Appendix 1: List of definitions of complications used by NSQIP (Source: https://www.facs.org/~/media/files/quality%20programs/nsqip/ug12.ashx)

1. Superficial Incisional Superficial Surgical Site Infection

   Superficial incisional SSI is an infection that occurs within 30 days after the operation and the infection involves only skin or subcutaneous tissue of the incision and at least one of the following: -Purulent drainage, with or without laboratory confirmation, from the superficial incision. -Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision. -At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat AND superficial incision is deliberately opened by the surgeon, unless incision is culture-negative. -Diagnosis of superficial incisional SSI by the surgeon or attending physician. Do not report the following conditions as SSI: -Stitch abscess (minimal inflammation and discharge confined to the points of suture penetration). -Infected burn wound. -Incisional SSI that extends into the fascial and muscle layers (see deep incisional SSI).

2. Deep Incisional Superficial Surgical Site Infection

   Deep Incision SSI is an infection that occurs within 30 days after the operation and the infection appears to be related to the operation and infection involved deep soft tissues (e.g., fascial and muscle layers) of the incision and at least one of the following: -Purulent drainage from the deep incision but not from the organ/space component of the surgical site. -A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (> 38 C), localized pain, or tenderness, unless site is culture-negative. -An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination. -Diagnosis of a deep incision SSI by a surgeon or attending physician. Note: -Infection that involves both superficial and deep incision sites is reported as deep incisional SSI. -An organ/space SSI that drains through the incision is reported as a deep incisional SSI.

3. Organ/Space Surgical Site Infection

   Organ/Space SSI is an infection that occurs within 30 days after the operation and the infection appears to be related to the operation and the infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following: -Purulent drainage from a drain that is placed through a stab wound into the organ/space. -Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space. -An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination. -Diagnosis of an organ/space SSI by a surgeon or attending physician.

4. Dehiscence

Abdominal site: refers primarily to loss of the integrity of fascial closure (or whatever closure was performed in the absence of fascial closure). Other Surgical Sites: there must be a total breakdown of the surgical closure compromising the integrity of the procedure. Example: tissue flap coverage where the surgical incisions, which were closed, have lost the integrity of closure An ostomy with a small separation around it would NOT qualify..

5. Pneumonia

Enter "Yes" if the patient has pneumonia meeting the definition below. Patients with pneumonia *must meet criteria from both* *Radiology* *and* *Signs/Symptoms/Laboratory* sections listed as follows:

Radiology:

One definitive chest radiological exam (x-ray or CT)* with at least one of the following:

•New or progressive and persistent infiltrate

•Consolidation or opacity

•Cavitation

Note: In patients with underlying pulmonary or cardiac disease (e.g. respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease)two or more serial chest radiological exams (x-ray or CT)are required. (Serial radiological exams should be taken no less than 12 hours apart, but not more than 7 days apart. The occurrence should be assigned on the date the patient first met all of the criteria of the definition (i.e, if the patient meets all PNA criteria on the day of the first xray, assign this date to the occurrence. Do not assign the date of the occurrence to when the second serial xray was performed).

Signs/Symptoms/Laboratory:

FOR ANY PATIENT, at least one of the following:

•Fever (>38 C or >100.4 F) with no other recognized cause

•Leukopenia (<4000 WBC/mm3) or leukocytosis(≥12,000 WBC/mm3)

•For adults ≥ 70 years old, altered mental status with no other recognized cause

And

At least one of the following:

•5% Bronchoalveolar lavage (BAL) -obtained cells contain intracellular bacteria on direct microscopic exam (e.g., Gram stain)

•Positive growth in blood culture not related to another source of infection

•Positive growth in culture of pleural fluid

•Positive quantitative culture from minimally contaminated lower respiratory tract (LRT) specimen (e.g. BAL or protected specimen brushing)

OR

At least two of the following:

•New onset of purulent sputum, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements

•New onset or worsening cough, or dyspnea, or tachypnea

•Rales or rhonchi

•Worsening gas exchange (e.g. O2 desaturations (e.g., PaO2/FiO2≤ 240), increased oxygen requirements, or increased ventilator demand)

6. Unplanned intubation

Patient required placement of an endotracheal tube or other similar breathing tube [Laryngeal Mask Airway (LMA), nasotracheal tube, etc] and ventilator support intraoperatively or within 30 days following surgery which was not intended or planned.
•The variable intent is to capture all cause unplanned intubations, including but not limited to unplanned intubations for refractory hypotension, cardiac arrest, inability to protect airway.
•Accidental self extubations requiring reintubation would be assigned.
•Emergency tracheostomy would be assigned. Patients with a chronic/long-term tracheostomy who are on and off the ventilator would not be assigned, unless the tracheostomy tube itself is removed and the patient requires reintubation (endotracheal or a new tracheostomy tube) or an emergency tracheostomy.
•Patients undergoing time off the ventilator during weaning trials and who fail the trail and are placed back on the ventilator would not be assigned.
•Intubations for an unplanned return to the OR would not be assigned, as the intubation is planned, it is the return to the OR which is unplanned.
•In patients who were intubated for a return to the OR for a surgical procedure unplanned intubation occurs after they have been extubated after surgery. In patients who were not intubated for a return to the OR, intubation at any time after their surgery is complete is considered unplanned.
•Intraoperative conversion from local or MAC anesthesia to general anesthesia, during the Principal Operative Procedure, with placement of a breathing tube and ventilator support, secondary to the patient not tolerating local or MAC anesthesia, in the absence of an emergency, would not be assigned.

7. Pulmonary embolism

Lodging of a blood clot in a pulmonary artery with subsequent obstruction of blood supply to the lung parenchyma. The blood clots usually originate from the deep leg veins or the pelvic venous system. "Yes" is entered if the patient has a V-Q scan interpreted as high probability of pulmonary embolism or a positive CT exam, TEE, pulmonary arteriogram, CT angiogram, or any other definitive modality. Treatment usually consists of: -Initiation of anticoagulation therapy - Placement of mechanical interruption (e.g. Greenfield Filter), for patients whom anticoagulation is contraindicated or already instituted.

8. Failure to wean

Total duration of ventilator-assisted respirations during postoperative hospitalization was greater than 48 hours. This can occur at any time during the 30-day period postoperatively. This time assessment is CUMULATIVE, not necessarily consecutive. Ventilator-assisted respirations can be via endotracheal tube, nasotracheal tube, or tracheostomy tube.

9. Renal insufficiency

The reduced capacity of the kidney to perform its function as evidenced by a rise in creatinine of >2 mg/dl from preoperative value, but with no requirement for dialysis within 30 days of the operation.

10. Acute renal failure

A patient who did not require dialysis preoperatively, worsening of renal dysfunction postoperatively requiring hemodialysis, peritoneal dialysis, hemofiltration, hemodiafiltration, or ultrafiltration.
- If the patient refuses a recommendation for dialysis, you would answer 'Yes' to this variable because the patient required dialysis -
Hemodialysis, peritoneal dialysis, hemofiltration, hemodiafiltration, or ultrafiltration all qualify -
Placement of a dialysis catheter is indicative of the need for dialysis, if used within 48 hours of placement

11. Urinary tract infection

Postoperative symptomatic urinary tract infection must meet one of the following TWO criteria within 30 days of the operation: 1. One of the following: . fever (>38 degrees C) . urgency . frequency . dysuria . suprapubic tenderness AND a urine culture of > 10^5 colonies/ml urine with no more than two species of organisms **OR** 2. Two of the following: . fever (>38 degrees C) . urgency . frequency . dysuria . suprapubic tenderness AND any of the following: -Dipstick test positive for leukocyte esterase and/or nitrate -Pyuria (>10 WBCs/cc or > 3 WBC/hpf of unspun urine) -Organisms seen on Gram stain of unspun urine -Two urine cultures with repeated isolation of the same uropathogen with >10^2 colonies/ml urine in non-voided specimen -Urine culture with < 10^5 colonies/ml urine of single uropathogen in patient being treated with appropriate antimicrobial therapy - Physician's diagnosis -Physician institutes appropriate antimicrobial therapy. Note: To assign a postoperative UTI, sign and symptoms should be reported within 72 hours prior to a urine culture being sent or 24 hours after the culture was sent.

12. Stroke/CVA

Patient develops an embolic, thrombotic, or hemorrhagic vascular accident or stroke with motor, sensory, or cognitive dysfunction (e.g., hemiplegia, hemiparesis, aphasia, sensory deficit, impaired memory) that persists for 24 or more hours. If a specific time frame for the dysfunction is not documented in the medical record, but there is a diagnosis of a stroke, assign the occurrence, unless documentation specifically states that the motor, sensory, or cognitive dysfunction resolved.

13. Coma

Patient is unconscious, or postures to painful stimuli, or is unresponsive to all stimuli (exclude transient disorientation or psychosis) for greater than 24 hours. Drug-induced coma (e.g. Propofol drips) are not entered within 30 days of the operation.

14. Peripheral nerve injury

Peripheral nerve damage may result from damage to the nerve fibers, cell body, or myelin sheath during surgery. Peripheral nerve injuries which result in motor deficits to the cervical plexus, brachial plexus, ulnar plexus, lumbar-sacral plexus (sciatic nerve), peroneal nerve, and/or the femoral nerve should be included.

15. Cardiac arrest requiring CPR

The absence of cardiac rhythm or presence of chaotic cardiac rhythm, intraoperatively or within 30 days following surgery, which results in a cardiac arrest requiring the initiation of CPR, which includes chest compressions. Patients are included who are in a pulseless VT or Vfib in which defibrillation is performed and PEA arrests requiring chest compressions. Patients with automatic implantable cardioverter defibrillator (AICD) that fire but the patient has no loss of consciousness should be excluded.

16. Acute myocardial infarction

An acute myocardial infarction which occurred intraoperatively or within 30 days following surgery as manifested by one of the following: *
Documentation of ECG changes indicative of acute MI (one or more of the following):
- ST elevation > 1 mm in two or more contiguous leads
- New left bundle branch
- New q-wave in two of more contiguous leads
* New elevation in troponin greater than 3 times upper level of the reference range in the setting of suspected myocardial ischemia □ * Physician diagnosis of myocardial infarction

17. Bleeding necessitating transfusion (2006-2009)

Any transfusion (including autologous) of packed red blood cells or whole blood given from the time the patient leaves the operating room up to and including 72 hours postoperatively. Bleeding Transfusion entered for five or more units of packed red blood cell units in the postoperative period including hanging blood from the OR that is finished outside of the OR. If the patient receives shed blood, autologous blood, cell saver blood or pleurovac postoperatively, this is counted if greater than four units. The blood may be given for any reason.

a. Bleeding necessitating transfusion (2010- definition)

At least 1 unit of packed or whole red blood cells given from the surgical start time up to and including 72 hours postoperatively. If the patient receives shed blood, autologous blood, cell saver blood or pleurovac postoperatively, count this blood in terms of equivalent units. For a cell saver, every 500 ml's of fluid will equal 1 unit of packed cells. If there are less than 250 ml of cell saver, round down and report as 0 units. If there are 250 cc, or more of cell saver, round up to 1 unit. The blood may be given for any reason. If greater than 200 units, enter 200 units. Record the number of units given. Record the date the blood was initially started (intra-operatively or postoperatively).
Note: Intra-operative blood to prime the by-pass pump for CABG is not shed blood and should not be included as cell-saver blood.

18. Graft/prosthesis/free flap failure

Mechanical failure of an extracardiac graft or prosthesis including myocutaneous flaps and skin grafts requiring return to the operating room, interventional radiology, or a balloon angioplasty within 30 days of the operation.

19. Deep venous thrombosis

The identification of a new blood clot or thrombus within the venous system which may be coupled with inflammation. The clot can be described in studies as present in the superficial or deep venous systems but requires therapy. This diagnosis is confirmed by a duplex, venogram or CT scan, AND the patient must be treated with anticoagulation therapy and/or placement of a vena cava filter or clipping of the vena cava.
Example of clots that should be considered for this variable include internal jugular (IJ) line clots, PICC line clots and those found in the abdomen (portal vein).
Clarification: the vein must be thrombosed to assign this occurrence. If only the catheter is thombosed and the vein is not, the occurrence of Vein Thrombosis Requiring Therapy would not be assigned.

20. Sepsis

Sepsis is a vast clinical entity that takes a variety of forms. The spectrum of disorders spans from relatively mild physiologic abnormalities to septic shock. The intent is to capture the patient whose physiology is compromised by an ongoing infectious process after surgery. Present at the time of surgery (PATOS) modifiers prevent patients from being counted as having complications if there is significant evidence that the sepsis or septic shock outcome was under way prior to the surgery performed. Please report the most significant level using the criteria below.
1.Sepsis: Sepsis is the systemic response to infection. Report this variable if the patient has two of the following clinical signs and symptoms of SIRS:
*Temp >38o C (100.4 o F) or < 36 o C (96.8 o F)
*HR >90 bpm
*RR >20 breaths/min or PaCO2 <32 mmHg(<4.3 kPa)
*WBC >12,000 cell/mm3, <4000 cells/mm3, or >10% immature (band) forms
*Anion gap acidosis: this is defined by either: [Na + K] – [Cl + HCO3 (or serum CO2)]. If this numbe is greater than 16, then an anion gap acidosis is present. Na – [Cl + HCO3 (or serum CO2)]. If this number is greater than 12, then an anion gap acidosis is present. *If anion gap lab values are performed at your facilities lab, ascertain which formula is utilized and follow guideline criteria.
And either A or B below:
A. One of the following:
*positive blood culture
*clinical documentation of purulence or positive culture from any site for which there is documentation noting the site as the acute cause of sepsis
B. One of the following findings during the Principal Operative Procedure:
*Confirmed infarcted bowel requiring resection
*Purulence in the operative site
*Enteric contents in the operative site, or
*Positive intra-operative cultures Guidance:
if the patient meets criteria to assign preop sepsis, assign the risk factor; if the patient meets the criteria to assign postop sepsis, assign the occurrence and then assess for PATOS and assign if appropriate.
2. Septic Shock: Sepsis is considered severe when it is associated with organ and/or circulatory dysfunction. Report this variable if the patient has sepsis AND documented organ and/or circulatory dysfunction. Examples of organ dysfunction include: oliguria, acute alteration in mental status, acute respiratory distress. Examples of circulatory dysfunction include: hypotension, requirement of inotropic or vasopressor agents. Septic Shock is assigned when it appears to be related to Sepsis and not a Cardiogenic or Hypovolemic etiology.
Guidance: if the patient meets criteria to assign preop septic shock assign the risk factor; if the patient meets the criteria to assign postop septic shock assign the occurrence and then assess for PATOS and assign if appropriate.

21. Septic shock

For Sepsis and Septic Shock within 30 days of the operation, please report the most significant level using the criteria that follow. Severe Sepsis/Septic Shock: Sepsis is considered severe when it is associated with organ and/or circulatory dysfunction. Report this variable if the patient has the clinical signs and symptoms of SIRS or sepsis **AND** documented organ and/or circulatory dysfunction. Examples of organ dysfunction include: oliguria, acute alteration in mental status, acute respiratory distress. Examples of circulatory dysfunction include: hypotension, requirement of inotropic or vasopressor agents. For the patient that had sepsis preoperatively, worsening of any of the above signs postoperatively would be reported as a postoperative sepsis.

Supplementary Appendix 2: Annotated version of the R code used for the primary analysis.

```
rm(list=ls());gc()

# Required R packages
library(rms)
library(foreign)
library(glmnet)
library(numDeriv)



#********************####
# (I) Main Analysis ####
#********************####

# Prespecified risk factors for generating design matrix
XX <- Cs(SUPINFEC,WNDINFD,ORGSPCSSI,DEHIS,OUPNEUMO,REINTUB,
         FAILWEAN,RENAINSF,OPRENAFL,URNINFEC,CNSCVA,CDARREST,CDMI,
         # OTHBLEED,VTE, # exclude from variable selection
         OTHSYSEP,OTHSESHOCK,  # Postop complications

         AGE,SEX,RACE2,HEIGHT,WEIGHT,
         WORKRVU,INOUT,TRANST2,ANESTHES2,SURGSPEC2,EMERGNCY,WNDCLAS,ASACLAS2,Class,
         DIABETES,SMOKE,DYSPNEA,FNSTATUS2.f,VENTILAT,HXCOPD,
         ASCITES,HXCHF,HYPERMED,RENAFAIL,DIALYSIS,DISCANCR,
         WNDINF,STEROID,WTLOSS,TRANSFUS,PRSEPIS,OPTIME,TOTHLOS,
         HTOODAY,RETURNOR,                  # Demos, Operations,Comobidities

         PRSODM0, PRBUN0, PRCREAT0, PRALBUM0, PRBILI0, PRSGOT0,
         PRALKPH0, PRWBC0, PRHCT0, PRPLATE0, PRPTT0, PRINR0, PRPT0,
         PRSODM.i,PRBUN.i,PRCREAT.i,PRALBUM.i,PRBILI.i,PRSGOT.i,
         PRALKPH.i,PRWBC.i,PRHCT.i,PRPLATE.i,PRPTT.i,PRINR.i,PRPT.i) # Labs

# Primary Analysis: all patients ###

# load cleaned data for regression
load('AM_Cleaned_Data2020.Rdata')

## 1. Year 2006 LASSO ####
# Relaxed LASSO for year 2005-2006 data

# Design matrix for LASSO
dat <- na.omit(dat06[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')]) # glmnet does not accept missing data
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data = dat)
Y <- dat$DEATH

# Step 1: variable selection using LASSO
Sys.time()
lasso.06 <- glmnet(X, Y, family = "binomial", alpha = 1) # alpha=1: LASSO
Sys.time()

plot(lasso.06)
vn <- colnames(X)
vnat06 <- coef(lasso.06)
vnat06 <- vnat06[-1, ncol(vnat06)] # remove the intercept, and get the coefficients at the end of the path
axis(4, at=vnat06, line=-.5, label=vn, las=1, tick=FALSE, cex.axis=0.8)

# Crossvalidation: cross-validated Lasso penalty parameter - lambda
Sys.time()
set.seed(123)
cv.06 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()

summary(cv.06)
plot(cv.06)  # top axis is number of variables in model
cbind(coef(cv.06, s="lambda.min"), coef(cv.06, s="lambda.1se"))

plot(lasso.06, label=TRUE, xvar="lambda")
abline(v=log(cv.06$lambda.min), lty=2, lwd=0.5)
abline(v=log(cv.06$lambda.1se), lty=2, lwd=0.5)

# Pick 'best' cross-validated lambda using 1 SE criteria
coef(lasso.06, s=log(cv.06$lambda.1se))
cv.06$lambda.1se

# Relaxed Lasso
b <- coef(cv.06, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1]    # lasso CV picked variables
dropped <- setdiff(colnames(X), subset) # lasso CV dropped variables
```

```
# Step 2: Rerun logistic regression using the selected variables

# index for age, weight
(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))

# revised design matrix that incoporates nonlinear effect of age and weight,
# and force VTE and OTHBLEED in the model
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )

Xi <- Xi[,-1]
fit.06  <- glm(Y ~ Xi, family=binomial(link="logit"))
print(fit.06)

save(lasso.06, cv.06, X, fit.06, subset, dropped, file='ModelResults_Y06.Rdata')


# We repeat the two steps (select and refit) procedure for each year

## 2. Year 2007 LASSO ####
dat <- na.omit(dat07[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH

lasso.07 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.07 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()
summary(cv.07)

# Relaxed Lasso
b <- coef(cv.07, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1]
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )

Xi <- Xi[,-1]
fit.07  <- glm(Y ~ Xi, family=binomial(link="logit"))
print(fit.07)

save(lasso.07, cv.07, X, fit.07, subset, dropped, file='ModelResults_Y07.Rdata')


## 3. Year 2008 LASSO ####
dat <- na.omit(dat08[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH

lasso.08 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.08 <- cv.glmnet(X, Y, family = "binomial")
summary(cv.08)

# Relaxed Lasso
b <- coef(cv.08, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1]
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))

Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )
Xi <- Xi[,-1]
fit.08  <- glm(Y ~ Xi, family=binomial(link="logit"))
print(fit.08)

save(lasso.08, cv.08, X, fit.08, subset, dropped, file='ModelResults_Y08.Rdata')
```

```
## 4. Year 2009 LASSO ####
dat <- na.omit(dat09[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH

lasso.09 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.09 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()
summary(cv.09)

b <- coef(cv.09, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1] # lasso cv picked x variables
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )

Xi <- Xi[,-1]
fit.09  <- glm(Y ~ Xi, family=binomial(link="logit"))
print(fit.09)

save(lasso.09, cv.09, X, fit.09, subset, dropped, file='ModelResults_Y09.Rdata')


## 5. Year 2010 LASSO ####
dat <- na.omit(dat10[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH

lasso.10 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.10 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()
summary(cv.10)

# Relaxed Lasso
b <- coef(cv.10, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1]
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )
Xi <- Xi[,-1]
fit.10  <- glm(Y ~ Xi, family=binomial(link="logit"))
print(fit.10)

save(lasso.10, cv.10, X, fit.10, subset, dropped, file='ModelResults_Y10.Rdata')


## 6. Year 2011 LASSO ####
dat <- na.omit(dat11[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH

lasso.11 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.11 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()
summary(cv.11)

# Relaxed Lasso
b <- coef(cv.11, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1]
```

```
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )
Xi <- Xi[,-1]

fit.11  <- glm(Y ~ Xi, family=binomial(link="logit"))
print(fit.11)

save(lasso.11, cv.11, X, fit.11, subset, dropped, file='ModelResults_Y11.Rdata')


## 7. Year 2012 LASSO ####
dat <- na.omit(dat12[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH

lasso.12 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.12 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()
summary(cv.12)

# Relaxed Lasso
b <- coef(cv.12, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1]
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )
Xi <- Xi[,-1];colnames(Xi);

fit.12  <- glm(Y ~ Xi, family=binomial(link="logit"))
summary(fit.12)

save(lasso.12, cv.12, X, fit.12, subset, dropped, file='ModelResults_Y12.Rdata')


## 8. Year 2013 LASSO ####
dat <- na.omit(dat13[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH

lasso.13 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.13 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()
summary(cv.13)

# Relaxed Lasso
b <- coef(cv.13, s="lambda.1se") # lambda.min
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1] # lasso cv picked x variables
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )
Xi <- Xi[,-1];colnames(Xi);

fit.13  <- glm(Y ~ Xi, family=binomial(link="logit"))
summary(fit.13)

save(lasso.13, cv.13, X, fit.13, subset, dropped, file='ModelResults_Y13.Rdata')


## 9. Year 2014 LASSO ####
dat <- na.omit(dat14[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH
```

```
lasso.14 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.14 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()
summary(cv.14)

# Relaxed Lasso
b <- coef(cv.14, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1]
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )
Xi <- Xi[,-1]; colnames(Xi);

fit.14  <- glm(Y ~ Xi, family=binomial(link="logit"))
summary(fit.14)

save(lasso.14, cv.14, X, fit.14, subset, dropped, file='ModelResults_Y14.Rdata')


## 10. Year 2015 LASSO ####
dat <- na.omit(dat15[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH

lasso.15 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.15 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()
summary(cv.15)

# Relaxed Lasso
b <- coef(cv.15, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1]
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )
Xi <- Xi[,-1]; colnames(Xi);

fit.15  <- glm(Y ~ Xi, family=binomial(link="logit"))
summary(fit.15)

save(lasso.15, cv.15, X, fit.15, subset, dropped,  file='ModelResults_Y15.Rdata')


## 11. Year 2016 LASSO ####
dat <- na.omit(dat16[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH

lasso.16 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.16 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()
summary(cv.16)

# Relaxed Lasso
b <- coef(cv.16, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1]
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )
```

```
Xi <- Xi[,-1]; colnames(Xi);

fit.16  <- glm(Y ~ Xi, family=binomial(link="logit"))
summary(fit.16)

save(lasso.16, cv.16, X, XX, fit.16, subset, dropped, file='ModelResults_Y16.Rdata')


## 12. Year 2017 LASSO ####
dat <- na.omit(dat17[, c(XX, 'OTHBLEED', 'VTE', 'DEATH')])
XX[c(65,78)]
XX <- XX[-c(65,78)] # Remove PRPT: PRPT not available in 2017 dataset
form <- as.formula(paste(" ~ ", paste0(XX, collapse = " + ")))
X <- model.matrix(form, data=dat)
Y <- dat$DEATH

lasso.17 <- glmnet(X, Y, family = "binomial")

# Crossvalidation: Lasso
Sys.time()
cv.17 <- cv.glmnet(X, Y, family = "binomial")
Sys.time()
summary(cv.17)

# Relaxed Lasso
b <- coef(cv.17, s="lambda.1se")
colnames(b) <- "lasso.1se"
subset <- colnames(X)[which(b!=0)-1]
dropped <- setdiff(colnames(X), subset)

(IND <- c(grep('AGE', subset),grep('WEIGHT', subset)))
Xi <- cbind( model.matrix( as.formula( '~ OTHBLEED + VTE + rcs(AGE,5) + rcs(WEIGHT,5)' ) , data=dat),
             X[, subset[-IND]] )
Xi <- Xi[,-1]; colnames(Xi);

fit.17  <- glm(Y ~ Xi, family=binomial(link="logit"))
summary(fit.17)

save(lasso.17, cv.17, X, XX, fit.17, subset, dropped, file='ModelResults_Y17.Rdata')


# Function for odds ratio
OR.cal <- function(obj=fit.06, YEAR='Year 2006') {

  ii <- c(grep('OTHBLEED', names(obj$coef)), grep('VTE', names(obj$coef)))
  COEF <- obj$coef[ii]
  se <- sqrt(diag(summary(obj)$cov.unscaled[ii, ii]))

  LOWCI <- UPPCI <- PVAL <- NULL
  COL.NAME <- gsub('Xi', '', names(beta))
  ROW.NAME <- YEAR

  LOWCI <- COEF - 1.96*se
  UPPCI <- COEF + 1.96*se
  PVAL <- 2*pnorm( abs(COEF/se), lower.tail=F)
  PVAL0 <- ifelse(PVAL < 0.001, '< 0.001',
                  ifelse(PVAL<0.01, format(round(PVAL,3),nsmall=3), format(round(PVAL,2),nsmall=2)))

  # Adj.OR <- exp(COEF)
  Adj.OR <- paste0(round(exp(COEF),2), ' (', round(exp(LOWCI),2), ', ', round(exp(UPPCI),2), '), ', PVAL0)
  Adj.OR <- matrix(Adj.OR, nrow=1, ncol=2, byrow=T)
  colnames(Adj.OR) <- COL.NAME
  rownames(Adj.OR) <- ROW.NAME

  OR <- exp(COEF)
  LOW <- exp(LOWCI)
  UPP <- exp(UPPCI)

  return(list(Adj.OR=Adj.OR, OR=OR, LOW=LOW, UPP=UPP, PVAL=PVAL0, Beta=COEF, SE=se))
}

# Function calculating attributable mortality
# a: number of complications
# b: number of no complications
# c: number of deaths
# p.c: proportion of death among those with complications
# p.nc: proportion of death among those with no complications
a.mort.cal <- function(a=150, b=850, c=110, OR=1.8, p.c=0.053, p.nc=0.013) {

  a0 <- b*OR-b
```

```
  b0 <- a*OR-c*OR+b+c
  c0 <- -c

  y <- (-b0 + sqrt( b0^2 -4*a0*c0))/(2*a0)
  x <- (c-b*y)/a
  af.adj <- x-y
  af.unadj <- p.c - p.nc
  AM.adj   <- a*(x-y)
  AM.unadj <- a*(p.c - p.nc)

  N <- a+b
  comp.perc  <- a/N
  death.perc <- c/N

  return(list(AM.adj=AM.adj, AM.unadj=AM.unadj,
              af.adj=af.adj, af.unadj=af.unadj,
              x=x, y=y,
              N=N, comp.perc=comp.perc, death.perc=death.perc))
}


# Calculate Odds Ratio and Attributable Mortality ####

# Year 2006 AM.OR ####
dat <-  dat06; YEAR <- '2006'
COMP <- c("OTHBLEED","VTE")

load('ModelResults_Y06.Rdata')

OR   <- OR.cal(obj=fit.06, YEAR='Year 2006')$OR
Beta <- OR.cal(obj=fit.06, YEAR='Year 2006')$Beta
SE   <- OR.cal(obj=fit.06, YEAR='Year 2006')$SE
PVAL <- OR.cal(obj=fit.06, YEAR='Year 2006')$PVAL
OR.LOW <- OR.cal(obj=fit.06, YEAR='Year 2006')$LOW
OR.UPP <- OR.cal(obj=fit.06, YEAR='Year 2006')$UPP

## Attributable mortality based on adjusted OR and observed complication prevalence
a.06 <- b.06 <- c.06 <- p.c.06 <- p.nc.06 <- Comp.Rate.06 <- Adj.AM.06 <- Unadj.AM.06 <- matrix(NA, nrow=1, ncol=2)
N.06 <- comp.perc.06 <- death.perc.06 <- x.06 <- y.06 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.06[, COMP[i] ] <- sum( dat[, COMP[i]] != 'NoComplication', na.rm = T)  # Complication
  b.06[, COMP[i] ] <- sum( dat[, COMP[i]] == 'NoComplication', na.rm = T)  # No Complication
  c.06[, COMP[i] ] <- sum( dat[, 'DEATH'] == 1, na.rm = T)                 # Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH', COMP[i])]
  p.c.06[, COMP[i] ]  <- mean(bla$DEATH == 1, na.rm = T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH', COMP[i])]
  p.nc.06[, COMP[i] ] <- mean(bla$DEATH == 1, na.rm = T)
  Comp.Rate.06[, COMP[i] ] <- mean(dat[[ COMP[i] ]] != 'NoComplication', na.rm = T)
}

for (j in 1:2) {

  lala <- a.mort.cal(a = a.06[1, j], b = b.06[1, j], c = c.06[1, j], OR = OR[j], p.c = p.c.06[1, j], p.nc = p.nc.06[1,
j])
  Adj.AM.06[1, j]   <- lala$AM.adj
  Unadj.AM.06[1, j] <- lala$AM.unadj
  x.06[1, j]        <- lala$x
  y.06[1, j]        <- lala$y
  N.06[1, j]        <- lala$N
  comp.perc.06[1, j]  <- lala$comp.perc
  death.perc.06[1, j] <- lala$death.perc
}

# Delta method for 95% CI of attributable mortality
# AM function feed to grad() to calculate 1st derivative
g.06.bleed <- function(x) {
  a0 <- 151358*exp(x)-151358
  b0 <- 929*exp(x)-2707*exp(x)+151358+2707
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-2707)))/(2*a0)
  x0 <- (2707-151358*y0)/929
  929*(x0-y0)
}
g.06.bleed(x=Beta[1] )
(g.prim <- grad(func=g.06.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.06.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.06[1,1] + c(-1, 1)*1.96*AM.se) # CI using delta method

g.06.thromb <- function(x=Beta[j] ) {
```

```
  a0 <- 150812*exp(x)-150812
  b0 <- 1475*exp(x)-2707*exp(x)+150812+2707
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-2707)))/(2*a0)
  x0 <- (2707-150812*y0)/1475
  1475*(x0-y0)
}
g.06.thromb(x=Beta[2])
(g.prim <- grad(func=g.06.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.06.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.06[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.06 <- rbind(
  data.frame(Comp='BLEED',
             AM=Adj.AM.06[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.06[1,1], Y=y.06[1,1], N=N.06[1,1], comp.perc=comp.perc.06[1,1], death.perc=death.perc.06[1,1]),
  data.frame(Comp='VTE',
             AM=Adj.AM.06[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.06[1,2], Y=y.06[1,2], N=N.06[1,2], comp.perc=comp.perc.06[1,2], death.perc=death.perc.06[1,2]))
)
rownames(OUTPUT.06) <- NULL
OUTPUT.06$YEAR <- 2006
OUTPUT.ALL <- rbind(OUTPUT.06)


# Year 2007 AM.OR ####
load('ModelResults_Y07.Rdata')

dat <-  dat07; YEAR <- '2007'
COMP <- c("OTHBLEED","VTE")

## Adjusted OR
OR   <- OR.cal(obj=fit.07, YEAR='Year 2007')$OR
Beta <- OR.cal(obj=fit.07, YEAR='Year 2007')$Beta
SE   <- OR.cal(obj=fit.07, YEAR='Year 2007')$SE
PVAL <- OR.cal(obj=fit.07, YEAR='Year 2007')$PVAL
OR.LOW <- OR.cal(obj=fit.07, YEAR='Year 2007')$LOW
OR.UPP <- OR.cal(obj=fit.07, YEAR='Year 2007')$UPP

a.07 <- b.07 <- c.07 <- p.c.07 <- p.nc.07 <- Comp.Rate.07 <- Adj.AM.07 <- Unadj.AM.07 <- matrix(NA, nrow=1, ncol=2)
N.07 <- comp.perc.07 <- death.perc.07 <- x.07 <- y.07 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.07[, COMP[i] ] <- sum( dat[, COMP[i]] != 'NoComplication', na.rm = T)  # Complication
  b.07[, COMP[i] ] <- sum( dat[, COMP[i]] == 'NoComplication', na.rm = T)  # No Complication
  c.07[, COMP[i] ] <- sum( dat[, 'DEATH'] == 1, na.rm = T)                 # Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH', COMP[i])]
  p.c.07[, COMP[i] ]  <- mean(bla$DEATH == 1, na.rm = T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH', COMP[i])]
  p.nc.07[, COMP[i] ] <- mean(bla$DEATH == 1, na.rm = T)
  Comp.Rate.07[, COMP[i] ] <- mean(dat[[ COMP[i] ]] != 'NoComplication', na.rm = T)
}


for (j in 1:2) {

  lala <- a.mort.cal(a = a.07[1, j], b = b.07[1, j], c = c.07[1, j], OR = OR[j], p.c = p.c.07[1, j], p.nc = p.nc.07[1,
j])
  Adj.AM.07[1, j]   <- lala$AM.adj
  Unadj.AM.07[1, j] <- lala$AM.unadj
  x.07[1, j]        <- lala$x
  y.07[1, j]        <- lala$y
  N.07[1, j]        <- lala$N
  comp.perc.07[1, j]  <- lala$comp.perc
  death.perc.07[1, j] <- lala$death.perc
}

g.07.bleed <- function(x) {
  a0 <- 210305*exp(x)-210305
  b0 <- 1044*exp(x)-3683*exp(x)+210305+3683
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-3683)))/(2*a0)
  x0 <- (3683-210305*y0)/1044
  1044*(x0-y0)
}
g.07.bleed(x=Beta[1] )
(g.prim <- grad(func=g.07.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.07.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.07[1,1] + c(-1, 1)*1.96*AM.se)
```

```
g.07.thromb <- function(x=Beta[j] ) {
  a0 <- 209328*exp(x)-209328
  b0 <- 2021*exp(x)-3683*exp(x)+209328+3683
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-3683)))/(2*a0)
  x0 <- (3683-209328*y0)/2021
  2021*(x0-y0)
}

g.07.thromb(x=Beta[2])
(g.prim <- grad(func=g.07.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.07.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.07[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.07 <- rbind(
  data.frame(Comp='BLEED',
             AM=Adj.AM.07[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.07[1,1], Y=y.07[1,1], N=N.07[1,1], comp.perc=comp.perc.07[1,1], death.perc=death.perc.07[1,1]),
  data.frame(Comp='VTE', AM=Adj.AM.07[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.07[1,2], Y=y.07[1,2], N=N.07[1,2], comp.perc=comp.perc.07[1,2], death.perc=death.perc.07[1,2]))
)

rownames(OUTPUT.07) <- NULL
OUTPUT.07$YEAR <- 2007
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.07)

# Year 2008 AM.OR ####
load('ModelResults_Y08.Rdata')

dat <-  dat08; YEAR <- '2008'
COMP <- c("OTHBLEED","VTE")

OR   <- OR.cal(obj=fit.08, YEAR='Year 2008')$OR
Beta <- OR.cal(obj=fit.08, YEAR='Year 2008')$Beta
SE   <- OR.cal(obj=fit.08, YEAR='Year 2008')$SE
PVAL <- OR.cal(obj=fit.08, YEAR='Year 2008')$PVAL
OR.LOW <- OR.cal(obj=fit.08, YEAR='Year 2008')$LOW
OR.UPP <- OR.cal(obj=fit.08, YEAR='Year 2008')$UPP

## Attributable mortality based on adjusted OR and observed complication prevalence
a.08 <- b.08 <- c.08 <- p.c.08 <- p.nc.08 <- Comp.Rate.08 <- Adj.AM.08 <- Unadj.AM.08 <- matrix(NA, nrow=1, ncol=2)
N.08 <- comp.perc.08 <- death.perc.08 <- x.08 <- y.08 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.08[, COMP[i] ] <- sum( dat[, COMP[i]] != 'NoComplication', na.rm = T)  # Complication
  b.08[, COMP[i] ] <- sum( dat[, COMP[i]] == 'NoComplication', na.rm = T)  # No Complication
  c.08[, COMP[i] ] <- sum( dat[, 'DEATH'] == 1, na.rm=T)                   # Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH', COMP[i])]
  p.c.08[, COMP[i] ]  <- mean(bla$DEATH == 1, na.rm = T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH', COMP[i])]
  p.nc.08[, COMP[i] ] <- mean(bla$DEATH == 1, na.rm = T)
  Comp.Rate.08[, COMP[i] ] <- mean(dat[[ COMP[i] ]] != 'NoComplication', na.rm = T)
}

for (j in 1:2) {

  lala <- a.mort.cal(a = a.08[1, j], b = b.08[1, j], c = c.08[1, j], OR = OR[j], p.c = p.c.08[1, j], p.nc = p.nc.08[1,
j])
  Adj.AM.08[1, j]   <- lala$AM.adj
  Unadj.AM.08[1, j] <- lala$AM.unadj
  x.08[1, j]        <- lala$x
  y.08[1, j]        <- lala$y
  N.08[1, j]        <- lala$N
  comp.perc.08[1, j]  <- lala$comp.perc
  death.perc.08[1, j] <- lala$death.perc
}

g.08.bleed <- function(x) {
  a0 <- 270026*exp(x)-270026
  b0 <- 1227*exp(x)-4629*exp(x)+270026+4629
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-4629)))/(2*a0)
  x0 <- (4629-270026*y0)/1227
  1227*(x0-y0)
}
g.08.thromb <- function(x) {
  a0 <- 268588*exp(x)-268588
  b0 <- 2665*exp(x)-4629*exp(x)+268588+4629
```

```
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-4629)))/(2*a0)
  x0 <- (4629-268588*y0)/2665
  2665*(x0-y0)
}

g.08.bleed(x=Beta[1] )
(g.prim <- grad(func=g.08.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.08.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.08[1,1] + c(-1, 1)*1.96*AM.se)

g.08.thromb(x=Beta[2])
(g.prim <- grad(func=g.08.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.08.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.08[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.08 <- rbind(
  data.frame(Comp='BLEED',
             AM=Adj.AM.08[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.08[1,1], Y=y.08[1,1], N=N.08[1,1], comp.perc=comp.perc.08[1,1], death.perc=death.perc.08[1,1]),
  data.frame(Comp='VTE',
             AM=Adj.AM.08[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.08[1,2], Y=y.08[1,2], N=N.08[1,2], comp.perc=comp.perc.08[1,2], death.perc=death.perc.08[1,2]))
)
rownames(OUTPUT.08) <- NULL
OUTPUT.08$YEAR <- 2008
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.08)

# Year 2009 AM.OR ####
load('ModelResults_Y09.Rdata')

dat <-  dat09; YEAR <- '2009'
COMP <- c("OTHBLEED","VTE")

OR   <- OR.cal(obj=fit.09, YEAR='Year 2009')$OR
Beta <- OR.cal(obj=fit.09, YEAR='Year 2009')$Beta
SE   <- OR.cal(obj=fit.09, YEAR='Year 2009')$SE
PVAL <- OR.cal(obj=fit.09, YEAR='Year 2009')$PVAL
OR.LOW <- OR.cal(obj=fit.09, YEAR='Year 2009')$LOW
OR.UPP <- OR.cal(obj=fit.09, YEAR='Year 2009')$UPP

## Attributable mortality based on adjusted OR and observed complication prevalence
a.09 <- b.09 <- c.09 <- p.c.09 <- p.nc.09 <- Comp.Rate.09 <- Adj.AM.09 <- Unadj.AM.09 <- matrix(NA, nrow=1, ncol=2)
N.09 <- comp.perc.09 <- death.perc.09 <- x.09 <- y.09 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.09[, COMP[i] ] <- sum( dat[, COMP[i]] != 'NoComplication', na.rm = T)  # Complication
  b.09[, COMP[i] ] <- sum( dat[, COMP[i]] == 'NoComplication', na.rm = T)  # No Complication
  c.09[, COMP[i] ] <- sum( dat[, 'DEATH'] == 1, na.rm = T)                 # Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH', COMP[i])]
  p.c.09[, COMP[i] ]  <- mean(bla$DEATH == 1, na.rm = T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH', COMP[i])]
  p.nc.09[, COMP[i] ] <- mean(bla$DEATH == 1, na.rm=T)
  Comp.Rate.09[, COMP[i] ] <- mean(dat[[ COMP[i] ]] != 'NoComplication', na.rm = T)
}

for (j in 1:2) {

  lala <- a.mort.cal(a = a.09[1, j], b = b.09[1, j], c = c.09[1, j], OR = OR[j], p.c = p.c.09[1, j], p.nc = p.nc.09[1,
j])
  Adj.AM.09[1, j]   <- lala$AM.adj
  Unadj.AM.09[1, j] <- lala$AM.unadj
  x.09[1, j]        <- lala$x
  y.09[1, j]        <- lala$y
  N.09[1, j]        <- lala$N
  comp.perc.09[1, j]  <- lala$comp.perc
  death.perc.09[1, j] <- lala$death.perc
}

g.09.bleed <- function(x) {
  a0 <- 334634*exp(x)-334634
  b0 <- 1464*exp(x)-5391*exp(x)+334634+5391
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-5391)))/(2*a0)
  x0 <- (5391-334634*y0)/1464
  1464*(x0-y0)
}
g.09.thromb <- function(x) {
  a0 <- 333069*exp(x)-333069
```

```
  b0 <- 3029*exp(x)-5391*exp(x)+333069+5391
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-5391)))/(2*a0)
  x0 <- (5391-333069*y0)/3029
  3029*(x0-y0)
}

g.09.bleed(x=Beta[1] )
(g.prim <- grad(func=g.09.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.09.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.09[1,1] + c(-1, 1)*1.96*AM.se)

g.09.thromb(x=Beta[2])
(g.prim <- grad(func=g.09.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.09.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.09[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.09 <- rbind(
  data.frame(Comp='BLEED',
             AM=Adj.AM.09[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.09[1,1], Y=y.09[1,1], N=N.09[1,1], comp.perc=comp.perc.09[1,1], death.perc=death.perc.09[1,1]),
  data.frame(Comp='VTE',
             AM=Adj.AM.09[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.09[1,2], Y=y.09[1,2], N=N.09[1,2], comp.perc=comp.perc.09[1,2], death.perc=death.perc.09[1,2]))
)
rownames(OUTPUT.09) <- NULL
OUTPUT.09$YEAR <- 2009
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.09)

# Year 2010 AM.OR ####
load('ModelResults_Y10.Rdata')

dat <-  dat10; YEAR <- '2010'
COMP <- c("OTHBLEED","VTE")

OR   <- OR.cal(obj=fit.10, YEAR='Year 2010')$OR
Beta <- OR.cal(obj=fit.10, YEAR='Year 2010')$Beta
SE   <- OR.cal(obj=fit.10, YEAR='Year 2010')$SE
PVAL <- OR.cal(obj=fit.10, YEAR='Year 2010')$PVAL
OR.LOW <- OR.cal(obj=fit.10, YEAR='Year 2010')$LOW
OR.UPP <- OR.cal(obj=fit.10, YEAR='Year 2010')$UPP

## Attributable mortality based on adjusted OR and observed complication prevalence
a.10 <- b.10 <- c.10 <- p.c.10 <- p.nc.10 <- Comp.Rate.10 <- Adj.AM.10 <- Unadj.AM.10 <- matrix(NA, nrow=1, ncol=2)
N.10 <- comp.perc.10 <- death.perc.10 <- x.10 <- y.10 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.10[, COMP[i] ] <- sum( dat[,COMP[i]]!='NoComplication', na.rm=T)  #Complication
  b.10[, COMP[i] ] <- sum( dat[,COMP[i]]=='NoComplication', na.rm=T)  #No Complication
  c.10[, COMP[i] ] <- sum( dat[,'DEATH']==1, na.rm=T) #Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH',COMP[i])]
  p.c.10[, COMP[i] ]  <- mean(bla$DEATH==1, na.rm=T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH',COMP[i])]
  p.nc.10[, COMP[i] ] <- mean(bla$DEATH==1, na.rm=T)
  Comp.Rate.10[, COMP[i] ] <- mean(dat[[ COMP[i] ]]!='NoComplication', na.rm=T)
}

for (j in 1:2) {

  lala <- a.mort.cal(a=a.10[1,j], b=b.10[1,j], c=c.10[1,j], OR=OR[j], p.c=p.c.10[1,j], p.nc=p.nc.10[1,j])
  Adj.AM.10[1,j]   <- lala$AM.adj
  Unadj.AM.10[1,j] <- lala$AM.unadj
  x.10[1,j]        <- lala$x
  y.10[1,j]        <- lala$y
  N.10[1,j]        <- lala$N
  comp.perc.10[1,j]  <- lala$comp.perc
  death.perc.10[1,j] <- lala$death.perc
}

g.10.bleed <- function(x) {
  a0 <- 341192*exp(x)-341192
  b0 <- 22182*exp(x)-6162*exp(x)+341192+6162
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-6162)))/(2*a0)
  x0 <- (6162-341192*y0)/22182
  22182*(x0-y0)
}
g.10.thromb <- function(x) {
  a0 <- 360013*exp(x)-360013
```

```
  b0 <- 3361*exp(x)-6162*exp(x)+360013+6162
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-6162)))/(2*a0)
  x0 <- (6162-360013*y0)/3361
  3361*(x0-y0)
}

g.10.bleed(x=Beta[1] )
(g.prim <- grad(func=g.10.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.10.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.10[1,1] + c(-1, 1)*1.96*AM.se)

g.10.thromb(x=Beta[2])
(g.prim <- grad(func=g.10.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.10.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.10[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.10 <- rbind(
  data.frame(Comp='BLEED',
             AM=Adj.AM.10[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.10[1,1], Y=y.10[1,1], N=N.10[1,1], comp.perc=comp.perc.10[1,1], death.perc=death.perc.10[1,1]),
  data.frame(Comp='VTE',
             AM=Adj.AM.10[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.10[1,2], Y=y.10[1,2], N=N.10[1,2], comp.perc=comp.perc.10[1,2], death.perc=death.perc.10[1,2]))
)
rownames(OUTPUT.10) <- NULL
OUTPUT.10$YEAR <- 2010
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.10)

# Year 2011 AM.OR ####
load('ModelResults_Y11.Rdata')

dat <- dat11; YEAR <- '2011'
COMP <- c("OTHBLEED","VTE")

OR   <- OR.cal(obj=fit.11, YEAR='Year 2011')$OR
Beta <- OR.cal(obj=fit.11, YEAR='Year 2011')$Beta
SE   <- OR.cal(obj=fit.11, YEAR='Year 2011')$SE
PVAL <- OR.cal(obj=fit.11, YEAR='Year 2011')$PVAL
OR.LOW <- OR.cal(obj=fit.11, YEAR='Year 2011')$LOW
OR.UPP <- OR.cal(obj=fit.11, YEAR='Year 2011')$UPP

a.11 <- b.11 <- c.11 <- p.c.11 <- p.nc.11 <- Comp.Rate.11 <- Adj.AM.11 <- Unadj.AM.11 <- matrix(NA, nrow=1, ncol=2)
N.11 <- comp.perc.11 <- death.perc.11 <- x.11 <- y.11 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.11[, COMP[i] ] <- sum( dat[,COMP[i]]!='NoComplication', na.rm=T)  #Complication
  b.11[, COMP[i] ] <- sum( dat[,COMP[i]]=='NoComplication', na.rm=T)  #No Complication
  c.11[, COMP[i] ] <- sum( dat[,'DEATH']==1, na.rm=T) #Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH',COMP[i])]
  p.c.11[, COMP[i] ]  <- mean(bla$DEATH==1, na.rm=T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH',COMP[i])]
  p.nc.11[, COMP[i] ] <- mean(bla$DEATH==1, na.rm=T)
  Comp.Rate.11[, COMP[i] ] <- mean(dat[[ COMP[i] ]]!='NoComplication', na.rm=T)
}

for (j in 1:2) {

  lala <- a.mort.cal(a=a.11[1,j], b=b.11[1,j], c=c.11[1,j], OR=OR[j], p.c=p.c.11[1,j], p.nc=p.nc.11[1,j])
  Adj.AM.11[1,j]   <- lala$AM.adj
  Unadj.AM.11[1,j] <- lala$AM.unadj
  x.11[1,j]        <- lala$x
  y.11[1,j]        <- lala$y
  N.11[1,j]        <- lala$N
  comp.perc.11[1,j]  <- lala$comp.perc
  death.perc.11[1,j] <- lala$death.perc
}

g.11.bleed <- function(x) {
  a0 <- 404959*exp(x)-404959
  b0 <- 37121*exp(x)-6982*exp(x)+404959+6982
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-6982)))/(2*a0)
  x0 <- (6982-404959*y0)/37121
  37121*(x0-y0)
}
g.11.thromb <- function(x) {
  a0 <- 438049*exp(x)-438049
  b0 <- 4031*exp(x)-6982*exp(x)+438049+6982
```

```
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-6982)))/(2*a0)
  x0 <- (6982-438049*y0)/4031
  4031*(x0-y0)
}

g.11.bleed(x=Beta[1] )
(g.prim <- grad(func=g.11.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.11.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.11[1,1] + c(-1, 1)*1.96*AM.se)

g.11.thromb(x=Beta[2])
(g.prim <- grad(func=g.11.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.11.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.11[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.11 <- rbind(
  data.frame(Comp='BLEED',
             AM=Adj.AM.11[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.11[1,1], Y=y.11[1,1], N=N.11[1,1], comp.perc=comp.perc.11[1,1], death.perc=death.perc.11[1,1]),
  data.frame(Comp='VTE',
             AM=Adj.AM.11[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.11[1,2], Y=y.11[1,2], N=N.11[1,2], comp.perc=comp.perc.11[1,2], death.perc=death.perc.11[1,2]))
)
rownames(OUTPUT.11) <- NULL
OUTPUT.11$YEAR <- 2011
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.11)

# Year 2012 AM.OR ####
load('ModelResults_Y12.Rdata')

dat <- dat12; YEAR <- '2012'
COMP <- c("OTHBLEED","VTE")

OR   <- OR.cal(obj=fit.12, YEAR='Year 2012')$OR
Beta <- OR.cal(obj=fit.12, YEAR='Year 2012')$Beta
SE   <- OR.cal(obj=fit.12, YEAR='Year 2012')$SE
PVAL <- OR.cal(obj=fit.12, YEAR='Year 2012')$PVAL
OR.LOW <- OR.cal(obj=fit.12, YEAR='Year 2012')$LOW
OR.UPP <- OR.cal(obj=fit.12, YEAR='Year 2012')$UPP

## Attributable mortality based on adjusted OR and observed complication prevalence
a.12 <- b.12 <- c.12 <- p.c.12 <- p.nc.12 <- Comp.Rate.12 <- Adj.AM.12 <- Unadj.AM.12 <- matrix(NA, nrow=1, ncol=2)
N.12 <- comp.perc.12 <- death.perc.12 <- x.12 <- y.12 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.12[, COMP[i] ] <- sum( dat[,COMP[i]]!='NoComplication', na.rm=T)  #Complication
  b.12[, COMP[i] ] <- sum( dat[,COMP[i]]=='NoComplication', na.rm=T)  #No Complication
  c.12[, COMP[i] ] <- sum( dat[,'DEATH']==1, na.rm=T) #Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH',COMP[i])]
  p.c.12[, COMP[i] ]  <- mean(bla$DEATH==1, na.rm=T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH',COMP[i])]
  p.nc.12[, COMP[i] ] <- mean(bla$DEATH==1, na.rm=T)
  Comp.Rate.12[, COMP[i] ] <- mean(dat[[ COMP[i] ]]!='NoComplication', na.rm=T)
}

for (j in 1:2) {

  lala <- a.mort.cal(a=a.12[1,j], b=b.12[1,j], c=c.12[1,j], OR=OR[j], p.c=p.c.12[1,j], p.nc=p.nc.12[1,j])
  Adj.AM.12[1,j]   <- lala$AM.adj
  Unadj.AM.12[1,j] <- lala$AM.unadj
  x.12[1,j]        <- lala$x
  y.12[1,j]        <- lala$y
  N.12[1,j]        <- lala$N
  comp.perc.12[1,j]  <- lala$comp.perc
  death.perc.12[1,j] <- lala$death.perc
}

g.12.bleed <- function(x) {
  a0 <- 503340*exp(x)-503340
  b0 <- 40500*exp(x)-6838*exp(x)+503340+6838
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-6838)))/(2*a0)
  x0 <- (6838-503340*y0)/40500
  40500*(x0-y0)
}
g.12.thromb <- function(x) {
  a0 <- 539133*exp(x)-539133
  b0 <- 4707*exp(x)-6838*exp(x)+539133+6838
```

```
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-6838)))/(2*a0)
  x0 <- (6838-539133*y0)/4707
  4707*(x0-y0)
}

g.12.bleed(x=Beta[1] )
(g.prim <- grad(func=g.12.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.12.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.12[1,1] + c(-1, 1)*1.96*AM.se)

g.12.thromb(x=Beta[2])
(g.prim <- grad(func=g.12.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.12.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.12[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.12 <- rbind(
  data.frame(Comp='BLEED',
             AM=Adj.AM.12[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.12[1,1], Y=y.12[1,1], N=N.12[1,1], comp.perc=comp.perc.12[1,1], death.perc=death.perc.12[1,1]),
  data.frame(Comp='VTE',
             AM=Adj.AM.12[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.12[1,2], Y=y.12[1,2], N=N.12[1,2], comp.perc=comp.perc.12[1,2], death.perc=death.perc.12[1,2]))
)
rownames(OUTPUT.12) <- NULL
OUTPUT.12$YEAR <- 2012
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.12)


# Year 2013 AM.OR ####
load('ModelResults_Y13.Rdata')

dat <- dat13; YEAR <- '2013'
COMP <- c("OTHBLEED","VTE")

OR   <- OR.cal(obj=fit.13, YEAR='Year 2013')$OR
Beta <- OR.cal(obj=fit.13, YEAR='Year 2013')$Beta
SE   <- OR.cal(obj=fit.13, YEAR='Year 2013')$SE
PVAL <- OR.cal(obj=fit.13, YEAR='Year 2013')$PVAL
OR.LOW <- OR.cal(obj=fit.13, YEAR='Year 2013')$LOW
OR.UPP <- OR.cal(obj=fit.13, YEAR='Year 2013')$UPP

## Attributable mortality based on adjusted OR and observed complication prevalence
a.13 <- b.13 <- c.13 <- p.c.13 <- p.nc.13 <- Comp.Rate.13 <- Adj.AM.13 <- Unadj.AM.13 <- matrix(NA, nrow=1, ncol=2)
N.13 <- comp.perc.13 <- death.perc.13 <- x.13 <- y.13 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.13[, COMP[i] ] <- sum( dat[,COMP[i]]!='NoComplication', na.rm=T)  #Complication
  b.13[, COMP[i] ] <- sum( dat[,COMP[i]]=='NoComplication', na.rm=T)  #No Complication
  c.13[, COMP[i] ] <- sum( dat[,'DEATH']==1, na.rm=T) #Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH',COMP[i])]
  p.c.13[, COMP[i] ]  <- mean(bla$DEATH==1, na.rm=T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH',COMP[i])]
  p.nc.13[, COMP[i] ] <- mean(bla$DEATH==1, na.rm=T)
  Comp.Rate.13[, COMP[i] ] <- mean(dat[[ COMP[i] ]]!='NoComplication', na.rm=T)
}

for (j in 1:2) {

  lala <- a.mort.cal(a=a.13[1,j], b=b.13[1,j], c=c.13[1,j], OR=OR[j], p.c=p.c.13[1,j], p.nc=p.nc.13[1,j])
  Adj.AM.13[1,j]   <- lala$AM.adj
  Unadj.AM.13[1,j] <- lala$AM.unadj
  x.13[1,j]        <- lala$x
  y.13[1,j]        <- lala$y
  N.13[1,j]        <- lala$N
  comp.perc.13[1,j]  <- lala$comp.perc
  death.perc.13[1,j] <- lala$death.perc
}

g.13.bleed <- function(x) {
  a0 <- 608469*exp(x)-608469
  b0 <- 43420*exp(x)-7877*exp(x)+608469+7877
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-7877)))/(2*a0)
  x0 <- (7877-608469*y0)/43420
  43420*(x0-y0)
}
g.13.thromb <- function(x) {
  a0 <- 646373*exp(x)-646373
```

```
  b0 <- 5516*exp(x)-7877*exp(x)+646373+7877
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-7877)))/(2*a0)
  x0 <- (7877-646373*y0)/5516
  5516*(x0-y0)
}

g.13.bleed(x=Beta[1] )
(g.prim <- grad(func=g.13.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.13.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.13[1,1] + c(-1, 1)*1.96*AM.se)

g.13.thromb(x=Beta[2])
(g.prim <- grad(func=g.13.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.13.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.13[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.13 <- rbind(
  data.frame(Comp='BLEED',
             AM=Adj.AM.13[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.13[1,1], Y=y.13[1,1], N=N.13[1,1], comp.perc=comp.perc.13[1,1], death.perc=death.perc.13[1,1]),
  data.frame(Comp='VTE',
             AM=Adj.AM.13[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.13[1,2], Y=y.13[1,2], N=N.13[1,2], comp.perc=comp.perc.13[1,2], death.perc=death.perc.13[1,2]))
)
rownames(OUTPUT.13) <- NULL
OUTPUT.13$YEAR <- 2013
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.13)

# Year 2014 AM.OR ####
load('ModelResults_Y14.Rdata')

dat <- dat14; YEAR <- '2014'
COMP <- c("OTHBLEED","VTE")

OR   <- OR.cal(obj=fit.14, YEAR='Year 2014')$OR
Beta <- OR.cal(obj=fit.14, YEAR='Year 2014')$Beta
SE   <- OR.cal(obj=fit.14, YEAR='Year 2014')$SE
PVAL <- OR.cal(obj=fit.14, YEAR='Year 2014')$PVAL
OR.LOW <- OR.cal(obj=fit.14, YEAR='Year 2014')$LOW
OR.UPP <- OR.cal(obj=fit.14, YEAR='Year 2014')$UPP

## Attributable mortality based on adjusted OR and observed complication prevalence
a.14 <- b.14 <- c.14 <- p.c.14 <- p.nc.14 <- Comp.Rate.14 <- Adj.AM.14 <- Unadj.AM.14 <- matrix(NA, nrow=1, ncol=2)
N.14 <- comp.perc.14 <- death.perc.14 <- x.14 <- y.14 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.14[, COMP[i] ] <- sum( dat[,COMP[i]]!='NoComplication', na.rm=T)  #Complication
  b.14[, COMP[i] ] <- sum( dat[,COMP[i]]=='NoComplication', na.rm=T)  #No Complication
  c.14[, COMP[i] ] <- sum( dat[,'DEATH']==1, na.rm=T) #Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH',COMP[i])]
  p.c.14[, COMP[i] ]  <- mean(bla$DEATH==1, na.rm=T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH',COMP[i])]
  p.nc.14[, COMP[i] ] <- mean(bla$DEATH==1, na.rm=T)
  Comp.Rate.14[, COMP[i] ] <- mean(dat[[ COMP[i] ]]!='NoComplication', na.rm=T)
}

for (j in 1:2) {

  lala <- a.mort.cal(a=a.14[1,j], b=b.14[1,j], c=c.14[1,j], OR=OR[j], p.c=p.c.14[1,j], p.nc=p.nc.14[1,j])
  Adj.AM.14[1,j]   <- lala$AM.adj
  Unadj.AM.14[1,j] <- lala$AM.unadj
  x.14[1,j]        <- lala$x
  y.14[1,j]        <- lala$y
  N.14[1,j]        <- lala$N
  comp.perc.14[1,j]  <- lala$comp.perc
  death.perc.14[1,j] <- lala$death.perc
}

g.14.bleed <- function(x) {
  a0 <- 707096*exp(x)-707096
  b0 <- 43805*exp(x)-9185*exp(x)+707096+9185
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-9185)))/(2*a0)
  x0 <- (9185-707096*y0)/43805
  43805*(x0-y0)
}
g.14.thromb <- function(x) {
  a0 <- 744593*exp(x)-744593
```

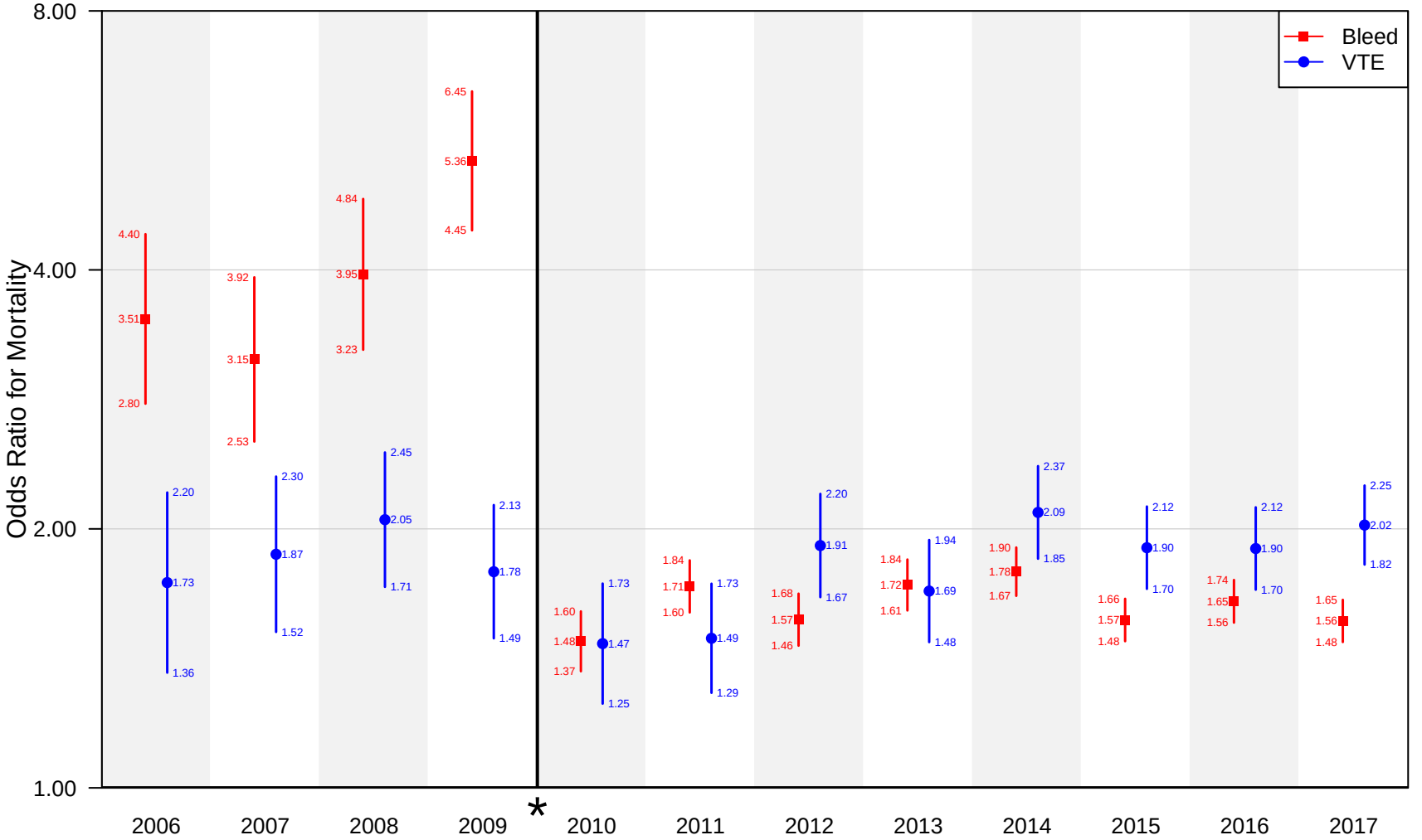
```
  b0 <- 6308*exp(x)-9185*exp(x)+744593+9185
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-9185)))/(2*a0)
  x0 <- (9185-744593*y0)/6308
  6308*(x0-y0)
}

g.14.bleed(x=Beta[1] )
(g.prim <- grad(func=g.14.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.14.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.14[1,1] + c(-1, 1)*1.96*AM.se)

g.14.thromb(x=Beta[2])
(g.prim <- grad(func=g.14.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.14.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.14[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.14 <- rbind(
  data.frame(Comp='BLEED',
             AM=Adj.AM.14[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.14[1,1], Y=y.14[1,1], N=N.14[1,1], comp.perc=comp.perc.14[1,1], death.perc=death.perc.14[1,1]),
  data.frame(Comp='VTE',
             AM=Adj.AM.14[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.14[1,2], Y=y.14[1,2], N=N.14[1,2], comp.perc=comp.perc.14[1,2], death.perc=death.perc.14[1,2]))
)
rownames(OUTPUT.14) <- NULL
OUTPUT.14$YEAR <- 2014
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.14)


# Year 2015 AM.OR ####
load('ModelResults_Y15.Rdata')

dat <- dat15; YEAR <- '2015'
COMP <- c("OTHBLEED","VTE")

OR   <- OR.cal(obj=fit.15, YEAR='Year 2015')$OR
Beta <- OR.cal(obj=fit.15, YEAR='Year 2015')$Beta
SE   <- OR.cal(obj=fit.15, YEAR='Year 2015')$SE
PVAL <- OR.cal(obj=fit.15, YEAR='Year 2015')$PVAL
OR.LOW <- OR.cal(obj=fit.15, YEAR='Year 2015')$LOW
OR.UPP <- OR.cal(obj=fit.15, YEAR='Year 2015')$UPP

## Attributable mortality based on adjusted OR and observed complication prevalence
a.15 <- b.15 <- c.15 <- p.c.15 <- p.nc.15 <- Comp.Rate.15 <- Adj.AM.15 <- Unadj.AM.15 <- matrix(NA, nrow=1, ncol=2)
N.15 <- comp.perc.15 <- death.perc.15 <- x.15 <- y.15 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.15[, COMP[i] ] <- sum( dat[,COMP[i]]!='NoComplication', na.rm=T)  # Complication
  b.15[, COMP[i] ] <- sum( dat[,COMP[i]]=='NoComplication', na.rm=T)  # No Complication
  c.15[, COMP[i] ] <- sum( dat[,'DEATH']==1, na.rm=T) #Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH',COMP[i])]
  p.c.15[, COMP[i] ]  <- mean(bla$DEATH==1, na.rm=T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH',COMP[i])]
  p.nc.15[, COMP[i] ] <- mean(bla$DEATH==1, na.rm=T)
  Comp.Rate.15[, COMP[i] ] <- mean(dat[[ COMP[i] ]]!='NoComplication', na.rm=T)
}
for (j in 1:2) {

  lala <- a.mort.cal(a=a.15[1,j], b=b.15[1,j], c=c.15[1,j], OR=OR[j], p.c=p.c.15[1,j], p.nc=p.nc.15[1,j])
  Adj.AM.15[1,j]   <- lala$AM.adj
  Unadj.AM.15[1,j] <- lala$AM.unadj
  x.15[1,j]        <- lala$x
  y.15[1,j]        <- lala$y
  N.15[1,j]        <- lala$N
  comp.perc.15[1,j]  <- lala$comp.perc
  death.perc.15[1,j] <- lala$death.perc
}

g.15.bleed <- function(x) {
  a0 <- 839838*exp(x)-839838
  b0 <- 45620*exp(x)-10683*exp(x)+839838+10683
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-10683)))/(2*a0)
  x0 <- (10683-839838*y0)/45620
  45620*(x0-y0)
}
g.15.thromb <- function(x) {
  a0 <- 878011*exp(x)-878011
```

```
  b0 <- 7447*exp(x)-10683*exp(x)+878011+10683
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-10683)))/(2*a0)
  x0 <- (10683-878011*y0)/7447
  7447*(x0-y0)
}

g.15.bleed(x=Beta[1] )
(g.prim <- grad(func=g.15.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.15.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.15[1,1] + c(-1, 1)*1.96*AM.se)

g.15.thromb(x=Beta[2])
(g.prim <- grad(func=g.15.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.15.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.15[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.15 <- rbind(
  data.frame(Comp='BLEED',
             AM=Adj.AM.15[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.15[1,1], Y=y.15[1,1], N=N.15[1,1], comp.perc=comp.perc.15[1,1], death.perc=death.perc.15[1,1]),
  data.frame(Comp='VTE',
             AM=Adj.AM.15[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.15[1,2], Y=y.15[1,2], N=N.15[1,2], comp.perc=comp.perc.15[1,2], death.perc=death.perc.15[1,2]))
)
rownames(OUTPUT.15) <- NULL
OUTPUT.15$YEAR <- 2015
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.15)


# Year 2016 AM.OR ####
load('ModelResults_Y16.Rdata')

dat <- dat16; YEAR <- '2016'
COMP <- c("OTHBLEED","VTE")

OR   <- OR.cal(obj=fit.16, YEAR='Year 2016')$OR
Beta <- OR.cal(obj=fit.16, YEAR='Year 2016')$Beta
SE   <- OR.cal(obj=fit.16, YEAR='Year 2016')$SE
PVAL <- OR.cal(obj=fit.16, YEAR='Year 2016')$PVAL
OR.LOW <- OR.cal(obj=fit.16, YEAR='Year 2016')$LOW
OR.UPP <- OR.cal(obj=fit.16, YEAR='Year 2016')$UPP

## Attributable mortality based on adjusted OR and observed complication prevalence
a.16 <- b.16 <- c.16 <- p.c.16 <- p.nc.16 <- Comp.Rate.16 <- Adj.AM.16 <- Unadj.AM.16 <- matrix(NA, nrow=1, ncol=2)
N.16 <- comp.perc.16 <- death.perc.16 <- x.16 <- y.16 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.16[, COMP[i] ] <- sum( dat[,COMP[i]]!='NoComplication', na.rm=T)  #Complication
  b.16[, COMP[i] ] <- sum( dat[,COMP[i]]=='NoComplication', na.rm=T)  #No Complication
  c.16[, COMP[i] ] <- sum( dat[,'DEATH']==1, na.rm=T) #Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH',COMP[i])]
  p.c.16[, COMP[i] ]  <- mean(bla$DEATH==1, na.rm=T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH',COMP[i])]
  p.nc.16[, COMP[i] ] <- mean(bla$DEATH==1, na.rm=T)
  Comp.Rate.16[, COMP[i] ] <- mean(dat[[ COMP[i] ]]!='NoComplication', na.rm=T)
}

for (j in 1:2) {

  lala <- a.mort.cal(a=a.16[1,j], b=b.16[1,j], c=c.16[1,j], OR=OR[j], p.c=p.c.16[1,j], p.nc=p.nc.16[1,j])
  Adj.AM.16[1,j]   <- lala$AM.adj
  Unadj.AM.16[1,j] <- lala$AM.unadj
  x.16[1,j]        <- lala$x
  y.16[1,j]        <- lala$y
  N.16[1,j]        <- lala$N
  comp.perc.16[1,j]  <- lala$comp.perc
  death.perc.16[1,j] <- lala$death.perc
}

g.16.bleed <- function(x) {
  a0 <- 953507*exp(x)-953507
  b0 <- 46844*exp(x)-11422*exp(x)+953507+11422
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-11422)))/(2*a0)
  x0 <- (11422-953507*y0)/46844
  46844*(x0-y0)
}
g.16.thromb <- function(x) {
```

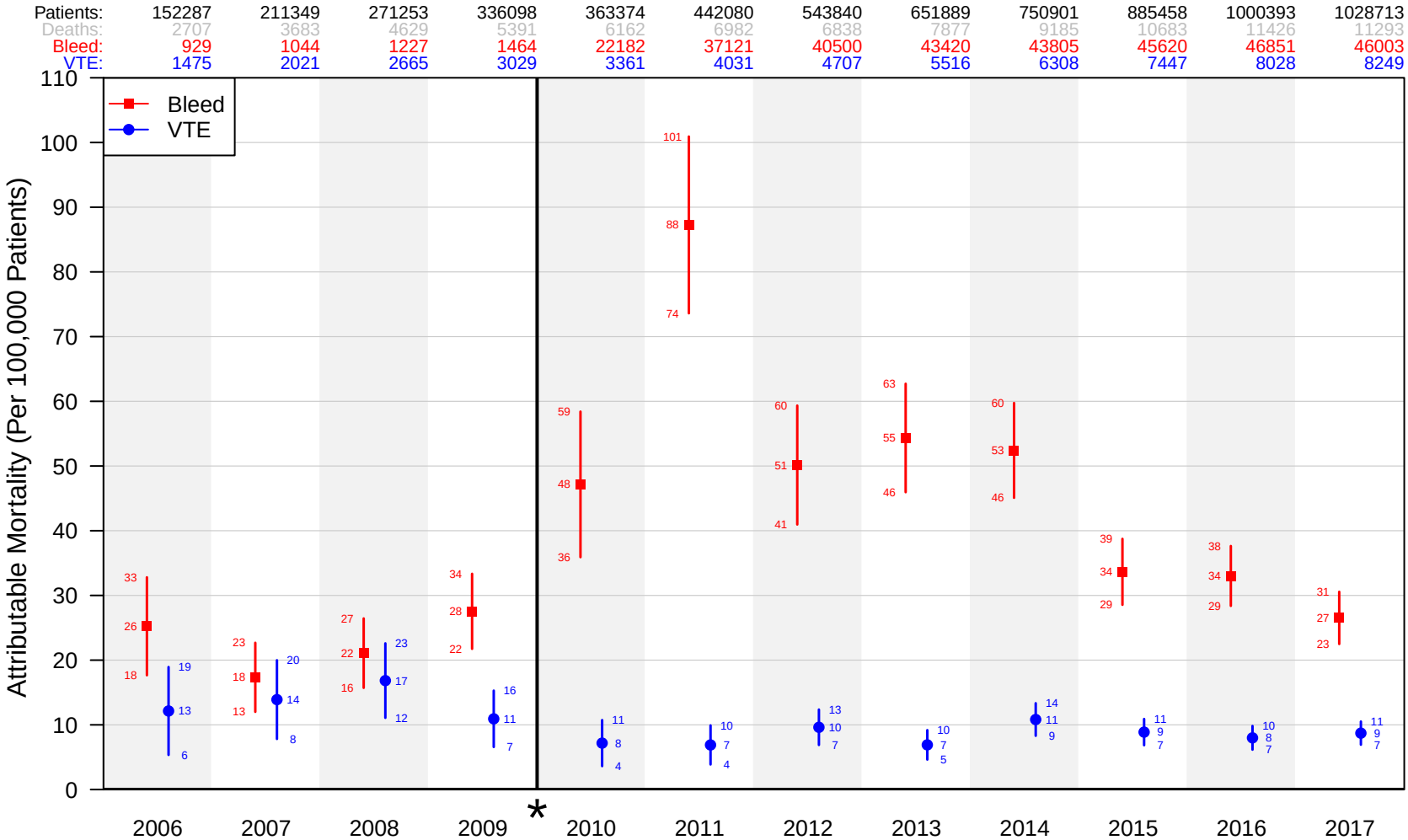
```
  a0 <- 992323*exp(x)-992323
  b0 <- 8028*exp(x)-11422*exp(x)+992323+11422
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-11422)))/(2*a0)
  x0 <- (11422-992323*y0)/8028
  8028*(x0-y0)
}

g.16.bleed(x=Beta[1] )
(g.prim <- grad(func=g.16.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.16.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.16[1,1] + c(-1, 1)*1.96*AM.se)

g.16.thromb(x=Beta[2])
(g.prim <- grad(func=g.16.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.16.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.16[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.16 <- rbind(
  data.frame(Comp='BLEED',  AM=Adj.AM.16[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],    OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.16[1,1], Y=y.16[1,1], N=N.16[1,1], comp.perc=comp.perc.16[1,1], death.perc=death.perc.16[1,1]),
  data.frame(Comp='VTE', AM=Adj.AM.16[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.16[1,2], Y=y.16[1,2], N=N.16[1,2], comp.perc=comp.perc.16[1,2], death.perc=death.perc.16[1,2]))
)
rownames(OUTPUT.16) <- NULL
OUTPUT.16$YEAR <- 2016
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.16)


# Year 2017 AM.OR ####
load('ModelResults_Y17.Rdata')

dat <- dat17; YEAR <- '2017'
COMP <- c("OTHBLEED","VTE")

OR   <- OR.cal(obj=fit.17, YEAR='Year 2017')$OR
Beta <- OR.cal(obj=fit.17, YEAR='Year 2017')$Beta
SE   <- OR.cal(obj=fit.17, YEAR='Year 2017')$SE
PVAL <- OR.cal(obj=fit.17, YEAR='Year 2017')$PVAL
OR.LOW <- OR.cal(obj=fit.17, YEAR='Year 2017')$LOW
OR.UPP <- OR.cal(obj=fit.17, YEAR='Year 2017')$UPP

## Attributable mortality based on adjusted OR and observed complication prevalence
a.17 <- b.17 <- c.17 <- p.c.17 <- p.nc.17 <- Comp.Rate.17 <- Adj.AM.17 <- Unadj.AM.17 <- matrix(NA, nrow=1, ncol=2)
N.17 <- comp.perc.17 <- death.perc.17 <- x.17 <- y.17 <- matrix(NA, nrow=1, ncol=2)

for ( i in 1:length(COMP) ) {
  a.17[, COMP[i] ] <- sum( dat[,COMP[i]]!='NoComplication', na.rm=T)  #Complication
  b.17[, COMP[i] ] <- sum( dat[,COMP[i]]=='NoComplication', na.rm=T)  #No Complication
  c.17[, COMP[i] ] <- sum( dat[,'DEATH']==1, na.rm=T) #Death

  bla <- dat[ dat[[ COMP[i] ]] != 'NoComplication', c('DEATH',COMP[i])]
  p.c.17[, COMP[i] ]  <- mean(bla$DEATH==1, na.rm=T)
  bla <- dat[ dat[[ COMP[i] ]] == 'NoComplication', c('DEATH',COMP[i])]
  p.nc.17[, COMP[i] ] <- mean(bla$DEATH==1, na.rm=T)
  Comp.Rate.17[, COMP[i] ] <- mean(dat[[ COMP[i] ]]!='NoComplication', na.rm=T)
}

for (j in 1:2) {

  lala <- a.mort.cal(a=a.17[1,j], b=b.17[1,j], c=c.17[1,j], OR=OR[j], p.c=p.c.17[1,j], p.nc=p.nc.17[1,j])
  Adj.AM.17[1,j]   <- lala$AM.adj
  Unadj.AM.17[1,j] <- lala$AM.unadj
  x.17[1,j]        <- lala$x
  y.17[1,j]        <- lala$y
  N.17[1,j]        <- lala$N
  comp.perc.17[1,j]  <- lala$comp.perc
  death.perc.17[1,j] <- lala$death.perc
}

g.17.bleed <- function(x) {
  a0 <- 982665*exp(x)-982665
  b0 <- 45999*exp(x)-11291*exp(x)+982665+11291
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-11291)))/(2*a0)
  x0 <- (11291-982665*y0)/45999
  45999*(x0-y0)
}
g.17.thromb <- function(x) {
  a0 <- 1020415*exp(x)-1020415
```

```
  b0 <- 8249*exp(x)-11291*exp(x)+1020415+11291
  y0 <- (-b0 + sqrt( b0^2 -4*a0*(-11291)))/(2*a0)
  x0 <- (11291-1020415*y0)/8249
  8249*(x0-y0)
}

g.17.bleed(x=Beta[1] )
(g.prim <- grad(func=g.17.bleed, x=Beta[1]))
(AM.se <- abs(grad(func=g.17.bleed, x=Beta[1])*SE[1]))
(AM.CI.1 <- Adj.AM.17[1,1] + c(-1, 1)*1.96*AM.se)

g.17.thromb(x=Beta[2])
(g.prim <- grad(func=g.17.thromb, x=Beta[2]))
(AM.se <- abs(grad(func=g.17.thromb, x=Beta[2])*SE[2]))
(AM.CI.2 <- Adj.AM.17[1,2] + c(-1, 1)*1.96*AM.se)

(OUTPUT.17 <- rbind(
  data.frame(Comp='BLEED',  AM=Adj.AM.17[1,1], AM.LOW=AM.CI.1[1], AM.UPP=AM.CI.1[2],
             OR=OR[1],          OR.LOW=OR.LOW[1],  OR.UPP=OR.UPP[1], OR.PVAL=PVAL[1],
             X=x.17[1,1], Y=y.17[1,1], N=N.17[1,1], comp.perc=comp.perc.17[1,1], death.perc=death.perc.17[1,1]),
  data.frame(Comp='VTE', AM=Adj.AM.17[1,2], AM.LOW=AM.CI.2[1], AM.UPP=AM.CI.2[2],
             OR=OR[2],          OR.LOW=OR.LOW[2],  OR.UPP=OR.UPP[2], OR.PVAL=PVAL[2],
             X=x.17[1,2], Y=y.17[1,2], N=N.17[1,2], comp.perc=comp.perc.17[1,2], death.perc=death.perc.17[1,2]))
)
rownames(OUTPUT.17) <- NULL
OUTPUT.17$YEAR <- 2017
OUTPUT.ALL <- rbind(OUTPUT.ALL, OUTPUT.17)
```

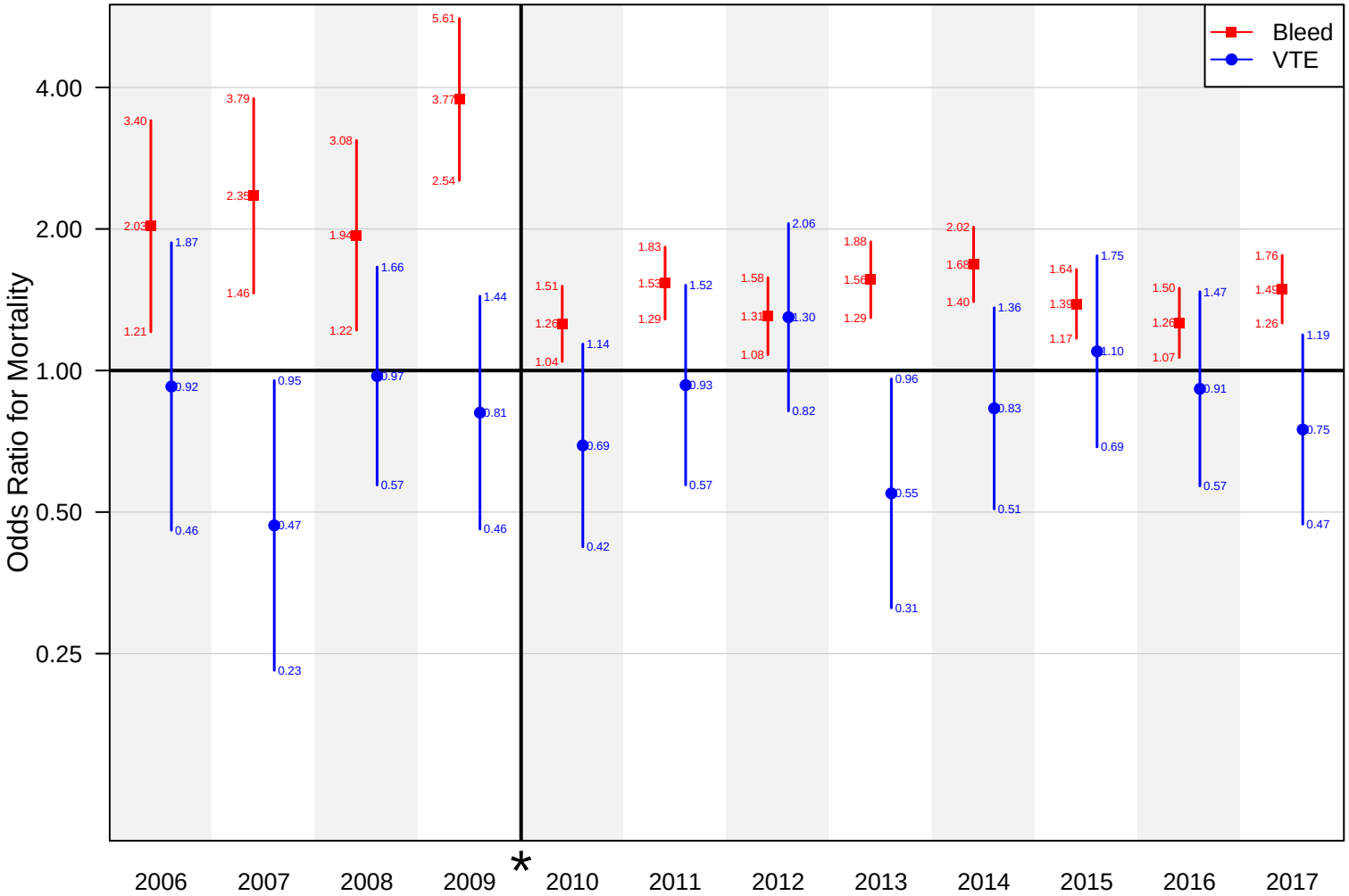
Supplementary Appendix 3: Sensitivity analysis excluding postoperative complications. The adjusted odds ratio for mortality by year, with break and * denoting definition change for bleeding starting in 2010. VTE= venous thromboembolism



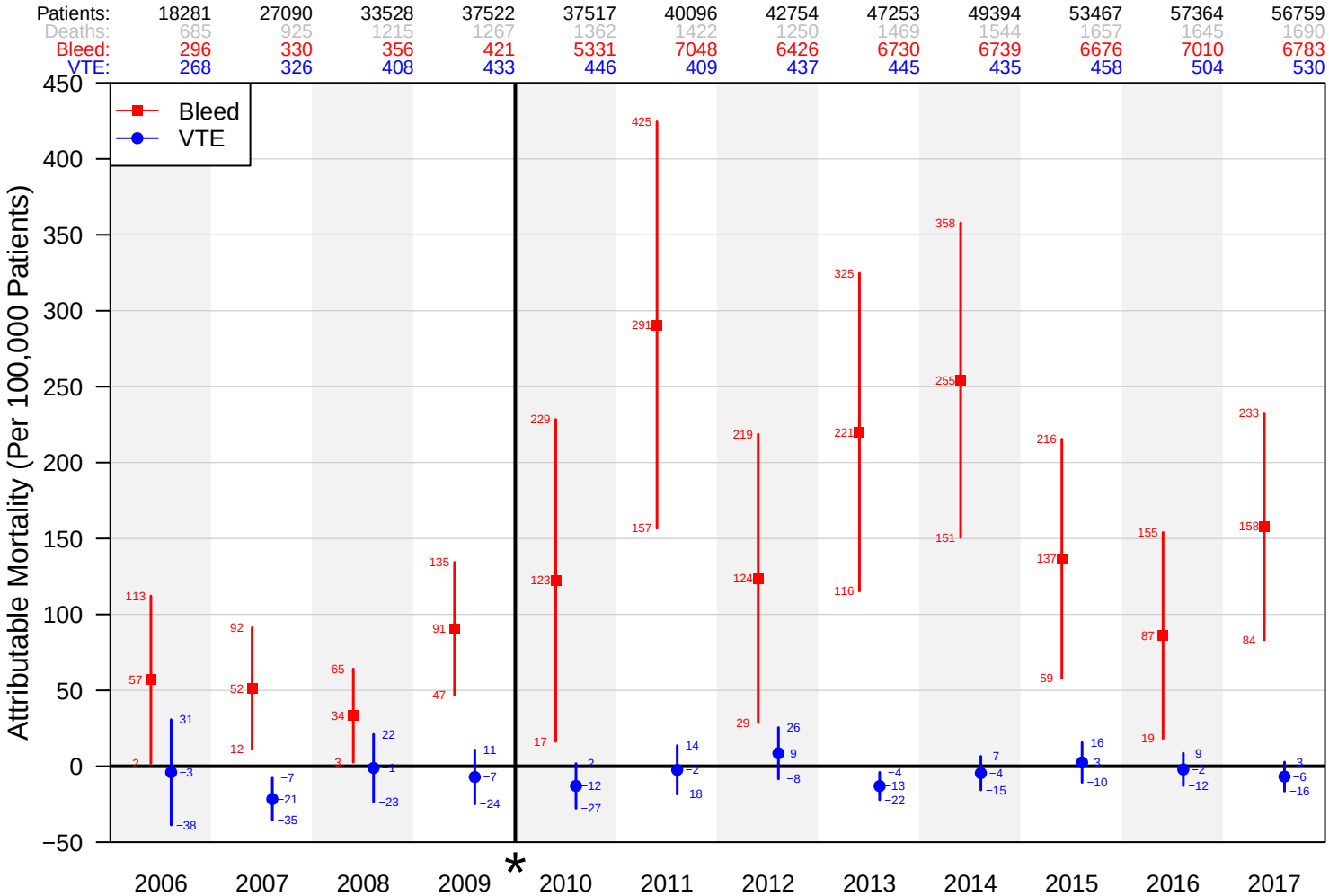
Supplementary Appendix 4: Sensitivity analysis excluding postoperative complications. The attributable mortality by year, normalized per 100,000 patients, with break and * denoting definition change for bleeding starting in 2010. VTE= venous thromboembolism



Supplementary Appendix 5: Sensitivity analysis of vascular surgery patients. The adjusted odds ratio for mortality by year, with break and * denoting definition change for bleeding starting in 2010. VTE= venous thromboembolism



Supplementary Appendix 6: Sensitivity analysis of vascular surgery patients. The attributable mortality by year, normalized per 100,000 patients, with break and * denoting definition change for bleeding starting in 2010. VTE= venous thromboembolism



Supplementary Appendix 7: Table of NSQIP variables adjusted for by year. X = included in analysis. Blank = not included. Variable names and definitions provided by ACS-NSQIP and available in the Participant Use Data File (PUF) by year at https://www.facs.org/quality-programs/acs-nsqip/participant-use.

ACS-NSQIP Variable	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
SUPINFEC	X	X	X	X	X	X	X	X	X	X	X	X
WNDINFD	X	X	X	X	X	X	X			X	X	X
ORGSPCSSI			X	X	X		X	X		X	X	
DEHIS		X		X	X		X	X	X	X		
OUPNEUMO	X	X	X	X	X	X	X	X	X	X	X	X
REINTUB	X	X	X	X	X	X	X	X	X	X	X	X
FAILWEAN	X	X	X	X	X	X	X	X	X	X	X	X
RENAINSF	X	X	X	X	X	X	X	X	X	X	X	X
OPRENAFL	X	X	X	X	X	X	X	X	X	X	X	X
URNINFEC		X	X	X	X		X	X		X	X	X
CNSCVA	X	X	X	X	X	X	X	X	X	X	X	X
CDARREST	X	X	X	X	X	X	X	X	X	X	X	X
CDMI	X	X	X	X	X	X	X	X	X	X	X	X
OTHSYSEP	X	X	X	X	X	X	X	X	X	X	X	X
OTHSESHOCK	X	X	X	X	X	X	X	X	X	X	X	X
AGE	X	X	X	X	X	X	X	X	X	X	X	X
SEX				X		X	X	X	X	X	X	X
RACE2		X	X	X		X	X	X	X	X	X	X
HEIGHT		X				X	X				X	X
WEIGHT	X	X	X	X	X	X	X	X	X	X	X	X
WORKRVU		X	X	X	X	X	X	X	X	X	X	X
INOUT	X	X	X	X	X	X	X	X	X	X	X	X
TRANST2	X	X	X	X	X	X	X	X	X	X	X	X
ANESTHES2			X	X			X	X				X
SURGSPEC2						X	X	X	X		X	X
EMERGNCY	X	X	X	X	X	X	X	X	X	X	X	X
WNDCLAS	X	X	X	X	X	X	X			X	X	
ASACLAS2	X	X	X	X	X	X	X	X	X	X	X	X
CLASS	X	X	X	X	X	X	X	X	X	X	X	X
DIABETES		X	X	X	X		X	X		X	X	X
SMOKE			X		X				X	X	X	X
DYSPNEA	X	X	X	X	X	X	X	X	X	X	X	X
FNSTATUS2.f	X	X	X	X	X	X	X	X	X	X	X	X

VENTILAT	X	X	X	X	X	X	X	X	X	X	X	X
HXCOPD	X	X	X	X	X	X	X	X	X	X	X	X
ASCITES	X	X	X	X	X	X	X	X	X	X	X	X
HXCHF	X	X	X	X	X	X	X	X	X	X	X	X
HYPERMED							X	X		X	X	X
RENAFAIL					X		X	X		X	X	X
DIALYSIS	X	X	X	X	X	X	X	X	X	X	X	X
DISCANCR	X	X	X	X	X	X	X	X	X	X	X	X
WNDINF	X	X	X	X	X	X	X	X	X	X	X	X
STEROID	X	X	X	X	X	X	X	X	X	X	X	X
WTLOSS	X	X	X	X	X	X	X	X	X	X	X	X
TRANSFUS	X	X	X	X	X	X	X	X	X	X	X	X
PRSEPIS	X	X	X	X	X	X	X	X	X	X	X	X
OPTIME	X	X	X	X	X	X	X	X	X	X	X	X
TOTHLOS	X	X	X	X	X	X	X	X	X	X	X	X
HTOODAY	X	X	X	X	X	X	X	X	X	X	X	X
RETURNOR	X	X	X	X	X	X	X	X	X	X	X	X
PRSODM0												
PRBUN0	X	X	X	X	X	X	X	X	X	X	X	X
PRCREAT0						X			X		X	
PRALBUM0		X	X	X	X	X	X	X	X	X	X	X
PRBILI0	X	X	X	X	X	X	X	X	X	X	X	X
PRSGOT0	X	X	X	X	X	X	X	X	X	X	X	X
PRALKPH0	X	X	X	X	X	X	X	X	X	X	X	X
PRWBC0	X	X	X	X	X	X	X	X	X	X	X	X
PRHCT0	X	X	X	X	X	X	X	X	X	X	X	X
PRPLATE0	X	X	X	X	X	X	X	X	X	X	X	X
PRPTT0	X	X	X			X						
PRINR0	X	X	X	X	X	X	X	X	X	X	X	X
PRPT0	X	X					X					X
PRSODM.i												
PRBUN.i									X			
PRCREAT.i												X
PRALBUM.i		X	X	X	X	X	X	X	X	X	X	X

PRBILI.i					
PRSGOT.i				X	
PRALKPH.i		X			
PRWBC.i					
PRHCT.i				X	X
PRPLATE.i		X			X
PRPTT.i		X	X	X	
PRINR.i				X	X
PRPT.i	X		X		X

All variable names and definitions are as provided by ACS-NSQIP

Supplementary Table 1: Population Demographics

	2006	**2007**	**2008**	**2009**	**2010**	**2011**
	N = 152,287	**N = 211,349**	**N = 271,253**	**N = 336,098**	**N = 363,374**	**N = 442,080**
Age	54 (42,67)	56 (43,68)	56 (43,68)	57 (44,68)	57 (44,68)	57 (45,69)
Female	88,363 (58)	120,853 (57)	155,265 (57)	192,505 (57)	206,306 (57)	252,186 (57)
Race						
White	120,983 (79)	169,938 (80)	236,959 (87)	291,735 (87)	304,359 (87)	379,494 (87)
Black	14,739 (10)	20,963 (10)	27,037 (10)	33,911 (10)	35,784 (10)	41,910 (10)
Other	16,565 (11)	20,448 (10)	7,257 (3)	10,452 (3)	11,052 (3)	16,471 (4)
Height (cm)	168 (160,175)	168 (160,175)	168 (160,175)	168 (160,175)	168 (160,175)	168 (160,175)
Weight (kg)	79 (66,95)	80 (67,96)	81 (67,97)	81 (68,98)	82 (68,98)	81 (68,97)
ASA						
1	17,656 (12)	21,955 (10)	26,509 (10)	31,230 (10)	33,477 (9)	40,551 (9)

2	72,118 (47)	95,042 (45)	122,264 (45)	153,278 (46)	165,303 (46)	199,600 (45)
3	53,002 (35)	78,324 (37)	101,778 (38)	126,713 (38)	138,336 (38)	170,524 (39)
4/5	9,511 (6)	15,086 (7)	19,638 (7)	23,628 (7)	24,907 (7)	29,899 (7)
	2012	**2013**	**2014**	**2015**	**2016**	**2017**
	N = 543,840	**N = 651,889**	**N = 750,901**	**N = 885,458**	**N = 1,000,393**	**N = 1,028,713**
Age	58 (45,69)	58 (45,69)	57 (44,68)	58 (45,69)	58 (45,69)	58 (45,69)
Female	311,667 (57)	375,105 (58)	426,707 (57)	501,385 (57)	565,490 (57)	585,478 (57)
Race						
White	471,886 (87)	563,340 (86)	645,450 (86)	763,493 (86)	864,187 (86)	885,013 (86)
Black	50,556 (9)	62,776 (10)	75,885 (10)	88,941 (10)	100,518 (10)	105,303 (10)
Other	21,398 (4)	25,771 (4)	29,566 (4)	33,024 (4)	35,688 (4)	38,397 (4)
Height (cm)	168 (160,175)	168 (160,175)	168 (160,175)	168 (160,175)	168 (160,175)	168 (160,175)

Weight (kg)	81 (68,97)	81 (68,97)	82 (68,98)	82 (69,98)	82 (69,98)	82 (68,98)
ASA						
1	51,843 (10)	59,685 (9)	69,676 (9)	79,479 (9)	86,036 (9)	84,803 (8)
2	248,058 (46)	294,615 (45)	337,674 (45)	396,550 (45)	444,683 (45)	456,322 (45)
3	208,612 (39)	255,592 (39)	296,028 (40)	352,733 (40)	404,839 (41)	423,328 (41)
4/5	33,658 (6)	40,172 (6)	45,522 (6)	54,236 (6)	62,076 (6)	61,921 (6)

Data are shown in median (25th, 75th percentile) for continuous variables, and n (%) for categorical variables. ASA = American Society of Anesthesiologists' Physical Status Classification

Supplementary Table 2: Complications By Year

	2006	**2007**	**2008**	**2009**	**2010**	**2011**
	N = 152287	**N = 211349**	**N = 271253**	**N = 336098**	**N = 363374**	**N = 442080**
Death	2707 (1.8)	3683 (1.7)	4629 (1.7)	5391 (1.6)	6162 (1.7)	6982 (1.6)
Bleeding	929 (0.6)	1044 (0.5)	1227 (0.5)	1464 (0.4)	22182 (6.1)	37121 (8.4)
VTE	1475 (1.0)	2021 (1.0)	2665 (1.0)	3029 (0.9)	3361 (0.9)	4031 (0.9)
Superficial SSI	5049 (3.3)	6523 (3.1)	7514 (2.8)	8495 (2.5)	8248 (2.3)	9171 (2.1)
Deep SSI	1417 (0.9)	1758 (0.8)	2029 (0.7)	2269 (0.7)	2308 (0.6)	3132 (0.7)
Organ Space SSI	2001 (1.3)	2922 (1.4)	3429 (1.3)	3990 (1.2)	4217 (1.2)	5244 (1.2)
Wound Dehiscence	1072 (0.7)	1373 (0.6)	1618 (0.6)	1839 (0.5)	1909 (0.5)	2136 (0.5)
Pneumonia	3138 (2.1)	3824 (1.8)	4105 (1.5)	4894 (1.5)	4774 (1.3)	5868 (1.3)
Reintubation	2385 (1.6)	3130 (1.5)	3677 (1.4)	4300 (1.3)	4395 (1.2)	4871 (1.1)
Pulmonary Embolism	422 (0.3)	654 (0.3)	893 (0.3)	1076 (0.3)	1206 (0.3)	1534 (0.3)
Failure to Wean	3875 (2.5)	5224 (2.5)	6198 (2.3)	6895 (2.1)	6892 (1.9)	7415 (1.7)
Renal Insufficiency	600 (0.4)	798 (0.4)	961 (0.4)	1123 (0.3)	1251 (0.3)	1523 (0.3)
Renal Failure	874 (0.6)	1094 (0.5)	1297 (0.5)	1644 (0.5)	1482 (0.4)	1749 (0.4)
Urinary Tract Infection	2696 (1.8)	3588 (1.7)	4406 (1.6)	5387 (1.6)	5881 (1.6)	7518 (1.7)
Stroke	395 (0.3)	520 (0.2)	739 (0.3)	872 (0.3)	887 (0.2)	1021 (0.2)
Cardiac Arrest	701 (0.5)	902 (0.4)	1162 (0.4)	1393 (0.4)	1398 (0.4)	1612 (0.4)
Myocardial Infarction	258 (0.2)	357 (0.2)	448 (0.2)	1519 (0.5)	1533 (0.4)	1780 (0.4)
Systemic Sepsis	4155 (2.7)	4862 (2.3)	5293 (2.0)	5662 (1.7)	5761 (1.6)	6613 (1.5)
Septic Shock	2621 (1.7)	3351 (1.6)	3221 (1.2)	2982 (0.9)	2863 (0.8)	3141 (0.7)
	2012	**2013**	**2014**	**2015**	**2016**	**2017**
	N = 543840	**N = 651889**	**N = 750901**	**N = 885458**	**N = 1000393**	**N = 1028713**

Death	6838 (1.3)	7877 (1.2)	9185 (1.2)	10683 (1.2)	11426 (1.1)	11293 (1.1)
Bleeding	40500 (7.4)	43420 (6.7)	43805 (5.8)	45620 (5.2)	46851 (4.7)	46003 (4.5)
VTE	4707 (0.9)	5516 (0.8)	6308 (0.8)	7447 (0.8)	8028 (0.8)	8249 (0.8)
Superficial SSI	10061 (1.8)	11064 (1.7)	12196 (1.6)	13071 (1.5)	14077 (1.4)	13713 (1.3)
Deep SSI	3149 (0.6)	4121 (0.6)	4846 (0.6)	5085 (0.6)	4226 (0.4)	3960 (0.4)
Organ Space SSI	5776 (1.1)	7543 (1.2)	9305 (1.2)	11146 (1.3)	13578 (1.4)	14664 (1.4)
Wound Dehiscence	2275 (0.4)	2783 (0.4)	3028 (0.4)	3391 (0.4)	3601 (0.4)	3493 (0.3)
Pneumonia	6196 (1.1)	8052 (1.2)	9736 (1.3)	11309 (1.3)	11835 (1.2)	11451 (1.1)
Reintubation	5010 (0.9)	5873 (0.9)	6352 (0.8)	6848 (0.8)	6925 (0.7)	6859 (0.7)
Pulmonary Embolism	1800 (0.3)	2131 (0.3)	2514 (0.3)	3066 (0.3)	3229 (0.3)	3367 (0.3)
Failure to Wean	6693 (1.2)	7506 (1.2)	7743 (1.0)	8720 (1.0)	8867 (0.9)	8411 (0.8)
Renal Insufficiency	1440 (0.3)	1692 (0.3)	1949 (0.3)	2249 (0.3)	2461 (0.2)	2409 (0.2)
Renal Failure	1730 (0.3)	1946 (0.3)	2178 (0.3)	2411 (0.3)	2577 (0.3)	2472 (0.2)
UTI	8465 (1.6)	9164 (1.4)	9998 (1.3)	11607 (1.3)	12168 (1.2)	12229 (1.2)
Stroke	1083 (0.2)	1318 (0.2)	1414 (0.2)	1742 (0.2)	1981 (0.2)	1971 (0.2)
Cardiac Arrest	1615 (0.3)	2004 (0.3)	2353 (0.3)	2827 (0.3)	2958 (0.3)	3056 (0.3)
Myocardial Infarction	1997 (0.4)	2103 (0.3)	2618 (0.3)	3339 (0.4)	3794 (0.4)	3858 (0.4)
Systemic Sepsis	7752 (1.4)	10168 (1.6)	13306 (1.8)	14594 (1.6)	16369 (1.6)	17252 (1.7)
Septic Shock	3743 (0.7)	5595 (0.9)	6961 (0.9)	7347 (0.8)	7852 (0.8)	7743 (0.8)

Cell values denote number and percentage. SSI= surgical site infection; DVT= deep venous thrombosis; UTI= urinary tract infection