# A Decision Theoretic Approach to Panel-Based, Pre-emptive Genotyping
# Appendix I

Table A1.1: C-index for the random survival forests as a function of node size (5, 25, and 50) and by the number of trees (100, 250, and 500) with number of splits for continuous variables equal to 10 and the number of variables tested at each split equal to 5. We boldfaced the model reported in the main text of the manuscript. We considered calibration and predicted risk distributions when choosing which set of parameters to report in the main text (see figure A1).

| N Tree | Node Size | Antiplatelet | | | Statin | | | Warfarin | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Original | Out of Bag | Testing | Original | Out of Bag | Testing | Original | Out of Bag | Testing |
| 100 | 5 | 0.9928 | 0.8496 | 0.7813 | 0.9607 | 0.737 | 0.6819 | 0.9869 | 0.761 | 0.6688 |
| | 25 | 0.9792 | 0.84 | 0.8023 | 0.8746 | 0.7111 | 0.6897 | 0.9675 | 0.7445 | 0.6871 |
| | 50 | 0.9538 | 0.8313 | 0.8075 | 0.8044 | 0.7008 | 0.693 | 0.9232 | 0.7338 | 0.6909 |
| 250 | 5 | 0.9928 | 0.868 | 0.7935 | 0.9613 | 0.749 | 0.6855 | 0.987 | 0.7814 | 0.6785 |
| | 25 | 0.98 | 0.8493 | 0.8073 | 0.8766 | 0.7163 | 0.6911 | 0.969 | 0.7542 | 0.691 |
| | 50 | 0.955 | 0.8379 | 0.8107 | 0.8059 | 0.7038 | 0.6922 | 0.925 | 0.7387 | 0.6939 |
| 500 | 5 | 0.9929 | 0.8742 | 0.7961 | **0.9615** | **0.7542** | **0.6864** | 0.987 | 0.7924 | 0.6808 |
| | 25 | **0.9804** | **0.8527** | **0.8088** | 0.8773 | 0.7177 | 0.6924 | **0.9698** | **0.7571** | **0.6912** |
| | 50 | 0.9552 | 0.8393 | 0.8099 | 0.8063 | 0.7046 | 0.6931 | 0.9259 | 0.741 | 0.6937 |

Table A1.2: Concordance C indices for two-year risks

| Model | Medication | Average across bootstrap samples in the 2010-2012 training cohort | Optimism corrected by applying constructed models to out of bag samples | Applying the final model based on the 2010-2012 cohort to the 2013-2015 cohort |
|---|---|---|---|---|
| Antiplatelet | Cox without interactions | 0.782 | 0.781 | 0.802 |
| | Cox with interactions | 0.792 | 0.789 | 0.806 |
| | RSF | 0.980 | 0.853 | 0.809 |
| | | | | |
| Statin | Cox without interactions | 0.676 | 0.676 | 0.697 |
| | Cox with interactions | 0.679 | 0.677 | 0.694 |
| | RSF | 0.962 | 0.754 | 0.686 |
| | | | | |
| Warfarin | Cox without interactions | 0.683 | 0.682 | 0.691 |
| | Cox with interactions | 0.687 | 0.685 | 0.692 |
| | RSF | 0.970 | 0.757 | 0.691 |

* Out of bag C index for RSF with optimal parameter selection: ntree = 500, nsplit = 10, mtry = 5, and node size = 25 (Antiplatelet, Warfarin), 5 (Statin)

Table A1.3: Adverse Events and medication failures included in Discrete Event Simulations

| Adverse Event | Clopidogrel | Simvastatin | Warfarin |
|---|---|---|---|
| Mild Myopathy | | X | |
| Moderate Myopathy | | X | |
| Severe Myopathy | | X | |
| Severe Myopathy Death | | X | |
| CVD | | X | |
| CVD Death | | X | |
| Non-fatal Gastrointestinal Bleed | | | X |
| Non-fatal Extracranial Bleed | X | | |
| Non-fatal Intracranial Bleed | X | | X |
| Non-fatal Minor Bleed | X | | X |
| Other Non-fatal Major Bleed | | | X |
| CABG-Related Bleed | X | | |
| Fatal Bleed | X | | |
| Fatal Intracranial Bleed | | | X |
| Fatal Gastrointestinal Bleed | | | X |
| Other Fatal Major Bleed | | | X |
| Fatal Stent Thrombosis | X | | |
| ST CABG | X | | |
| ST PCI | X | | |
| MI CABG | X | | |
| MI Medical Management | X | | |
| MI PCI | X | | |
| Revascularization CABG | X | | |
| Revascularization PCI | X | | |
| Non-fatal Deep Vein Thrombosis | | | X |
| Non-fatal Pulmonary Embolism | | | X |
| Stroke Minor Deficit | | | X |
| Stroke Major Deficit | | | X |
| Fatal Stroke | | | X |
| Fatal DVTPE | | | X |

Figure A1.1: Calibration and distribution for predicted two-year risks. Risk estimates were calculated by applying random survival forests developed on the training data and applying them to the testing data. We fixed nsplit=10 and mtry=5, and then examine model performance for ntree=100, 250, and 500 and for node size= 5, 25, and 50. Each dot represents 1/500$^{th}$ of the data in each plot, and the smooth lines and the 95% confidence band were calculated using the local polynomial regression fitting (LOESS). The "syringe" plot or extended boxplot shows the 1$^{st}$, 10$^{th}$, 25$^{th}$, 50$^{th}$, 75$^{th}$, 90$^{th}$, 99$^{th}$ percentiles, and the standard deviation of the predicted risk distribution is displayed numerically.

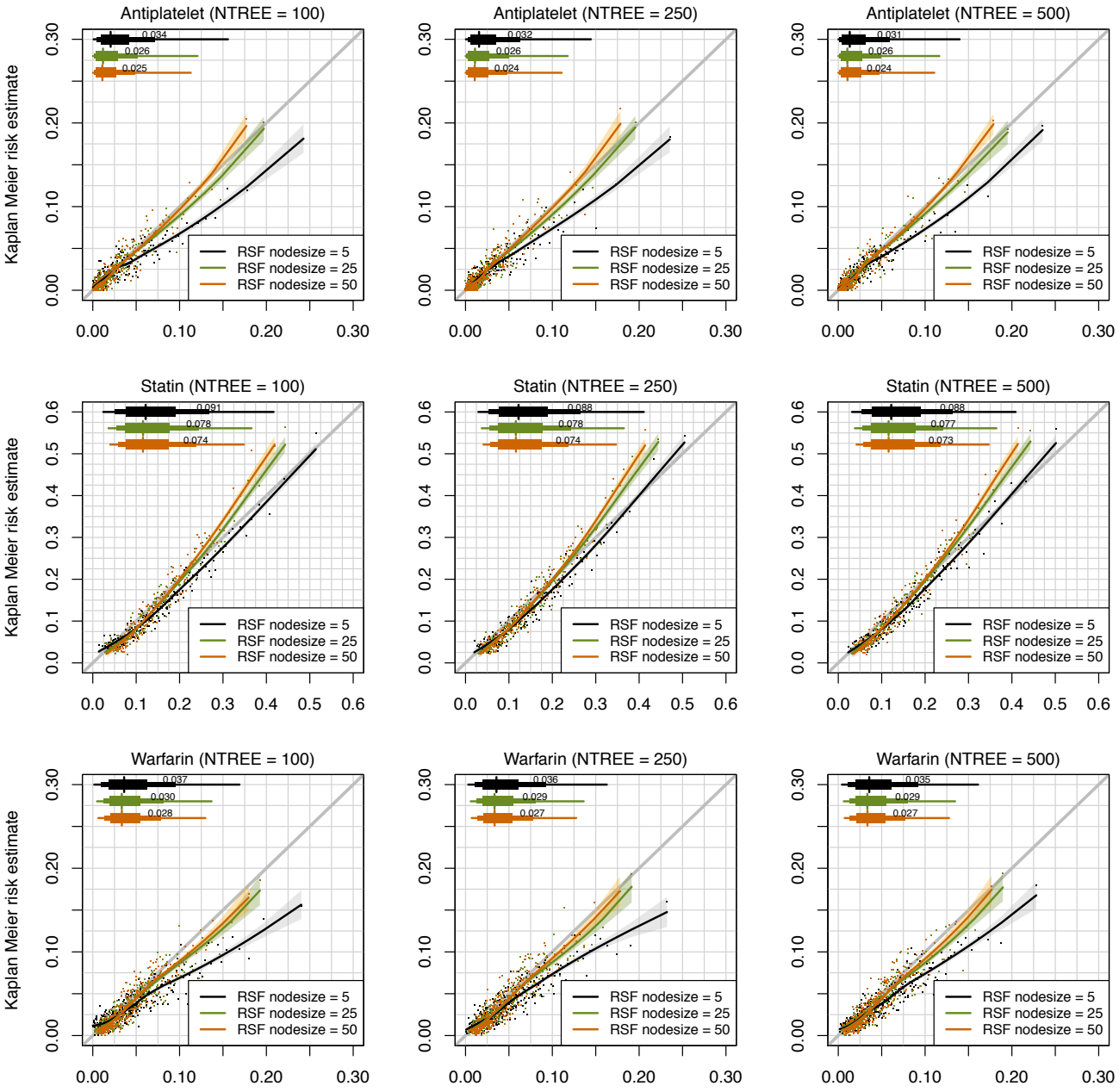


Figure A1.2: The Cox proportional hazard model effect estimates and 95% confidence intervals for antiplatelet model.

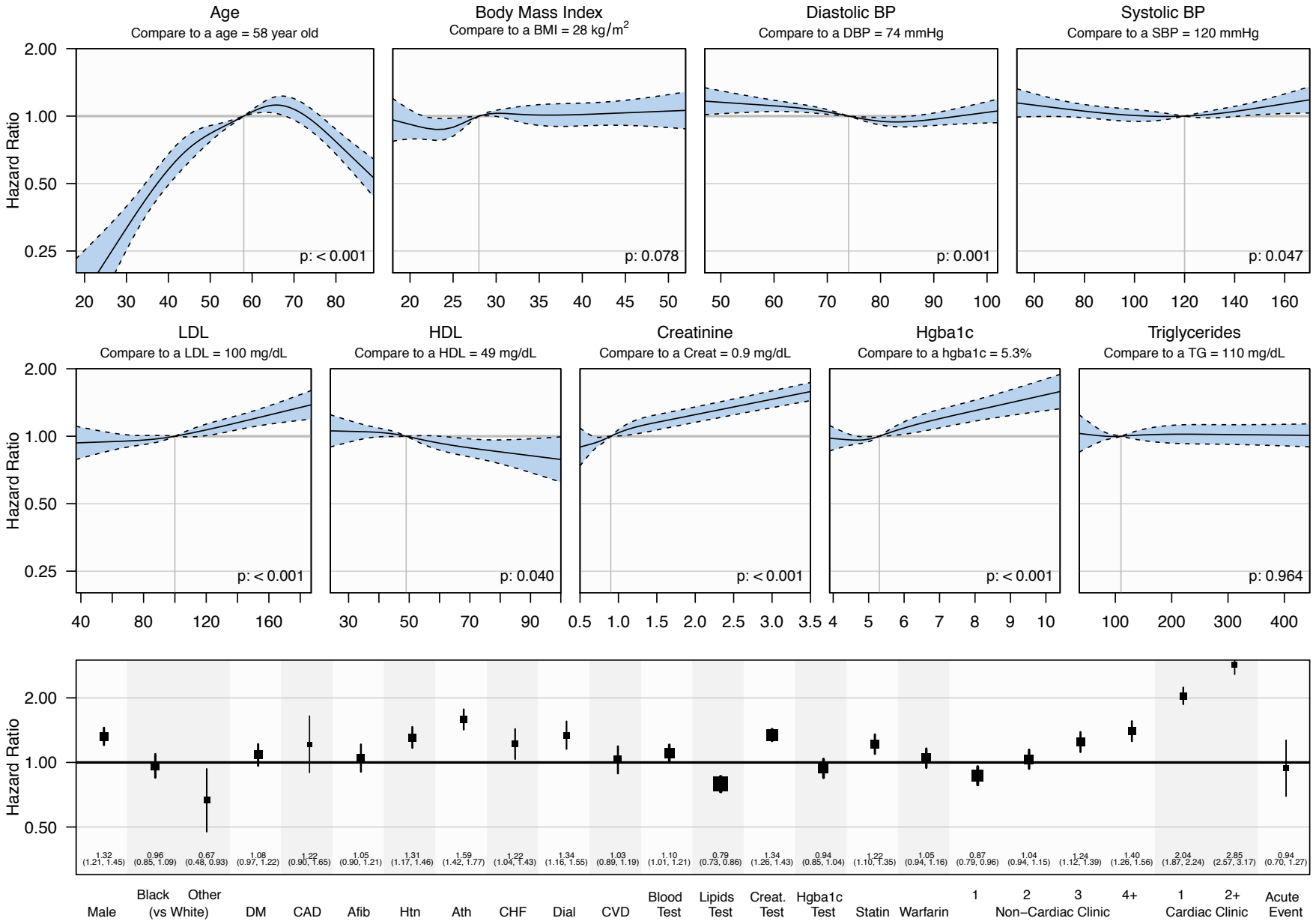


Figure A1.3: Nomogram to calculate one-year and two-year risk for an antiplatelet prescription using the model shown in Figure A2.

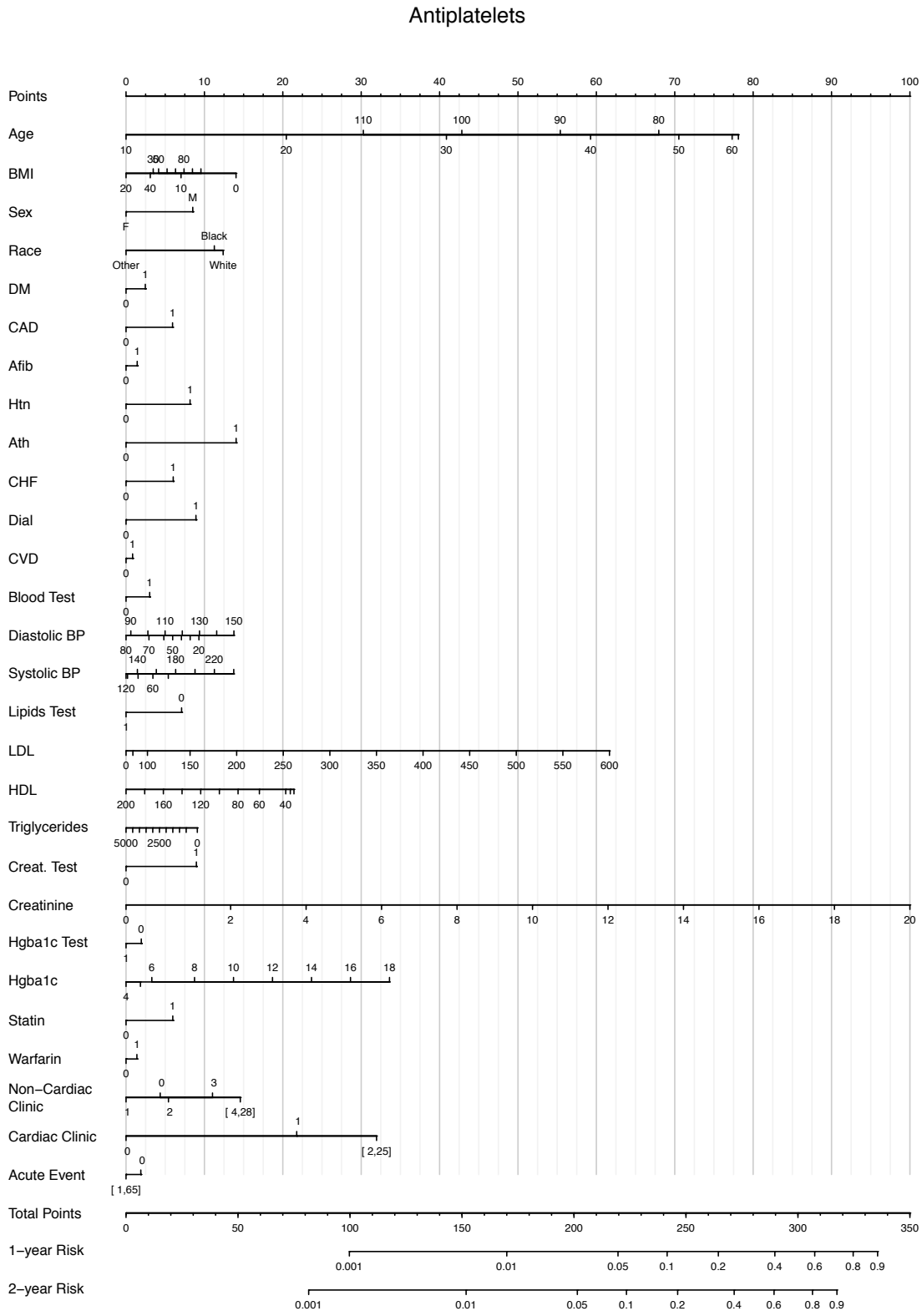


Figure A1.4: The Cox proportional hazard model effect estimates and 95% confidence intervals for statin model.

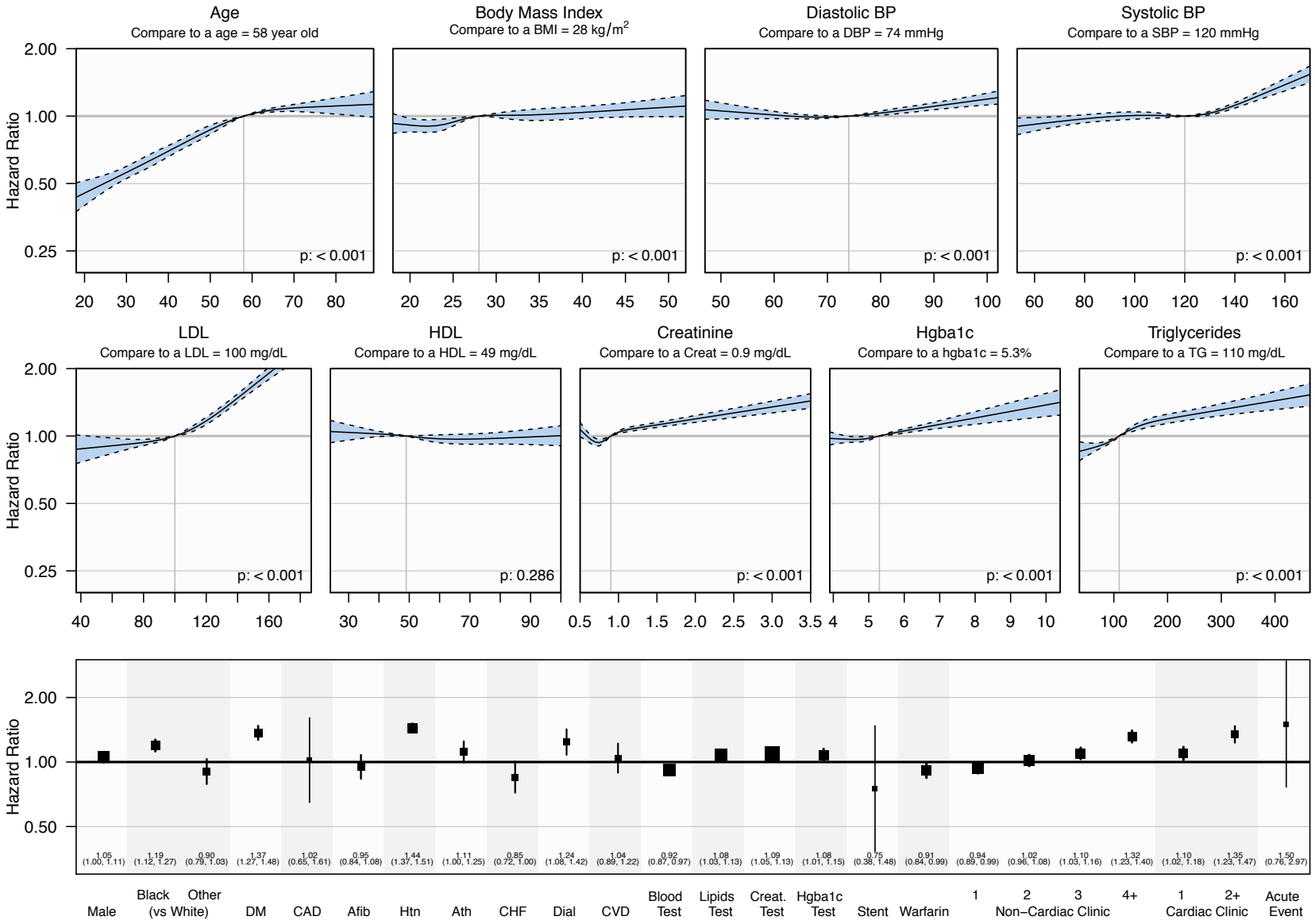


Figure A1.5: Nomogram to calculate one-year and two-year risk for a statin prescription using the model shown in Figure A4.

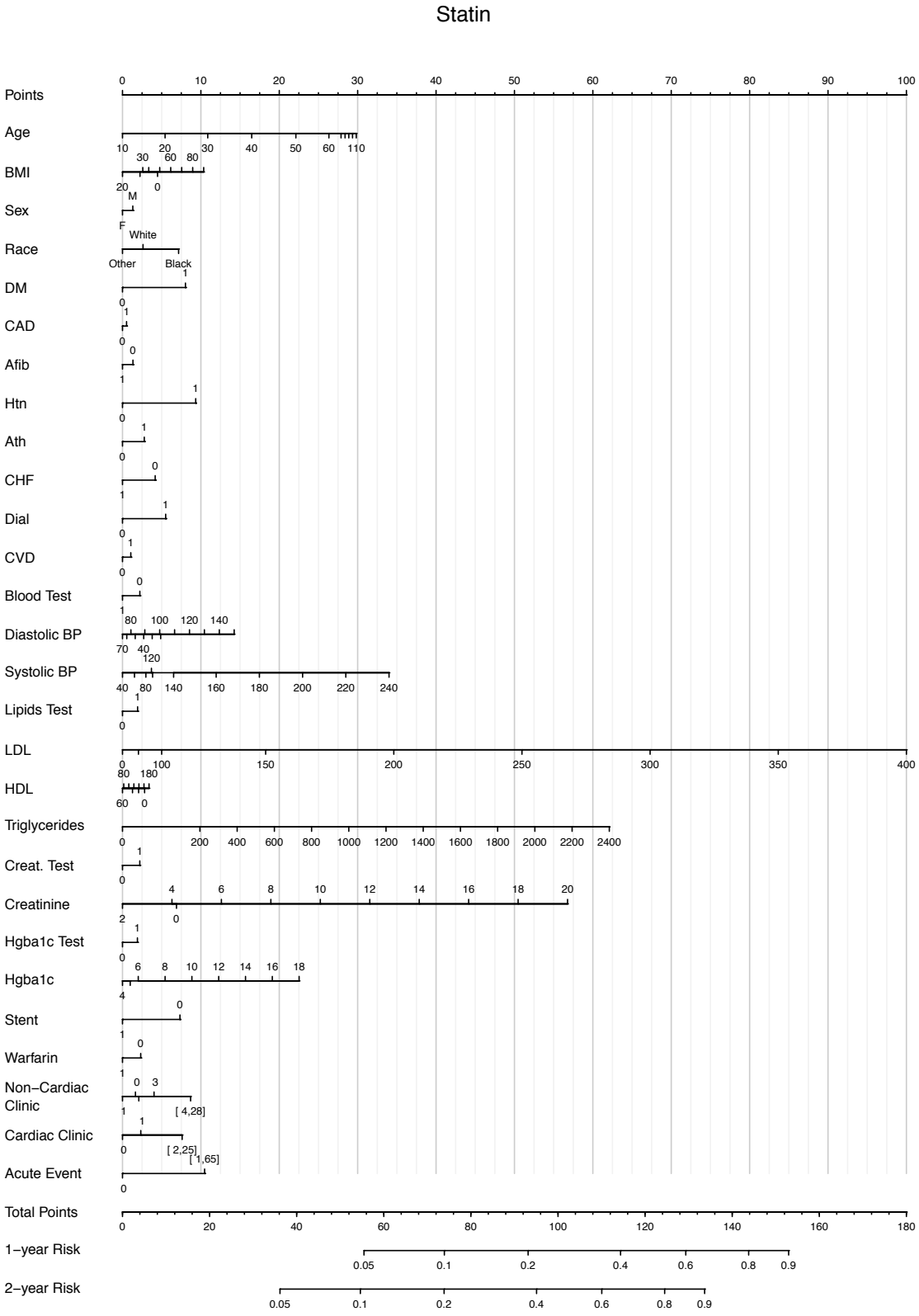


Figure A1.6: The Cox proportional hazard model effect estimates and 95% confidence intervals for warfarin model.

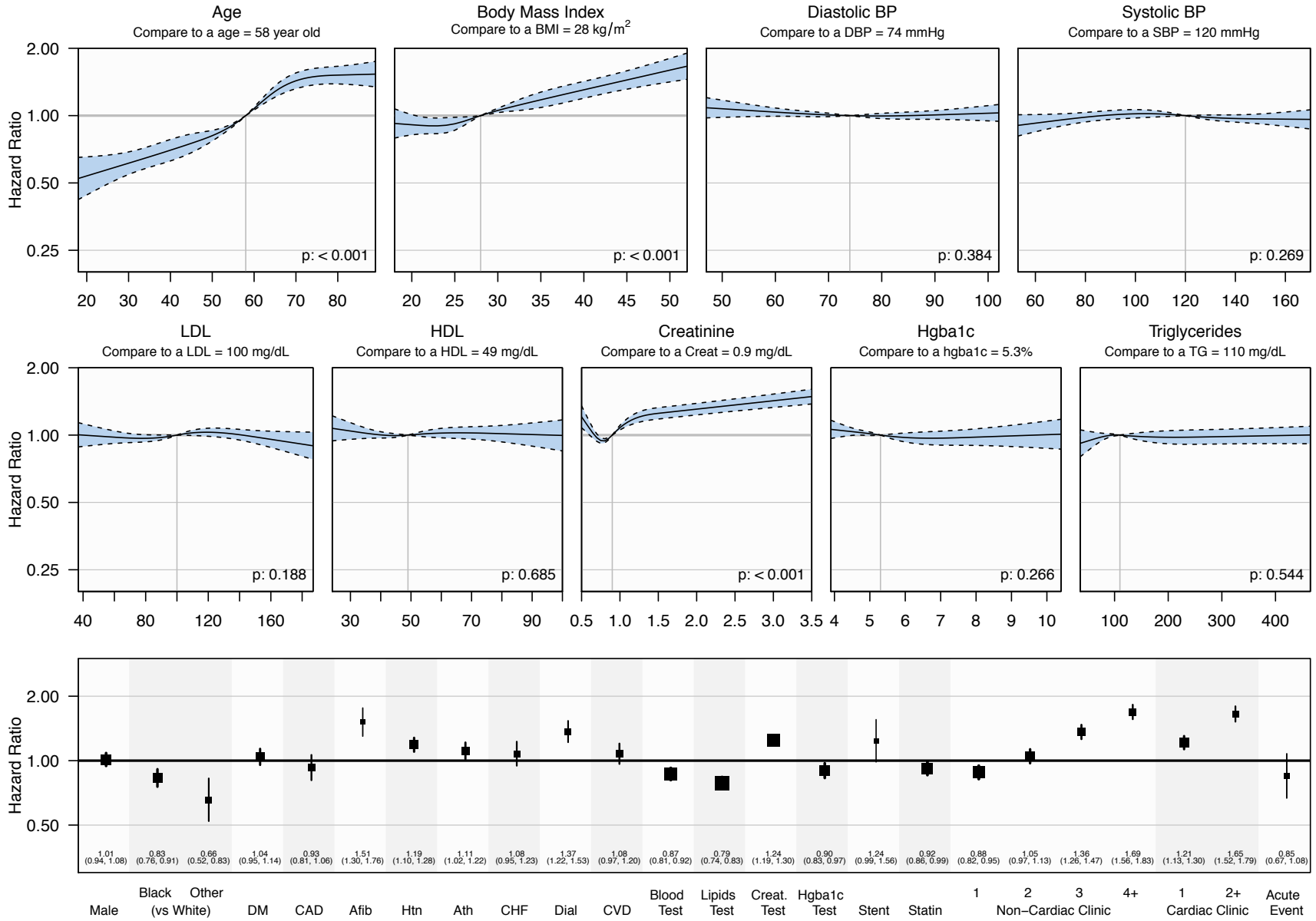
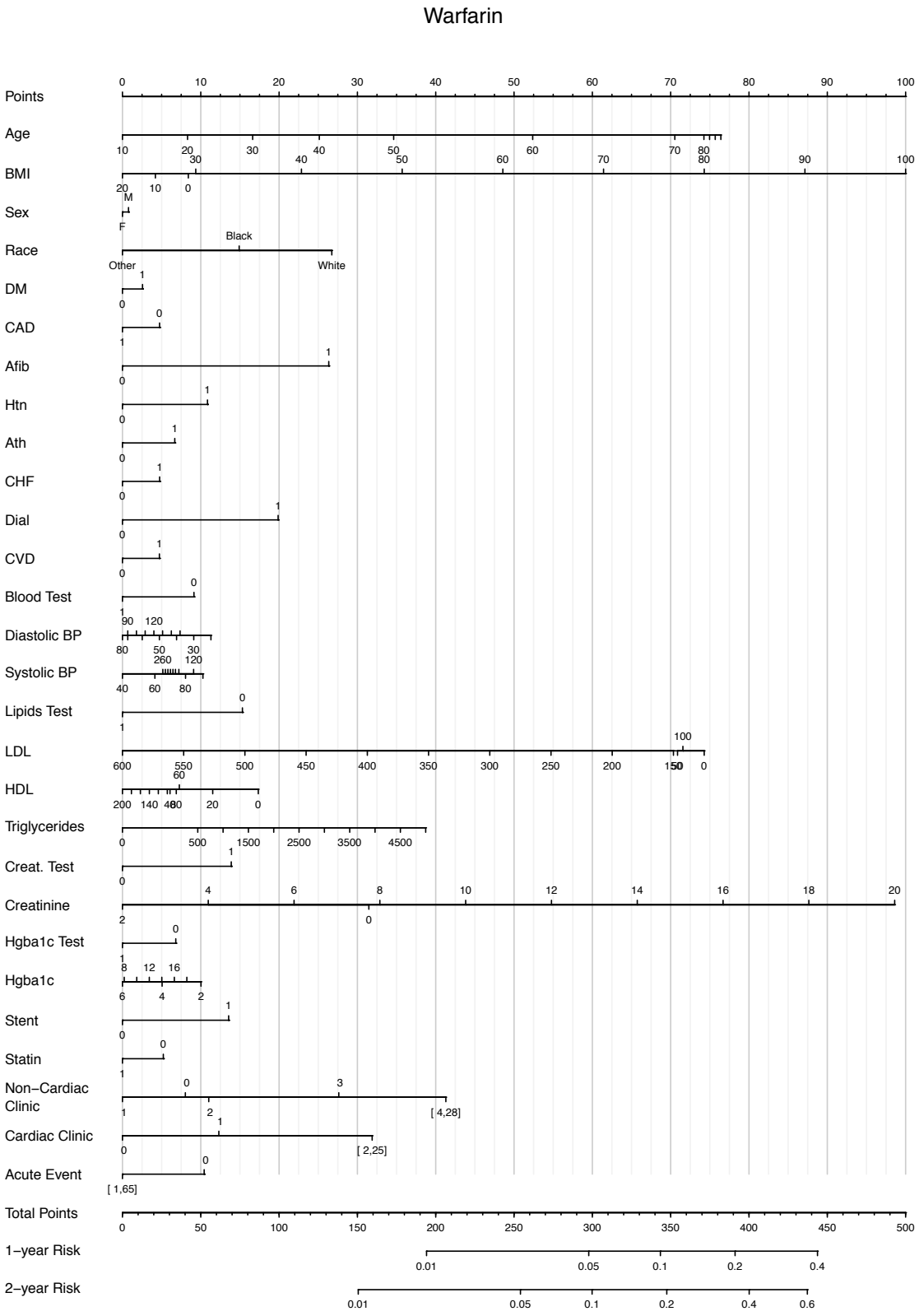


Figure A1.7: Nomogram to calculate one-year and two-year risk for a warfarin prescription using the model shown in Figure A6.



# A Decision Theoretic Approach to Panel-based, Pre-emptive Genotyping

Appendix II: Description of the discrete event simulation models

This appendix details the discrete event simulation (DES) methods employed in this paper. The underlying DES model jointly models the prescription incidence, health, and mortality outcomes among patients prescribed antiplatelet therapy, a statin, or warfarin. The model assumes the health sector perspective and incorporates medical costs, pharmaceutical costs and clinical outcomes based on prior randomized trials and on previous cost-effectiveness studies of antiplatelet therapy, simvastatin and warfarin. The DES compared a base case scenario under which no genetic testing is used to guide therapeutic decisions to a genotype-tailored scenario under which a genetic test is ordered and acted upon when appropriate (i.e., all patients with the genetic variant are switched to an alternative therapy). Each drug scenario is evaluated independently.

## Context

The demographic profile of the simulated patient population was matched to the Vanderbilt University Medical Center (VUMC) medical home (MH) population based on age and gender. Each drug and strategy (genomic test or none) was run on 10 million individual trajectories in a discrete event simulation with a 1 year time horizon.

We used R 3.5.1 and the package simmer version 4.0 for simulations. The code used is available at the link: `https://github.com/spgarbet/des3drugmodel`

Secular mortality rates were estimated from 2011 Social Security mortality data and each age in years was fit with a Gompertz distribution for random draws of life span.

Risks are specified as risk of event over a time period. Relative risks modify a risk based on state of individual in a trajectory. Probabilities are used for branching decisions. Costs are given with a year they are fixed within.

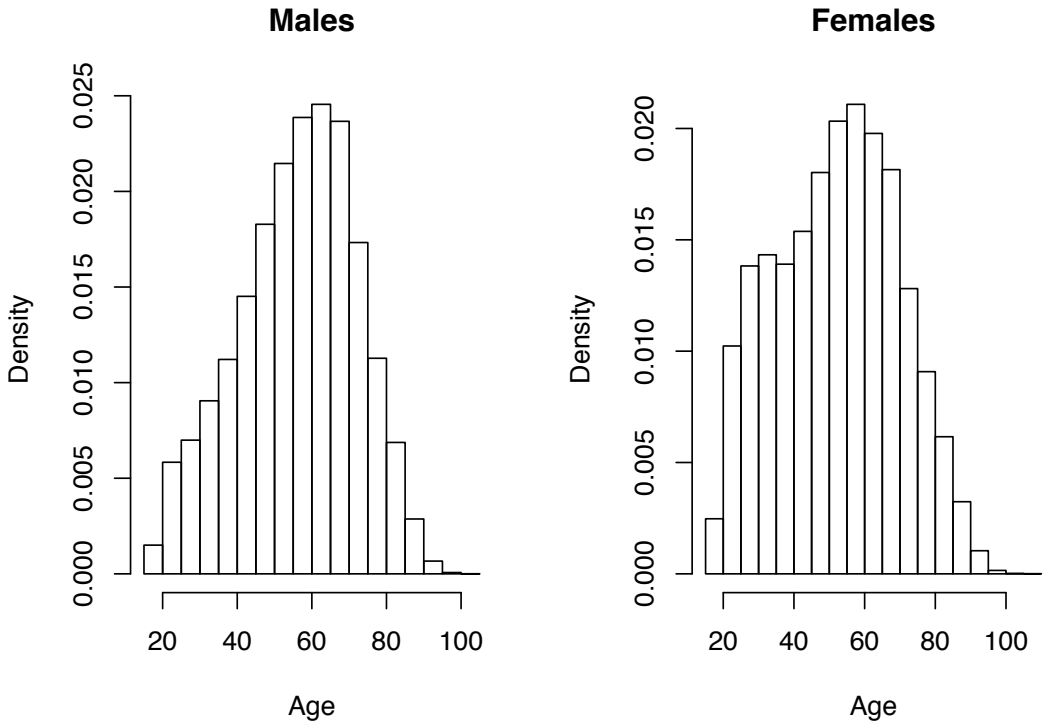



Figure 2.1: Age Distribution of Medical Home Establishment for Vanderbilt Population

## Antiplatelet Model

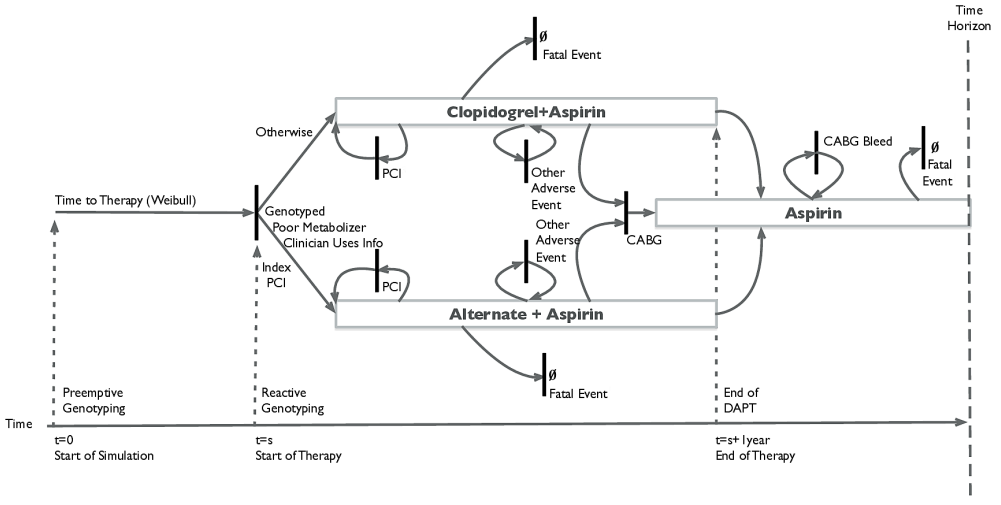



Figure 2.2: Antiplatelet Therapy Model. Clopidogrel with aspirin was considered with an alternate therapy of Ticagrelor for those with genetic indication.

| Value | Parameter | Source |
|---|---|---|
| 0.59 | Weibull Shape | VUMC PREDICT data |
| 1e-12 | Weibull Scale (forces Rx at $t = 0$ start of run) | Model Specification |
| 365 | Time Horizon (days) | Model Specification |
| 1.0 | Probability of physician using test results | Model Specification |
| 1.0 | Probability of physician ordering test | Model Specification |
| † | CYP2C19 poor metabolizer population proportion | Kazi DS 2014 |
| 0 | Relative Risk of repeating therapy | Model Specification |
| 1 | Maximum DAPT therapies allowed | Model Specification |
| 365 | Treatment duration in days | Kazi DS 2014 |
| 0.55 | Probability of switching treatments | VUMC PREDICT data |
| 0.0150 | Risk of Stent Thrombosis for 30 days | Kazi DS 2014 |
| 0.0060 | Risk of ST for 31-365 days | Kazi DS 2014 |
| 0.0022 | Risk of ST for >365 days | Kazi DS 2014 |
| 0.75 | Relative risk of ST on Ticagrelor | Kazi DS 2014 |
| 1.29 | Relative risk of ST on Aspirin | Kazi DS 2014 |
| 0.20 | ST Case Fatality | Kazi DS 2014 |
| 0.10 | ST Coronary artery bypass grafting (CABG) Probability | Kazi DS 2014 |
| 0.035 | Risk of Myocardial Infarction (MI) in 1 year | Kazi DS 2014 |
| 0.84 | Relative Risk of MI on Ticagrelor | Kazi DS 2014 |
| 1.29 | Relative Risk of MI on Aspirin | Kazi DS 2014 |
| 0.08 | MI CABG Probability | Kazi DS 2014 |
| 0.55 | MI PCI Probability | Kazi DS 2014 |
| 0.10 | Risk of Revascularization 1-365 days | Kazi DS 2014 |
| 0.03 | Risk of Revascularization >365 days | Kazi DS 2014 |
| 0.25 | Probability of CABG with Revascularization | Kazi DS 2014 |
| 0.0230 | Risk of External Bleed (1 year) | Kazi DS 2014 |
| 0.0015 | Risk of Internal Bleed (1 year) | Kazi DS 2014 |
| 0.0200 | Risk of Thrombolysis in Myocardial Infarction (TIMI) Minor Bleed (1 year) | Kazi DS 2014 |
| 0.0015 | Risk of Fatal Bleed (1 year) | Kazi DS 2014 |
| 1.30 | Relative Risk of External Bleed Ticagrelor | Kazi DS 2014 |
| 0.72 | Relative Risk of External Bleed Aspirin | Kazi DS 2014 |
| 1.15 | Relative Risk of Internal Bleed Ticagrelor | Kazi DS 2014 |
| 0.71 | Relative Risk of Internal Bleed Aspirin | Kazi DS 2014 |
| 1.07 | Relative Risk of TIMI Minor Ticagrelor | Kazi DS 2014 |
| 0.47 | Relative Risk of TIMI Minor Aspirin | Kazi DS 2014 |
| 0.87 | Relative Risk of Fatal Bleed Ticagrelor | Kazi DS 2014 |
| 1.35 | Relative Risk of Fatal Bleed Aspirin | Kazi DS 2014 |
| 0.022 | Risk of CABG TIMI Major (1 year) | Kazi DS 2014 |
| 1.08 | Relative Risk of CABG TIMI Major Ticagrelor | Kazi DS 2014 |
| 1.08 | Relative Risk of CABG TIMI Major Aspirin | Kazi DS 2014 |
| 1.75 | Relative Risk of ST w/ loss of function on Clopidogrel (LOF) | Kazi DS 2014 |
| 1.48 | Relative Risk of MI w/ LOF | Kazi DS 2014 |
| 0.84 | Relative Risk of Bleed w/ LOF | Kazi DS 2014 |
| 100 | Cost Genetic Variant Test (2012 US Dollars) | Assumption |
| 4 | Cost 30 days of Aspirin (2011 US Dollars) | Kazi DS 2014 |
| 30 | Cost 30 days of Clopidogrel (2011 US Dollars) | Kazi DS 2014 |
| 220 | Cost 30 days of Ticagrelor (2011 US Dollars) | Kazi DS 2014 |
| 10120 | Cost External Major Bleed (2011 US Dollars) | Kazi DS 2014 |
| 20740 | Cost Internal Major Bleed (2011 US Dollars) | Kazi DS 2014 |
| 79 | Cost Minor Non Fatal Bleed (2011 US Dollars) | Kazi DS 2014 |
| 17920 | Cost Fatal Bleed (2011 US Dollars) | Kazi DS 2014 |
| 24540 | Cost ST Fatal (2011 Dollars) | Kazi DS 2014 |
| 67720 | Cost ST CABG (2011 Dollars) | Kazi DS 2014 |
| 27840 | Cost ST PCI (2011 Dollars) | Kazi DS 2014 |
| 67720 | Cost MI CABG (2011 Dollars) | Kazi DS 2014 |
| 17200 | Cost MI Med Manage (2011 Dollars) | Kazi DS 2014 |
| 27840 | Cost MI PCI (2011 Dollars) | Kazi DS 2014 |
| 50560 | Cost Revascularization CABG (2011 Dollars) | Kazi DS 2014 |
| 20670 | Cost Revascularization PCI (2011 Dollars) | Kazi DS 2014 |
| 35570 | Cost CABG Bleed (2011 Dollars) | Kazi DS 2014 |
| 0.20 | Temporary Disutility of Major Ext Bleed | Kazi DS 2014 |
| 14 | Length of Major Ext Bleed | Kazi DS 2014 |
| 0.61 | Permanent Disutility of Major Int Bleed | Kazi DS 2014 |
| 0.20 | Temporary Disutility of Minor Bleed | Kazi DS 2014 |
| 2 | Length of Minor Bleed (days) | Kazi DS 2014 |
| 0.12 | Permanent Disutility of ST CABG | Kazi DS 2014 |
| 0.12 | Permanent Disutility of ST PCI | Kazi DS 2014 |
| 0.12 | Permanent Disutility of MI CABG | Kazi DS 2014 |
| 0.12 | Permanent Disutility of MI Med Manage | Kazi DS 2014 |
| 0.12 | Permanent Disutility of MI PCI | Kazi DS 2014 |
| 0.50 | Temporary Disutility of CABG Revascularization | Kazi DS 2014 |
| 14 | Length of CABG Revascularization (days) | Kazi DS 2014 |
| 0.50 | Temporary Disutility of PCI Revascularization | Kazi DS 2014 |
| 7 | Length of PCI Revascularization (days) | Kazi DS 2014 |
| 0.50 | Temporary Disutility of CABG Bleed | Kazi DS 2014 |
| 7 | Length of CABG Bleed (days) | Kazi DS 2014 |
| Varies | Secular Death Rate | 2011 US SS Deaths |

Table 2.1: Parameters used for the Antiplatelet Therapy Discrete Event Simulation. Simvastatin was considered as an alternative for Atorvastatin for those with genetic indication.
†See Table 2 in Main Text

## Statin Therapy

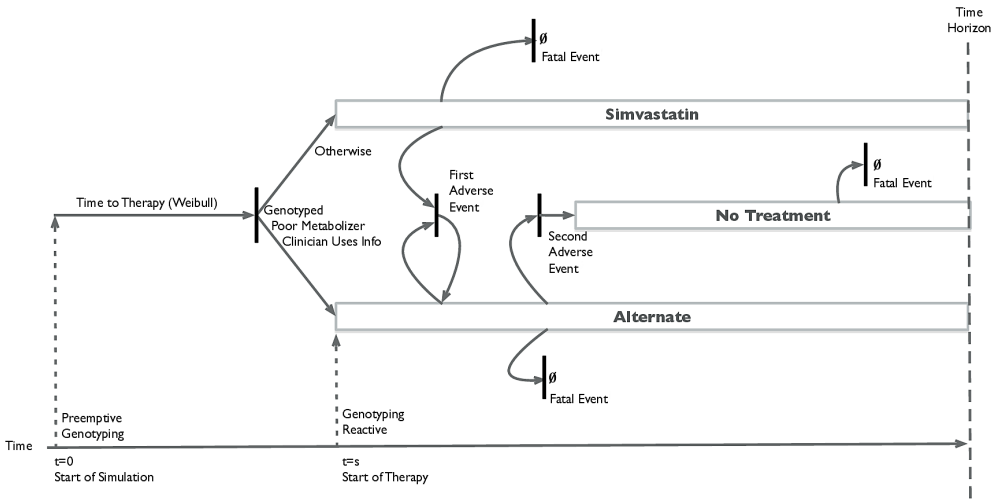



Figure 2.3: Statin Therapy Model. Clopidogrel with aspirin was considered with an alternate therapy of Ticagrelor for those with genetic indication.

| Value | Parameter | Source |
|---|---|---|
| 0.54 | Weibull Shape | VUMC PREDICT data |
| 1e-12 | Weibull Scale (forces Rx at start of run) | Model Specification |
| 365 | Time Horizon (days) | Model Specification |
| 1.0 | Probability of physician using test results | Model Specification |
| 1.0 | Probability of physician ordering test | Model Specification |
| † | Poor metabolizer population proportion | SEARCH Collaborative Group 2008 |
| † | Medium metabolizer population proportion | SEARCH Collaborative Group 2008 |
| 1.00 | Probability of prescribing alternate therapy | Model Specification |
| 0.23 | Probability of stopping from mild myopathy | Bruckert, E 2005 |
| 0.23 | Probability of stopping from moderate myopathy | Bruckert, E 2005 |
| 1.00 | Probability of stopping from severe myopathy | Bruckert, E 2005 |
| 1e-7 | 5yr Risk of Mild Myopathy with no Rx | Assumption |
| 0.05 | 5yr Risk of Mild Myopathy Simvastatin | Law 2006 |
| 2.727 | Relative Risk of Mild Myopathy Simvastatin Medium Metabolizer | Hou, Q 2015 |
| 6.429 | Relative Risk of Mild Myopathy Simvastatin Poor Metabolizer | Hou, Q 2015 |
| 0.05 | 5yr Risk of Mild Myopathy Alternate | Assumption |
| 1 | Relative Risk of Mild Myopathy Alternate Medium Metabolizer | Assumption |
| 1 | Relative Risk of Mild Myopathy Alternate Poor Metabolizer | Assumption |
| 1e-10 | 5yr Risk of Moderate Myopathy with no Rx | Assumption |
| 0.00011 | 5yr Risk of Moderate Myopathy Simvastatin | Law 2006 |
| 2.999 | Relative Risk of Moderate Myopathy Simvastatin Medium Metabolizer | Hou, Q 2015 |
| 8.992 | Relative Risk of Moderate Myopathy Simvastatin Poor Metabolizer | Hou, Q 2015 |
| 0.00011 | 5yr Risk of Severe Myopathy Alternate | Assumption |
| 1 | Relative Risk of Alternate Medium Metabolizer | Assumption |
| 1 | Relative Risk of Alternate Poor Metabolizer | Assumption |
| 1e-16 | 5yr Risk of Severe Myopathy with no Rx | Assumption |
| 0.000034 | 5yr Risk of Severe Myopathy Simvastatin | Law 2006 |
| 3 | Relative Risk of Severe Myopathy Simvastatin Medium Metabolizer | Hou, Q 2015 |
| 9 | Relative Risk of Severe Myopathy Simvastatin Poor Metabolizer | Hou, Q 2015 |
| 0.000034 | 5yr Risk of Severe Myopathy Alternate | Assumption |
| 1 | Relative Risk of Alternate Medium Metabolizer | Assumption |
| 1 | Relative Risk of Alternate Poor Metabolizer | Assumption |
| 0.1 | Probability of Rahbdo Death for Severe Myopathy | Law 2006 |
| 0.117 | CVD Mortality Rate | Ergin 2004 |
| 100 | Cost Genetic Variant Test (2012 US Dollars) | Assumption |
| 147 | Cost of 1 year Simvastatin (2012 US Dollars) | AWP, Red Book Online 2015 |
| 173.10 | Cost of 1 year Alternate (2012 US Dollars) | AWP, Red Book Online 2015 |
| 129 | Cost of Mild Myopathy (2012 US Dollars) | Healthcare Bluebook |
| 2255 | Cost of Moderate Myopathy (2012 US Dollars) | Healthcare Bluebook |
| 12811 | Cost of Severe Myopathy (2012 US Dollars) | Healthcare Bluebook |
| 12811 | Cost of Rahbdo Death (2012 Dollars) | Healthcare Bluebook |
| 20347 | Cost of CVD (2012 Dollars) | Healthcare Bluebook |
| 20347 | Cost of CVD Death (2012 Dollars) | Healthcare Bluebook |
| 0.01 | Temporary Disutility of Mild Myopathy | Assumption |
| 30 | Length of Mild Myopathy (days) | Healthcare Bluebook |
| 0.05 | Temporary Disutility of Moderate Myopathy | Sullivan 2006 |
| 60 | Length of Moderate Myopathy (days) | Healthcare Bluebook |
| 0.53 | Temporary Disutility of Moderate Myopathy | Vegter 2014 |
| 60 | Length of Moderate Myopathy (days) | Healthcare Bluebook |
| 0.2445 | Temporary Disutility of CVD | Sullivan 2006 |
| 30 | Length of CVD | Korsnes, J 2015 |
| Varies | Secular Death Rate | 2011 US SS Deaths |

Table 2.2: Parameters used for the Statin Therapy Discrete Event Simulation. Simvastatin was considered as an alternative for Atorvastatin for those with genetic indication.
†See Table 2 in Main Text

## Warfarin Therapy

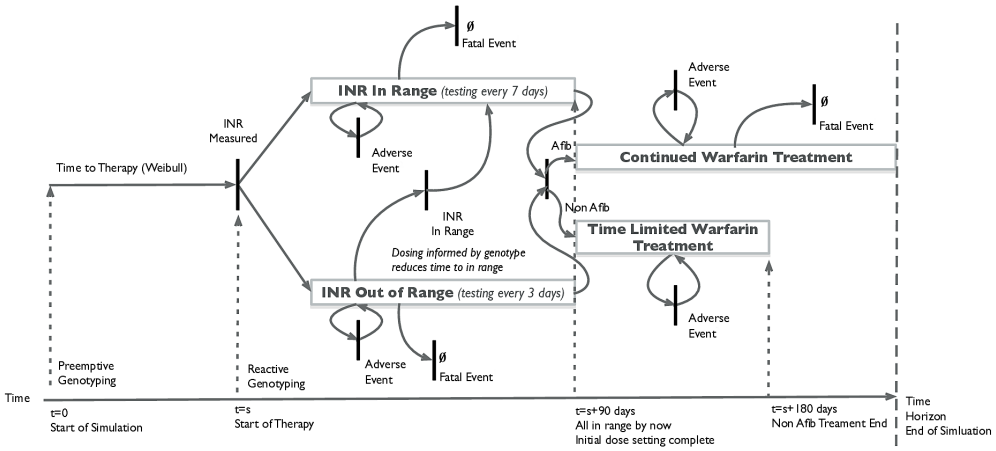



Figure 2.4: Warfarin Therapy Model. Warfarin was considered with an alternate therapy of different dosing for those with genetic indication. The effect is indirect in that genotyping reduces median time to INR in range.

| Value | Parameter | Source |
|---|---|---|
| 0.66 | Weibull Shape | VUMC PREDICT data |
| 1e-12 | Weibull Scale (forces Rx at start of run) | Model Specification |
| 365 | Time Horizon (days) | Model Specification |
| 1.0 | Probability of physician using test results | Model Specification |
| 1.0 | Probability of physician ordering test | Model Specification |
| Dist | Initial INR (see following distribution) | VUMC Study |
| 0.0239 | Exponential rate of time to in range (IR) non-genotyped | Pirmohamed, M 2013 |
| 0.02888 | Exponential rate of time to IR genotyped | Pirmohamed, M 2013 |
| 0.09 | Percent Atrial Fibrillation (AF) at Warfarin Indication | VUMC Study |
| 0.01497 | Risk of major bleed INR < 3 (90 day) | Patrick, AR 2009 |
| 0.06224 | Risk of major bleed 3 < INR < 4 (90 day) | Patrick, AR 2009 |
| 0.39118 | Risk of major bleed INR > 3 (90 day) | Patrick, AR 2009 |
| 0.0936 | Risk of minor bleed INR < 3 (90 day) | Patrick, AR 2009 |
| 0.389 | Risk of minor bleed 3 < INR < 4 (90 day) | Patrick, AR 2009 |
| 0.9999 | Risk of minor bleed INR > 3 (90 day) | Patrick, AR 2009 |
| 0.144 | Major bleed: Probability of non-fatal intracranial bleed | Patrick, AR 2009 |
| 0.156 | Major bleed: Probability of fatal intracranial bleed | Patrick, AR 2009 |
| 0.557 | Major bleed: Probability of non-fatal gastrointestinal bleed | Patrick, AR 2009 |
| 0.043 | Major bleed: Probability of fatal gastrointestinal bleed | Patrick, AR 2009 |
| 0.098 | Major bleed: Probability of other non-fatal major bleed | Patrick, AR 2009 |
| 0.002 | Major bleed: Probability of other fatal major bleed | Patrick, AR 2009 |
| 0.077 | Risk of stroke events for INR < 1.5 & AF indication (1 year) | Patrick, AR 2009 |
| 0.019 | Risk of stroke events for 1.5 <= INR <2 & AF indication (1 year) | Patrick, AR 2009 |
| 0.006 | Risk of stroke events for INR >=2 & AF indication (1 year) | Patrick, AR 2009 |
| 1e-5 | Risk of stroke events for INR < 3 & non-AF indication (1 year) | Assumption |
| 0.006 | Risk of stroke events for INR >=3 & non-AF indication (1 year) | Assumption |
| 0.4116 | Probability of stroke minor deficit for INR < 2 | Patrick, AR 2009 |
| 0.4284 | Probability of stroke major deficit for INR < 2 | Patrick, AR 2009 |
| 0.16 | Probability of stroke fatal stroke for INR < 2 | Patrick, AR 2009 |
| 0.5358 | Probability of stroke minor deficit for INR >= 2 | Patrick, AR 2009 |
| 0.4042 | Probability of stroke major deficit for INR >= 2 | Patrick, AR 2009 |
| 0.06 | Probability of stroke fatal stroke for INR >= 2 | Patrick, AR 2009 |
| 0.019 | Risk of DVTPE events for INR < 2 & non-AF indication (1 year) | Kearon 2003 |
| 0.007 | Risk of DVTPE events for INR >= 2 & non-AF indication (1 year) | Kearon 2003 |
| 0.4 | Probability of non-fatal deep vein thrombosis | Assumption |
| 0.1 | Probability of non-fatal pulmonary embolism | Assumption |
| 0.5 | Probability of fatal DVTPE | Assumption |
| 71 | Cost of warfarin 3 months (2007 US Dollars) | Patrick, AR 2009 |
| 20740 | Cost of non-fatal intracranial bleed (2011 US Dollars) | Kazi, DS 2014 |
| 2328 | Cost of non-fatal gastrointestinal bleed (2011 US Dollars) | Dorian, P 2014 |
| 6154 | Cost of other non-fatal major bleed | Dorian, P 2014 |
| 179920 | Cost of fatal intracranial bleed (2011 US Dollars) | Kazi, DS 2014 |
| 179920 | Cost of fatal gastrointestinal bleed (2011 US Dollars) | Kazi, DS 2014 |
| 179920 | Cost of other fatal major bleed (2011 US Dollars) | Kazi, DS 2014 |
| 79 | Cost of non-fatal minor bleed (2011 US Dollars) | Kazi, DS 2014 |
| 21537 | Cost of stroke major deficit (2007 US Dollars) | Patrick, AR 2009 |
| 15499 | Cost of stroke minor deficit (2007 US Dollars) | Patrick, AR 2009 |
| 10396 | Cost of fatal stroke (2007 US Dollars) | Patrick, AR 2009 |
| 7594 | Cost of deep vein thrombosis (2004 US Dollars) | Spyropoulos, AC 2007 |
| 13018 | Cost of pulmonary embolism (2004 US Dollars) | Spyropoulos, AC 2007 |
| 7000 | Cost of fatal DVTPE | Assumption |
| 29 | Cost of INR test | Patrick, AR 2009 |
| 0.61 | Permanent disutility of non-fatal intracranial bleed | Kazi, DS 2014 |
| 0.1511 | Temporary disutility of non-fatal gastrointestinal bleed | Dorian, P 2014 |
| 14 | Length of non-fatal gastrointestinal bleed | Dorian, P 2014 |
| 0.1511 | Temporary disutility of other non-fatal major bleed | Dorian, P 2014 |
| 14 | Length of other non-fatal major bleed (days) | Dorian, P 2014 |
| 0.2 | Temporary disutility of non-fatal minor bleed | Kazi, DS 2014 |
| 2 | Length of non-fatal minor bleed (days) | Kazi, DS 2014 |
| 0.65 | Permanent disutility of stroke major deficit | Patrick, AR 2009 |
| 0.24 | Permanent disutility of stroke minor deficit | Patrick, AR 2009 |
| 0.16 | Permanent disutility of deep vein thrombosis | Locadia, M 2004 |
| 0.37 | Permanent disutility of pulmonary embolism | Locadia, M 2004 |
| 0.012 | Temporary disutility of INR test for out of range | Marchetti, M 2001 |
| 3 | Length of INR test for out of range | Marchetti, M 2001 |
| 0.012 | Temporary disutility of INR test for in range | Marchetti, M 2001 |
| 7 | Length of INR test for in range | Marchetti, M 2001 |

Table 2.3: Parameters used for the Warfarin Therapy Discrete Event Simulation. Warfarin was considered with an alternate therapy of different dosing for those with genetic indication. The effect is indirect in that genotyping reduces median time to INR in range..

## Parameter Sources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