Prediction of 90-day mortality after Total Hip Arthroplasty: a simplified and externally validated model based on observational registry data from Sweden, England and Wales

Anne Garland\*1,2,3, Erik Bulow\*2,4, Erik Lenguerrand5, Ashley Blom5,6, J. Mark Wilkinson7, Adrian Sayers5, Ola Rolfson2,4, Nils P. Hailer1,2

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\* Authors contributed equally.

## Affiliations

1. Department of Orthopaedics, Institute of Surgical Sciences, Uppsala University Hospital, Uppsala, Sweden (postal: Akademiska sjukhuset, ingång 61, 6 tr, SE-751 85 Uppsala, Sweden)
2. The Swedish Hip Arthroplasty Register, Gothenburg, Sweden (postal: Registercentrum Västra Götaland, SE-413 45 Gothenburg, Sweden)
3. Department of Orthopaedics, Visby Hospital, Visby, Sweden (postal: S:t Göransgatan 5, SE-621 55 Visby, Sweden)
4. Department of Orthopaedics, Institute of Clinical Sciences, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden (postal: Avdelningen för ortopedi, Mölndals sjukhus, Göteborgsvägen 31, SE-431 80 Mölndal, Sweden)
5. Translational Health Sciences, Bristol Medical School, University of Bristol, UK (postal: Bristol Medical School, University of Bristol, First Floor, 5 Tyndall Avenue Bristol, BS8 1UD, United Kingdom).
6. The National Institute of Health Research Biomedical Research Centre Bristol (postal: NIHR Biomedical Research Centre Bristol, University Hospitals Bristol and Weston NHS Foundation Trust, University of Bristol, Oakfield House, Oakfield Grove, Bristol BS8 2BN, United Kingdom)
7. Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK. (postal: The Medical School, The University of Sheffield, Beech Hill Road, Sheffield, S10 2RX, UNited Kingdom)

## Correspondence

Erik Bulow. + 46 70 08 234 28. [erik.bulow@vgregion.se](mailto:erik.bulow@vgregion.se). Postal: Svenska Hoftprotesregistret, Registercentrum Vastra Gotaland, SE-413 45 Gothenburg, SWEDEN

## Titles

**AG:** MD, PhD, orthopaedic surgeon  
**EB:** MSc (PhD after 2020-09-18), statistician  
**EL:** PhD, statistician, Senior Research Fellow  
**AB:** MB, ChB, FRCS, MD, PhD, Head of Bristol Medical School, Professor of Orthopaedic Surgery, orthopaedic surgeon  
**MJW:** MB, ChB, PhD, FRCS, professor of orthopaedics, orthopaedic surgeon  
**AS:** MSc, statistician, senior research fellow  
**OR:** MD, PhD, orthopaedic surgeon, professor of orthopaedics, head of department, registry director of the Swedish Hip Arthroplasty Register  
**NPH:** MD, PhD, orthopaedic surgeon, professor of orthopaedics, research leader

# Contribution of authors

AG and NPH initiated the study and managed the ethical review board application in Sweden. AB and JMW conceptualized the external validation and managed the ethical review board application in the UK. EB developed the statistical model. EL and AS performed external validation with data from NJR. AG and EB drafted, and all authors edited and finalized the manuscript.

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# Abstract

**Aims:**  To develop and externally validate a parsimonious statistical prediction model of 90-day mortality after elective Total Hip Arthroplasty (THA), and to provide a web-calculator for clinical usage.

**Patients and methods:**  We included 53,099 patients with cemented THA due to osteoarthritis from the Swedish Hip Arthroplasty Register for model derivation and internal validation, as well as 125,428 patients from the National Joint Register from England and Wales for external model validation. A model was developed using a bootstrap ranking procedure with a least absolute shrinkage and selection operator (LASSO) logistic regression model combined with piecewise linear regression. Discriminative ability was evaluated by the area under the receiver operating characteristics curve (AUC). Calibration belt plots were used for model calibration.

**Results:**  A main effects model combining age, sex, American Society for Anesthesiologists (ASA) class, the presence of cancer, diseases of the central nervous system, kidney disease, and obesity had good discrimination, both internally (AUC = 0.78, 95 % CI 0.75 - 0.81) and externally (AUC = 0.75, 95 % CI 0.73 - 0.76). This model was superior to traditional models based on the Charlson (AUC = 0.66, 95 % CI 0.62 - 0.70) and Elixhauser (AUC = 0.64, 95 % CI 0.59 - 0.68) co-morbidity indices. The model was well calibrated for predicted probabilities up to 5%.

**Concusion:**  We developed a parsimonious model which may facilitate individualized risk assessment prior to one of the most common surgical interventions. We published a web-calculator to aid clinical decision-making (<https://shpr.registercentrum.se/om-registret-1/forskning/prediktion-av-90-dagarsmortalitet/p/SkyeTsTFB>).

**Clinical relevance:**

* We developed a parsimonious model for risk assessment of 90-day mortality after elective THA.
* The model considers age, sex, ASA class, the presence of cancer, diseases of the central nervous system, kidney disease, and obesity.
* We published an on-line web-calculator (<https://shpr.registercentrum.se/om-registret-1/forskning/prediktion-av-90-dagarsmortalitet/p/SkyeTsTFB>).

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# Introduction

Shared decision making has evolved into an integral part of patient-physician interactions prior to surgical interventions, and the weighing of risks against benefits is central to this process. 90-day mortality after THA performed due to osteoarthritis is low, ranging from 0.2 % to 0.6 %.1 The risk of short-term mortality is nevertheless an essential part of preoperative discussions between patients and surgeons.

Co-morbidity is associated with a shorter remaining life span, but the Charlson and Elixhauser co-morbidity indices poorly predict mortality after THA.1,2,2–5 Additionally, these complex co-morbidity instruments are based on information from extensive in- or out-patient databases, each measure being defined by 1,178 and 1,516 individual International Classification of Diseases (ICD)-10 codes, respectively. The use of these indices is therefore limited to research settings.

Pre-operative co-morbidity data have been used for prediction models of early mortality and adverse events such as surgical site infection, in the context of THA surgery.6–12 The first prediction model based on a European cohort was developed in the UK (<https://jointcalc.shef.ac.uk/>). However, it remains unclear to what level the depth of co-morbidity characterization influences the accuracy of mortality prediction models.

We aimed to develop a parsimonious prediction model of 90-day mortality after THA with internal and external validation of discrimination and calibration, and to compare this to the accuracy of prediction models based on existing co-morbidity measures.13

# Participants and Methods

We used data from the Swedish Hip Arthroplasty Register (SHAR) for model derivation and internal validation. The model was then validated externally on patients from England and Wales recorded in the National Joint Registry for England, Wales, Northern Ireland, the Isle of Man and the States of Guernsey (NJR). We focused on patients with cemented THA due to osteoarthritis. Cementation is the most common fixation technique used in Sweden, thus used as inclusion criteria to decrease heterogeneity. Only the last operated hip was accounted for in patients with bilateral THA (Figure 1).14

## Derivation cohort (Sweden)

The inclusion period started 2008 since the American Society for Anesthesiologists (ASA) class and Body Mass Index (BMI) were systematically recorded in SHAR from then on. The observation period ended 2015, since we had access to co-morbidity from the national patient register up to this point. Deterministic data linkage was performed by 10-digit identity numbers, assigned to all Swedish residents at birth or immigration. The data linkage has been described previously.15 Age, sex, BMI, ASA class, type of hospital and year of surgery were collected from the SHAR, with a completeness of 96-98 %.16 Data on educational level were recorded for more than 98 % of the population with 85 % accuracy in the longitudinal integration database for health insurance and labor market studies (LISA) from Statistics Sweden.17 Civil status, were also collected from LISA and co-morbidity during the year preceding index surgery from the National Patient Register (NPR). NPR contains diagnoses coded by ICD-10 from in- and outpatient episodes in all private and public hospitals. Completeness for NPR is above 99 % and 85-95 % of all diagnostic codes are valid.18 Death dates were linked from the national population register.

Patients with missing information on BMI or a measurement above 50 were excluded, as were patients with missing information on ASA class or class IV and above, as well as patients with unknown educational level or type of hospital. 53,099 patients (mean age 72.68 years, range 35 - 99 and 61 % females) were included (Figure 1).

## External validation cohort (England and Wales)

Similar inclusion criteria were applied to the validation cohort. We excluded no patients based on missing information on BMI, educational level, or civil status however, since those variables were not used in the final model. 125,428 patients were included (Figure 2). NJR data was linked to the secondary uses service database from the National Health Service (NHS) with co-morbidity from the hospital episode statistics (HES) database in England, and the patient episode database for Wales.19 Out-patient deaths were linked from the office of national statistics based on NHS-numbers, as well as patient name, age, sex and address.20

## Defining co-morbidity

Co-morbidity was defined by individual ICD-10 codes grouped into 17 categories by Charlson and 31 by Elixhauser.21 Some conditions were identified by both indices, and some were closely related and therefore merged (such as hypertension with and without complications, or abuse of either drugs or alcohol). We combined individual diagnostic groups to establish 21 broader categories of co-morbidity (Table 1).

## Statistical analysis for model development

We used Kaplan–Meier and a procedure with bootstrap ranking and a logistic least absolute shrinkage and selection operator (LASSO).22 Age and BMI were normalized to have mean = 0 and standard deviation = 1. Co-morbidities recorded for at least one patient who died within 90 days, and one who did not, were included in the modelling process. 1,000 bootstrap samples were drawn from the observed data set. We used 10-fold cross validation for every bootstrap sample with a range of potential penalty values (:s) in a logistic LASSO model. We kept :s minimizing the mean cross-validated deviances and those were used to estimate model coefficients for each potential predictor. The magnitude (absolute values) of those estimates were used as a measure of variable importance. Piece-wise linear regression was used to detect a breaking point where a significant drop in variable importance was observed. Potential predictors with variable importance above this breaking point were kept as model candidates. The whole process was repeated 100 times. Covariates that were selected at least once were used in a main effects model of multivariable logistic regression without penalty, and without pre-normalization of numeric variables (main model). A reduced model with variables chosen at least 33 out of the 100 times were used as a simpler alternative. This model was also evaluated without cancer as a predictor, considering that medical indications for THA surgery may be different for patients with cancer or without cancer. Univariable models with the ASA class, Charlson or Elixhauser co-morbidity indices were used for benchmarking, as well as a model including only age and sex. Each model including age was fitted three times, once with age as a main effect and twice with restricted cubic splines, either by two or three knots. Odds ratios for the final model were estimated with 95 % confidence intervals and -values below 0.05 were considered statistically significant.

## Statistical analysis for model validation

Each model was used to predict the probability of death within 90 days for patients from the SHAR (internal validation). Receiver operating characteristic (ROC) curves were drawn and the area under those curves (AUC) were used as a measure of discriminative ability. Models with a lower bootstrap-based 95 % confidence limit above 0.7, were considered good. We used the bias-corrected Somers’ rank correlation based on 100 resamples to adjust for optimism.23 Calibration bands were made to graphically assess model calibration, comparing predicted probabilities and observed proportions.24 The reduced model was then evaluated externally. An AUC with 95 % CI was calculated for the model as-is. Re-calibration of the model intercept was then performed to account for different mortality rates in Sweden compared to England and Wales. An updated over-all slope was also calculated to account for country-specific treatment differences.25

## Statistical tools

We built an online web calculator (<https://shpr.registercentrum.se/om-registret-1/forskning/prediktion-av-90-dagarsmortalitet/p/SkyeTsTFB>) to be used in clinical practice.

We used R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria) with significant packages tidyverse, tidymodels, furrr, pROC and shiny. All R-scripts and necessary configurations (but no personal data) is available at <http://doi.org/10.5281/zenodo.3732852>. A linked Binder environment is also available for interactive usage.

## Ethical approval

Ethical approval for this study was obtained from the Regional Ethical Review Board in Gothenburg (360-13) and by the NJR in the UK (RSC2017/21). Informed consent was not mandatory according to the Swedish patient data law from 2009, and the UK law for pseudonymised data.

# Results

## Study participants

175 (0.33 %) of the patients from SHAR died within 90 days (0.33 % (95 % CI 0.28 - 0.38) according to Kaplan–Meier) and no one was censored before that. Patients from NJR had an unadjusted risk of 90 day mortality of 0.52 % (95 % CI 0.49 - 0.56). Further cohort characteristics are presented in Table 2.

## Model development and internal validation

There were five co-morbidities not recorded for any patient who died in the Swedish derivation cohort and therefore not considered as potential predictors: acquired immunodeficiency syndrome by the human immunodeficiency virus (AIDS/HIV), coagulopathy, fluid electrolyte disorders, liver disease, and weight loss. The derived main model included age, sex, ASA class, the presence of cancer, diseases of the central nervous system, kidney disease, diagnosed obesity, heart condition, anemia, and myocardial infarction. The reduced model was restricted to age, sex, ASA class, the presence of cancer, diseases of the central nervous system, kidney disease, and diagnosed obesity (Table 3).

There were no differences between models including age as a main effect or as restricted cubic splines. We therefore focused on the more parsimonious models with age as a main effect. Similarly, the correction for optimism only affected the third decimals of the AUC confidence intervals and was therefore omitted.

The main and reduced models were no different regarding discriminative ability (AUC = 0.79, 95 % CI 0.75 - 0.82 versus AUC = 0.78, 95 % CI 0.75 - 0.81). We therefore considered the reduced model as superior due to its simplicity. Traditional models performed poorly with 95 % confidence intervals not above 0.7: The Charlson co-morbitiy index had an AUC of (AUC = 0.66, 95 % CI 0.62 - 0.70) and the Elixhauser co-morbidity an AUC of (AUC = 0.64, 95 % CI 0.59 - 0.68; Figure 4 and Figure 5).

The ability of the reduced model to estimate probabilities of death within 90 days is further illustrated in Figure 6 and 7. Model calibration was good for estimated probabilities up to 3 % and acceptable up to 5 % (Figure 8). Estimated model coefficients and corresponding odds ratios for the reduced model are presented in Table 4. Omitting cancer from the reduced model did not affect the AUC or calibration for estimated probabilities below 3 %, but calibration outside this range deteriorated, and we thus retained cancer as an important predictor.

## External validation

The discriminative ability for the reduced model was not statistically significantly different when applied to the external validation cohort (AUC = 0.75, 95 % CI 0.73 - 0.76) compared to the internal validation (AUC = 0.78, 95 % CI 0.75 - 0.81) (Figure 4 and Figure 5). Calibration of the re-calibrated model was slightly inferior compared to the internal calibration. Predicted probabilities between 0.5 % and 1.5 % were lower than observed proportions and the estimated 95 % confidence bands were wider. Over-all, calibration was good for predicted probabilities below 3 % and acceptable below 5 % (Figure 8).

# Discussion

We found that a multivariable main effects logistic regression model with age, sex, ASA class, the presence of cancer, diseases of the central nervous system, kidney disease, and diagnosed obesity was better at predicting death within 90 days after THA than traditional models based on the Charlson or Elixhauser co-morbidity indices. The resulting model predicted the probability of death within 90 days as: where is the vector of estimated coefficients (including intercept) presented in table 4. This formula is considered valid for patients aged 35–99 years and for predicted probabilities up to 5 %.

## Clinical usage

Our model could be used in clinical practice, either by the formula, or by the web calculator (<https://shpr.registercentrum.se/om-registret-1/forskning/prediktion-av-90-dagarsmortalitet/p/SkyeTsTFB>). A 35-year-old woman with ASA class I and none of the important co-morbidities would have a 0.028 ‰ risk to die within 90 days of surgery. A woman, 67 years old, would have an elevated risk of 0.37 ‰. A 99-year-old man with ASA class III and cancer, would have a risk of 8.8 %. Note, however, that covariate patterns with observed probabilities above 5 % were rare (0.13 %, n = 70). Risks above 5 % are therefore subject to extrapolation. The true proportions are likely lower (as indicated by Figure 8). Some risk calculators ignore this problem,6,12 but we think this should be acknowledged.

Variables in our model were chosen based on statistical properties and should therefore not be assigned any exact epidemiological and/or causal meaning per se. Nevertheless, age and sex are well-known predictors of remaining life span.~~26,27~~ ASA class III has the largest estimated coefficient among all predictors, indicating large relative importance. This is clinically reasonable since a label of “severe systemic disease” should be based on a relevant patient assessment prior to surgery.

Obesity was not statistically significant ( 0.05) but was still relevant as a predictor due to unobserved heterogeneity. We noted that the proportion of patients in the SHAR with BMI above 30, the WHO definition of obesity, was much higher (23 %, n = 12,336) than the proportion of patients with a diagnosis code for obesity (ICD-10 = E66) recorded in the NPR (1.9 %, n = 1,000). BMI is systematically recorded in the SHAR, but the diagnosis of obesity might not have been made during previous contacts with the healthcare system.

## Strengths and limitations

The nationwide design with data from both Sweden, England and Wales is a strength. The Swedish registers are valid with low proportions of missing data.16,18 Some concerns have been raised regarding the HES database from UK, but a systematic review found that the overall median diagnostic accuracy (comparing ICD-codes to individual case notes) was 80 %.28 Both in- and outpatient co-morbidity data were available for Sweden, but only in-patient data for England and Wales. The linkage between NJR and HES has been previously described,29 where it was noted that privately funded patients were not included in HES. 17 % of the patients had missing personal data or did not allow linkage, and 6 % were not found in HES although their data were available from the NJR.

The indications for different fixation techniques differ between the cohorts. Cementation is commonly used in Sweden but not so in England and Wales, where younger patients are more likely to be operated with cementless implants. To only include cemented THA therefore implies an over-representation of older and frailer patients from England and Wales. Those patients might be more likely to die within 90 days, and this assumption would be in agreement with the calibration plot where estimated probabilities below 1.5 % underestimated the observed proportion of deaths in the external validation cohort.

We investigated whether the effect of age on mortality was non-linear using restricted cubic splines. A similar approach might be relevant for BMI. A U-shaped association between mortality and BMI categorized as underweight (below 18.5 kg/m2), normal (18.5 to 25 kg/m2), or obese (above 25 kg/m2) has been reported.30 Our recordings of BMI might be imprecise however. Some hospitals report actual measurements but it is unknown to what extent those data are self-estimated by the patients or by health care personnel. Therefore, we aimed to avoid overfitting BMI based on too elaborate transformations.

It should be noted that the risk model does not study THA as an observed intervention. We merely followed the cohort who already had THA. Deaths within 90 days might occur for those patients regardless if THA is inserted or not. The proximity in time however, the maximum of 90 days from THA to death, is an indication that the operation might be the main cause of death for the majority of deceased patients.

## Conclusion

Our results indicate that the risk of early postoperative mortality after cemented THA can be pre-operatively assessed by a parsimonious prediction model. We hope that this model, with its accompanying web calculator, will facilitate shared decision-making.

# Acknowledgement

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Figure 1: Flowchart depicting inclusion criteria and number of patients from the Swedish derivation cohort.



Figure 2: Flowchart depicting inclusion criteria and number of patients for the external validation cohort from England and Wales.



Figure 3: Receiver Operation Characteristics (ROC) curves. The area under the ROC curve (AUC) for the reduced model derived on data from the SHAR was very similar to the main model



Figure 4: Receiver Operation Characteristics (ROC) curves. There was no difference when applying the reduced model to the external validation cohort from England and Wales ,compared to the Swedish derivation cohort.



Figure 5: Area Under the Receiver Operation Characteristics Curve (AUC) as a measure of predictive discriminative ability with 95 % bootstrap confidence intervals. AUC above 0.7 were considered good. The reduced model was similar to the main model, and not statistically significantly inferior when used with external data from the NJR.



Figure 6: The vast majority of patients survived more than 90 days after THA, and therefore the blue bars dominate the histogram (note the scales). There were very few observations with covariate patterns resulting in death probabilities higher than 5 % (green line). Estimated probabilities above this limit are therefore subject to extrapolation.



Figure 7: A normalized density plot reveals that patients who died within 90 days were, on average, estimated to have a higher probability to do so. There were very few observations with covariate patterns resulting in death probabilities higher than 5 % (green line). Estimated probabilities above this limit are therefore subject to extrapolation.



Figure 8: This figure illustrates calibration between observed proportions and predicted probabilities with 95 % confidence intervals. Deviations above the diagonal line indicated that the model under-estimated the probability of death within 90 days. Such deviation was statistically significant for the external validation for predictions below 1.5 %. In contrast, with higher predicted probabilities, the model over-estimated the observed proportions of deaths.

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Table 1: Categorization of co-morbidities based on diagnostic groups according to Charlson and Elixhauser. (CNS = central nervous system.)

|  |  |  |
| --- | --- | --- |
| Comorbidities by groups | Charlson | Elixhauser |
| AIDS/HIV | AIDS/HIV | AIDS/HIV |
| Anemia |  | Blood loss anemia, Deficiency anemia |
| Arrhythmia |  | Cardiac arrhythmias |
| Arterial hypertension |  | Hypertension uncomplicated, Hypertension complicated |
| Cancer | Malignancy, Metastatic solid tumor | Lymphoma, Metastatic cancer, Solid tumor |
| CNS disease | Dementia, Hemiplegia or paraplegia | Depression, Paralysis, Other neurological disorders, Psychoses |
| Coagulopathy |  | Coagulopathy |
| Diabetes | Diabetes without complication, Diabetes complication | Diabetes uncomplicated, Diabetes complicated |
| Drug alcohol abuse |  | Alcohol abuse, Drug abuse |
| Fluid electrolyte disorders |  | Fluid electrolyte disorders |
| Heart condition | Congestive heart failure | Congestive heart failure, Valvular disease |
| Myocardial infarction | Myocardial infarction |  |
| Hypothyroidism |  | Hypothyroidism |
| Kidney disease | Renal disease | Renal failure |
| Liver disease | Mild liver disease, Moderate or severe liver disease | Liver disease |
| Lung airways disease | Chronic pulmonary disease | Chronic pulmonary disease, Pulmonary circulation disorder |
| Obesity |  | Obesity |
| Peptic ulcer | Peptic ulcer disease | Peptic ulcer disease |
| Rheumatic disease | Rheumatic disease | Rheumatoid arthritis |
| Vascular disease | Peripheral vascular disease, Cerebrovascular disease | Peripheral vascular disorder |
| Weight loss |  | Weight loss |

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Table 2: Characteristics of the study population in the model derivation cohort (SHAR) and external validation cohort (NJR). Educational levels were classified as low (up to 9 years), middle (10-12 years) and high (at least 12 years). BMI = Body mass index. ASA = American Society for Anesthesiologists classification. CNS = central nervous system.

|  |  |  |  |
| --- | --- | --- | --- |
| what | level | SHAR | NJR |
| n |  | 53,099 | 125,428 |
| Age (mean (SD)) |  | 72.68 (7.76) | 73.51 (8.67) |
| Sex = Female (%) |  | 32,440 (61.1) | 82,247 (65.6) |
| BMI (mean (SD)) |  | 27.19 (4.39) |  |
| ASA class (%) |  |  |  |
|  | I | 9,589 (18.1) | 10,890 (8.7) |
|  | II | 33,881 (63.8) | 89,388 (71.3) |
|  | III | 9,629 (18.1) | 25,150 (20.05) |
| Hospital (%) |  |  |  |
|  | University | 24,460 (46.1) |  |
|  | County | 16,507 (31.1) |  |
|  | Rural | 9,940 (18.7) |  |
|  | Private | 2,192 ( 4.1) |  |
| Education (%) |  |  |  |
|  | Low | 11,645 (21.9) |  |
|  | Middle | 20,604 (38.8) |  |
|  | High | 20,850 (39.3) |  |
| Civil status (%) |  |  |  |
|  | Married | 29,436 (55.4) |  |
|  | Single | 12,888 (24.3) |  |
|  | Widow/widower | 10,775 (20.3) |  |
| Charlson (%) |  |  |  |
|  | 0 | 39,256 (73.9) | 80,236 (64.0) |
|  | 1 | 8,117 (15.3) | 33,447 (26.7) |
|  | 2 | 3,762 ( 7.1) | 9,049 (7.2) |
|  | 3 | 1,176 ( 2.2) | 2,116 (1.7) |
|  | 4+ | 788 ( 1.5) | 580 (0.5) |
| Elixhauser (%) |  |  |  |
|  | 0 | 27,773 (52.3) | 33,546 (26.8) |
|  | 1 | 13,766 (25.9) | 42,467 (33.9) |
|  | 2 | 7,239 (13.6) | 28,188 (22.5) |
|  | 3+ | 4,321 ( 8.1) | 21,227 (16.9) |
| AIDS/HIV (%) |  | 5 ( 0.0) | 0 |
| Anemia (%) |  | 416 ( 0.8) | 2,306 (1.8) |
| Arrhythmia (%) |  | 4,505 ( 8.5) | 13,040 (10.4) |
| Arterial hypertension (%) |  | 16,677 (31.4) | 66,837 (53.3) |
| Cancer (%) |  | 2,715 ( 5.1) | 3,055 (2.4) |
| CNS disease (%) |  | 1,682 ( 3.2) | 7,075 (5.6) |
| Coagulopathy (%) |  | 192 ( 0.4) | 583 (0.5) |
| Diabetes (%) |  | 4,077 ( 7.7) | 13,874 (11.1) |
| Drug alcohol abuse (%) |  | 223 ( 0.4) | 2,057 (1.6) |
| Fluid electrolyte disorders (%) |  | 304 ( 0.6) | 2,774 (2.2) |
| Heart condition (%) |  | 2,639 ( 5.0) | 5,746 (4.6) |
| Myocardial infarction (%) |  | 2,186 ( 4.1) | 3,774 (3.0) |
| Hypothyroidism (%) |  | 1,791 ( 3.4) | 10,453 (8.3) |
| Kidney disease (%) |  | 551 ( 1.0) | 7,370 (5.9) |
| Liver disease (%) |  | 207 ( 0.4) | 630 (0.5) |
| Lung airways disease (%) |  | 2,878 ( 5.4) | 18,337 (14.6) |
| Obesity (%) |  | 1,000 ( 1.9) | 10,380 (8.3) |
| Peptic ulcer (%) |  | 341 ( 0.6) | 685 (0.6) |
| Rheumatic disease (%) |  | 1,922 ( 3.6) | 5,956 (4.8) |
| Vascular disease (%) |  | 1,686 ( 3.2) | 3,656 (2.9) |
| Weight loss (%) |  | 35 ( 0.1) | 509 (0.4) |

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Table 3: Variables selected by the bootstrap ranking procedure, and therefore kept in the main model. Variables chosen at least 33 times out of 100 were kept in the reduced model as well. ASA class II and III were kept in both models, since those are usually distinguished anyway. To simplify the models further would be possible by lumping class I and II together. Variables chosen more frequently are likely more important predictors. This is not necessarily true however since one of several strongly correlated variables might be chosen spuriously. (CNS = central nervous system.)

|  |  |
| --- | --- |
| variable | n |
| Cancer | 100 |
| CNS disease | 100 |
| Kidney disease | 100 |
| ASA class III | 100 |
| Age | 50 |
| Obesity | 49 |
| Male sex | 38 |
| Heart condition | 20 |
| Anemia | 9 |
| ASA class II | 8 |
| Myocardial infarction | 6 |

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Table 4: Estimated coefficients (beta) and odds ratios (OR) with 95 % confidence intervals for the reduced model.

|  |  |  |  |
| --- | --- | --- | --- |
| term | beta | OR 95 % CI | p |
| (intercept) | -13.28 |  |  |
| Cancer | 0.71 | 2.04 (1.30-3.08) | <0.01 |
| CNS disease | 0.90 | 2.45 (1.35-4.11) | <0.01 |
| Kidney disease | 1.33 | 3.79 (2.04-6.52) | <0.01 |
| ASA class II | 0.88 | 2.42 (1.20-5.78) | 0.03 |
| ASA class III | 1.66 | 5.27 (2.56-12.77) | <0.01 |
| Age | 0.08 | 1.08 (1.06-1.11) | <0.01 |
| Obesity | 0.77 | 2.17 (0.91-4.36) | 0.05 |
| Male sex | 0.61 | 1.85 (1.36-2.52) | <0.01 |

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