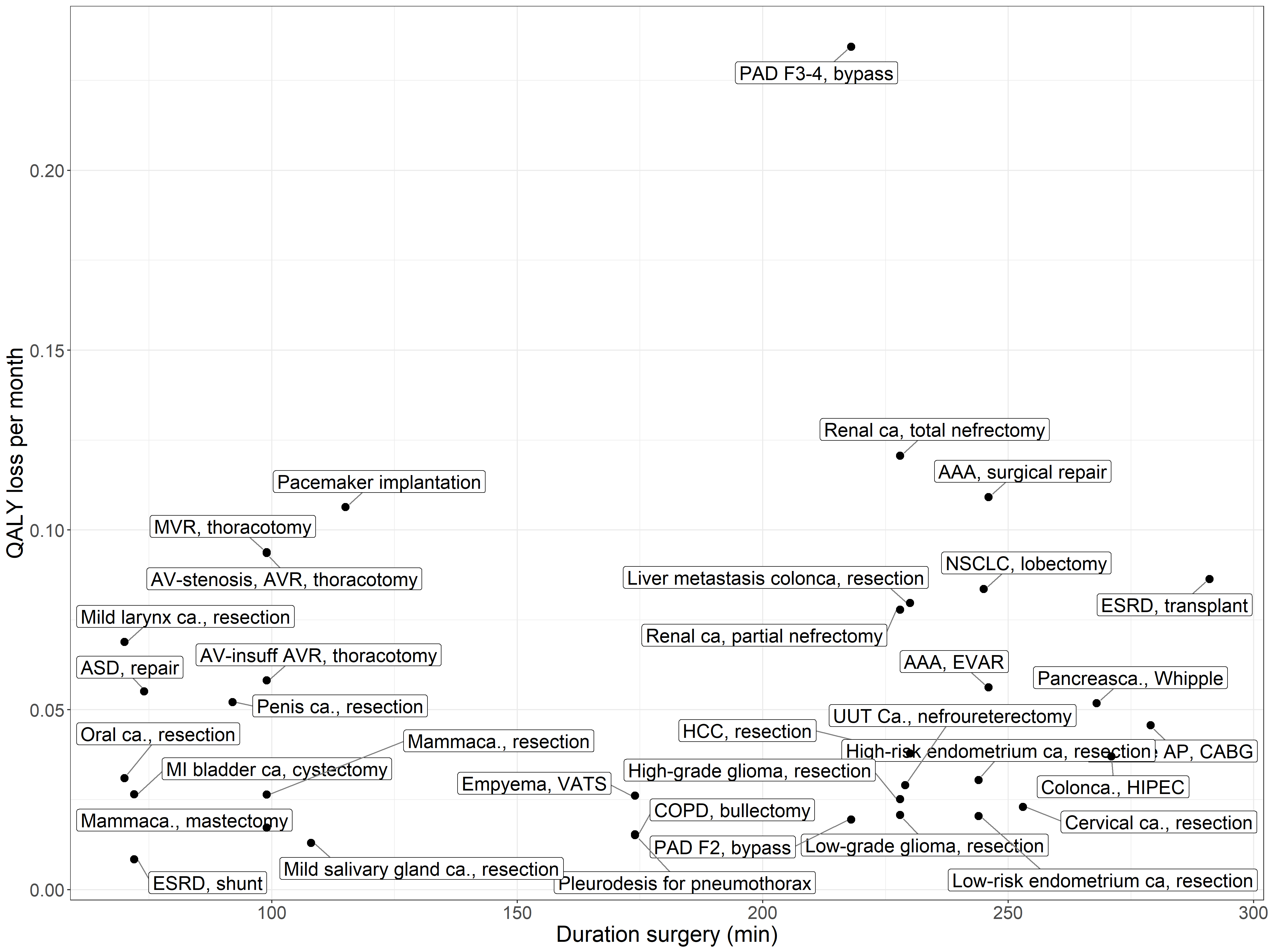


Figure 5, showing the mean duration of the surgeries and the urgency in terms of QALY loss per month. Liver transplant is excluded in this plot, because it was an outlier in terms of duration of surgeries (median: 875 minutes, IQR: 797-957 and -0.08 QALY per month, 95% CI: -0.09 - -0.07). **Abbreviations Figure titles**: QALY: Quality of Life without treatment. **Disease abbreviations**: AAA: aneurysm of the abdominal aorta; AP: angina pectoris; ESRD: end-stage renal disease; ASD: atrial septum defect; ca.: carcinoma; CABG: coronary artery bypass graft; ESHF: end-stage heart failure; ESLD: end-stage liver disease; EVAR: endovascular aortic repair; HIPEC: hyperthermic intraperitoneal chemotherapy; HCC: hepatocellular carcinoma; NSCLC: non-small cell lung carcinoma; PAD: peripheral arterial disease; PCI: percutaneous coronary intervention; UUT: upper urinary track; VATS: video assisted thoracoscopic surgery; COPD: chronic obstructive pulmonary disease; PAD: peripheral arterial disease (F: Fontaine classification); AV: aortic valve; AVR: aortic valve replacement; MVR: mitral valve replacement; TAVI: transaortic valve implantation.

Disclosures

No specific funds were rewarded for this project.

Isabel Retel Helmrich and Ernest van Veen are supported by the European Union 7th Framework program (Center-TBI, EC grant 602150). Eline Krijkamp is supported by the Society for Medical Decision Making (SMDM) fellowship through a grant by the Gordon and Betty Moore Foundation (GBMF7853).

Acknowledgement

We are grateful for Lisa Caulley for her revision of 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.

References

1. Office of the Assistant Secretary for Preparedness H. Pandemic Influenza Plan - Update IV (December 2017). 2017.

2. 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;1–7.

3. D’Agostino A, Demartini B, Cavallotti S, Gambini O. Mental health services in Italy during the COVID-19 outbreak. The Lancet Psychiatry. 2020;7(5):385–7.

4. 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. Heal. 2020;4(5):e10–1.

5. 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 Pandemic J Pediatr [Internet] 2020 [cited 2020 May 15];Available from: https://doi.org/10.1016/j.jpeds.2020.04.052.

6. NZA. Analyse van de gevolgen van de coronacrisis voor de reguliere zorg [Internet]. 2020 [cited 2020 May 17]. Available from: https://zorgdomein.com/media/documents/NZa-analyse\_van\_de\_gevolgen\_van\_de\_coronacrisis\_voor\_de\_reguliere\_zorg\_-....pdf

7. Dinmohamed AG, Visser O, Verhoeven RHA, et al. Fewer cancer diagnoses during the COVID-19 epidemic in the Netherlands. Lancet Oncol. 2020;0(0).

8. 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 [Internet] 2004;94(4):562–4. Available from: http://ajph.aphapublications.org/doi/10.2105/AJPH.94.4.562

9. 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;13:19.

10. 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;

11. Salenger R, Etchill EW, Ad N, et al. The Surge after the Surge: Cardiac Surgery post-COVID-19. Ann Thorac Surg [Internet] 2020 [cited 2020 Jun 15];Available from: https://linkinghub.elsevier.com/retrieve/pii/S0003497520306937

12. Vergano M, Bertolini G, Giannini A, et al. Clinical Ethics Recommendations for the Allocation of Intensive Care Treatments in exceptional, resource-limited circumstances [Internet]. 2020 [cited 2020 May 17]. Available from: http://www.siaarti.it/SiteAssets/News/COVID19 - documenti SIAARTI/SIAARTI - Covid-19 - Clinical Ethics Reccomendations.pdf

13. 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(4 Suppl):e145S-e155S.

14. Bayer R. Ethical Considerations for Decision Making Regarding Allocation of Mechanical Ventilators during a Severe Influenza Pandemic or Other Public Health Emergency. 2011.

15. York State Department of Health N. VENTILATOR ALLOCATION GUIDELINES New York State Task Force on Life and the Law New York State Department of Health. 2015.

16. Toner E, Waldhorn R. Responding to pandemic influenza - The ethical framework for policy and planning | Information | Health Service Journal [Internet]. 2020 [cited 2020 May 17];Available from: https://www.hsj.co.uk/swine-flu/responding-to-pandemic-influenza-the-ethical-framework-for-policy-and-planning/5005219.article

17. Garner RT, Rosen B. Moral Philosophy: A Systematic Introduction to Normative Ethics and Meta-Ethics. New York: Macmillan; 1967.

18. 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;1.

19. MacCormick AD, Parry BR. Judgment analysis of surgeons’ prioritization of patients for elective general surgery. Med Decis Making [Internet] 2006 [cited 2020 Mar 27];26(3):255–64. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16751324

20. Kankersoorten - IKNL [Internet]. [cited 2020 May 19];Available from: https://iknl.nl/kankersoorten

21. NHR [Internet]. [cited 2020 May 19];Available from: https://nederlandsehartregistratie.nl/

22. CBS. Sterftekansen naar leeftijd, geslacht, opleidingsniveau [Internet]. [cited 2020 May 19];Available from: https://www.cbs.nl/nl-nl/maatwerk/2017/23/sterftekansen-naar-leeftijd-geslacht-opleidingsniveau

23. Hunink M, Mc E, Glasziou P, Elstein A. Decision Making in Health and Medicine: Integrating Evidence and Values [Internet]. 2nd ed. Cambridge: Cambridge University Press; 2003 [cited 2020 May 19]. Available from: http://www.cambridge.org

24. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2016 (GBD 2016) Disability Weights. Seattle, United States: Institute for Health Metrics and Evaluation (IHME): 2017.

25. General Guidance for DALYs calculation [Internet]. [cited 2020 May 19]. Available from: https://montagu.vaccineimpact.org/contribution/resources/c978e5a1acf6a502679c92200e78ef61.pdf

26. Disability-adjusted life years (DALYs) [Internet]. [cited 2020 May 19];Available from: https://www.who.int/data/gho/indicator-metadata-registry/imr-details/158

27. 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 [Internet] 2000 [cited 2020 May 14];10(1):24–30. Available from: https://academic.oup.com/eurpub/article-abstract/10/1/24/490779

28. 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 Heal [Internet] 2012;15(6):812–20. Available from: http://eprints.gla.ac.uk/73437/

29. Sonnenberg FA, Beck JR. Markov Models in Medical Decision Making. Med Decis Mak [Internet] 1993 [cited 2018 Nov 15];13(4):322–38. Available from: http://journals.sagepub.com/doi/10.1177/0272989X9301300409

30. Klarman H, Rosenthal GD. Cost Effectiveness Analysis Applied to the Treatment of Chronic Renal Disease. Med Care [Internet] 1968 [cited 2020 May 11];6.1:48–54. Available from: https://www.jstor.org/stable/3762651?casa\_token=PBjn8CVNsEUAAAAA:Qz-0ARl86RMuto-iy4CfBlNhpHIEvFPKiQ5MyuBfuZOih82MBB5dYOsKO-P4wZX9\_J1Qh92HEUHDel6W2TO172lSHMIoHJx4KeMoP03NLSvVyss5wKaP&seq=7#metadata\_info\_tab\_contents

31. Torgerson DJ, Raftery J. Economic notes. Discounting. BMJ [Internet] 1999;319(7214):914–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10506056

32. Zorginstituut Nederland. Richtlijn voor het uitvoeren van economische evaluaties in de gezondheidszorg. 2016;

33. Zorginstituut Nederland. Richtlijn voor het uitvoeren van economische evaluaties in de gezondheidszorg. 2016.

34. Husereau D, Drummond M, Petrou S, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. Eur J Heal Econ 2013;

35. R Core Team. R: A language and Environment for Statistical Computing. 2013;

36. Alarid-Escudero F, Krijkamp EM, Enns EA, Hunink MGM, Pechlivanoglou P, Jalal H. Cohort state-transition models in R: From conceptualization to implementation. 2020 [cited 2020 May 19];Available from: http://arxiv.org/abs/2001.07824

37. 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(11):1329–39.

38. Salomon JA, Haagsma JA, Davis A, et al. Disability weights for the Global Burden of Disease 2013 study [Internet]. 2015 [cited 2020 May 14]. Available from: www.thelancet.com/lancetgh

39. Chen EY, Mayo SC, Sutton T, et al. Effect of Time to Surgery of Colorectal Liver Metastases on Survival. J Gastrointest Cancer 2020;

40. 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(8922):563–70.

41. 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(1):31–9.

42. 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. Surg (United States) 2018;164(2):219–26.

43. 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(4):468–75.

44. 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(1):100–8.

45. Moss AJ, Jackson Hall W, Cannom 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(26):1933–40.

46. 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(4):444–9.

47. Nyboe C, Karunanithi Z, Nielsen-Kudsk JE, Hjortdal VE. Long-term mortality in patients with atrial septal defect: a nationwide cohort-study. [cited 2020 May 19];Available from: https://academic.oup.com/eurheartj/article-abstract/39/12/993/4675086

48. 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(44):e17552.

49. Brewster DC, Jones JE, Chung TK, et al. Long-term outcomes after endovascular abdominal aortic aneurysm repair: The First Decade. Ann. Surg. 2006;244(3):426–36.

50. 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(1):88–95.

51. 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(20):1435–43.

52. 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(2):105-113.e2.

53. 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;134:44–9.

54. 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(45):79876–83.

55. Shalowitz DI, Epstein AJ, Ko EM, Giuntoli RL. Non-surgical management of ovarian cancer: Prevalence and implications. Gynecol Oncol 2016;142(1):30–7.

56. 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 Oto-Rhino-Laryngology 2018;275(8):2071–7.

57. Kim WR, Lake JR, Smith JM, et al. OPTN/SRTR 2016 Annual Data Report: Liver. Am J Transplant 2018;18:172–253.

58. 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(2):251–8.

59. 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(9):2426–32.

60. Holtzman A, Morris CG, Amdur RJ, Dziegielewski PT, Boyce B, Mendenhall WM. Outcomes after primary or adjuvant radiotherapy for salivary gland carcinoma. Acta Oncol (Madr) 2017;56(3):484–9.

61. Murphy MM, Simons JP, Hill JS, et al. Pancreatic resection: A key component to reducing racial disparities in pancreatic adenocarcinoma. Cancer 2009;115(17):3979–90.

62. Mikkola R, Kelahaara J, Heikkinen J, Lahtinen J, Biancari F. Poor late survival after surgical treatment of pleural empyema. World J Surg 2010;34(2):266–71.

63. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet [Internet] 2003 [cited 2020 May 19];361(9351):13–20. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673603121137

64. Piehler JM, Crichlow RW. Primary Carcinoma of the Gallbladder. Arch Surg 1977;112(1):26–30.

65. 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(12).

66. 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(9113):1379–87.

67. 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(11):3141–9.

68. Ginsberg RJ, Rubinstein L V. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Ann Thorac Surg 1995;60(3):615–23.

69. Redden MD, Chin TY, van Driel ML. Surgical versus non-surgical management for pleural empyema. Cochrane Database Syst. Rev. 2017;2017(3).

70. 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(8):469–73.

71. Sørensen VR, Heaf J, Wehberg S, Sørensen SS. Survival Benefit in Renal Transplantation Despite High Comorbidity. Transplantation 2016;100(10):2160–7.

72. 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(3):268.e1-268.e18.

73. 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 [Internet] 2014 [cited 2020 May 19];50(4):282–90. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24405882

74. Stewart JM, Tone AA, Jiang H, et al. The optimal time for surgery in women with serous ovarian cancer. Can J Surg 2016;59(4):223–32.

75. Davies L, Welch G. Thyroid cancer survival in the United States: Observational data from 1973 to 2005. Arch Otolaryngol - Head Neck Surg 2010;136(5):440–4.

76. Bleicher RJ, Ruth K, Sigurdson ER, et al. Time to surgery and breast cancer survival in the United States. JAMA Oncol 2016;2(3):330–9.

77. Morse E, Fujiwara RJT, Judson B, Mehra S. Treatment Times in Salivary Gland Cancer: National Patterns and Association with Survival. Otolaryngol - Head Neck Surg (United States) 2018;159(2):283–92.

78. USRDS [Internet]. [cited 2020 May 19];Available from: https://www.usrds.org/2015/view/

79. Kirkegård J, Mortensen FV, Hansen CP, Mortensen MB, Sall M, Fristrup C. Waiting time to surgery and pancreatic cancer survival: A nationwide population-based cohort study. Eur J Surg Oncol 2019;45(10):1901–5.

80. 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(1):224–9.

81. 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(4):358–65.

82. Organ Procurement and Transplantation Network [Internet]. [cited 2020 May 19];Available from: https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/

83. 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 [Internet] 2015 [cited 2020 Jun 17];132(19):1805–15. Available from: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.115.016424

84. Bonow RO, Greenland P. Population-wide trends in aortic stenosis incidence and outcomes. Circulation. 2015;131(11):969–71.

85. 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(10):1471–7.

86. 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(4):1262–7.

87. 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 Investig 2020;38(3):74.e13-74.e20.

88. Janssen MWW, 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(5).

89. Jakola AS, Myrmel KS, Kloster R, et al. Comparison of a strategy favoring early surgical resection vs a strategy favoring watchful waiting in low-grade gliomas. JAMA - J Am Med Assoc 2012;308(18):1881–8.

90. Haruna A, Muro S, Nakano Y, et al. CT scan findings of emphysema predict mortality in COPD. Chest 2010;138(3):635–40.

91. 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 2014;16(5):469–74.

92. 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(8):2468–76.

93. Petrides GA, Subramaniam N, Pham M, et al. Reducing the morbidity of parotidectomy for benign pathology. 2020;

94. 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;20:417–35.

95. Kennedy-Martin M, Slaap B, Herdman M, et al. Which multi-attribute utility instruments are recommended for use in cost-utility analysis? A review of national health technology assessment (HTA) guidelines. Eur J Heal Econ 2020;1–13.

96. Pettitt D, Raza S, Naughton B, et al. The Limitations of QALY: A Literature Review. J Stem Cell Res Ther 2016;6(4).

97. Elliott JH, Synnot A, Turner T, et al. Living systematic review: 1. Introductiondthe why, what, when, and how on behalf of the Living Systematic Review Network. [cited 2020 Jun 15];Available from: http://dx.doi.org/10.1016/j.jclinepi.2017.08.010

## Appendix A

An overview per disease of the distribution and source of the input parameters and a graphical representation of the output of the model.

## Appendix B

A summary of the estimates of the decision model and an overview of the counts, duration, and length of stay of the included surgeries in our hospital.

## Appendix C

Detailed model description

## Appendix D

Calibrated visual analogue scale based on the Global burden of disease study and description of expert panel that participated.

## Appendix E

Formulas to convert survival data into risk per week.