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Differences in Predicted Risk of Mortality after Coronary Artery Bypass Graft Between Black and White Patients with Identical Clinical Profiles Using the Society of Thoracic Surgeons Calculator: an in-silico Cohort Study

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Title: Differences in Predicted Risk of Mortality after Coronary Artery Bypass Graft between Black and White patients with identical clinical profiles using the Society of Thoracic Surgeons calculator: an in-silico cohort study.

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Abstract/Summary:

Background: "The Society of Thoracic Surgeons mortality risk calculator", which includes a race variable, is recommended for estimating Short- term (30 day) predicted risk of mortality after isolated coronary artery bypass graft, with a risk estimate of 3-4% stratifying patients into intermediate risk, a risk estimate above 5% stratifying patients into high risk for surgery and a risk estimate above 8% stratifying patients into the very high-risk category. We compared differences between Black and White individuals in Society of Thoracic Surgeons-predicted risk of mortality across various plausible risk factor combinations with the aim of evaluating if using the predictive calculator might result in different surgical decisions in Black versus White individuals with identical risk profiles.

Methods: We generated in silico patient risk profiles by combining numerical risk factors (age {10 year intervals 60-70}, ejection fraction {5% intervals 30-40}, weight {50 kg, 80kg 130kg, hematocrit {25%,40%}, creatinine {0.8, 1, 1.3, 1.7, 2}) and binary risk factors (gender, insurance status, peripheral arterial disease, diabetes on insulin, lung disease, and number of diseased vessels). We compared Society of Thoracic Surgeons predicted risk of mortality in Black and White individuals with identical risk profiles. Secondary outcomes measured included total morbidity/mortality, risk of stroke, risk of renal failure, risk of prolonged ventilation, and risk of long stay >14days.

Findings: For our in-silico analysis, we evaluated 5,041 risk profiles for men and 4,768 risk profiles for women after excluding risk profiles that generated risk of mortality below 2% or above 10%. There were 703 risk profiles associated with Society of Thoracic Surgeon Predicted risk of mortality (PROM) above 5% for Black men but not for White men (median risk difference [RD] .827%, range 0.32-2.83; median relative risk [RR] 1.18, range 1.06-1.89). There were 189 risk profiles associated with a predicted risk of mortality (PROM) above 8% for Black men but not for White men (median risk difference [RD] .81% , range 0.77-3.24; median relative risk [RR] 1.11, range 1.10-1.54). There were 616 risk profiles associated with a predicted risk of mortality (PROM) above 5% for Black women but not for White women (median risk difference [RD] 0.80%, range 0.49%-0.91%; median relative risk [RR] 1.18, range 1.11-1.18). Lastly, there were 347 risk profiles associated with a predicted risk of mortality (PROM) above 8% for Black women but not for White women (median risk difference [RD] 0.81% , range 0.77%-2.81%; median relative risk [RR] 1.11, range 1.10-1.50). There were no risk profiles using the Society of Thoracic Surgeons short term calculator in which predicted risk of mortality for White individuals was above 5% risk and PROM for Black individuals was below 5%, nor any risk profiles which PROM for White individuals was above 8% risk and PROM for Black individuals was below 8%.

Interpretation: The STS calculator might produce divergent risk of mortality estimates for Black and White individuals with identical risk profiles, leading to a difference in treatment plans, timing of surgery, or long-term outcomes.

Introduction:

The STS database was originally created in 1989 for monitoring surgeon outcomes and hospital performance reports using data from Adult Cardiac Surgery Database (ACSD) participants. The database includes participation of approximately 3,800 surgeons and anesthesiologists, and previous research suggests the STS captures 90% of all coronary artery bypass operations in the US. In 1986, at the advent of public reporting, CMS (what was then HCFA) released unadjusted mortality data that were criticized and labeled as "death lists" by cardiac surgeons. In response, surgeons, professional groups, and hospitals developed statistical models to risk-adjust the mortality rates in order to account for the inherent risk of their patients when reporting outcomes. This led to the development of risk-adjustment of relevant predictors of mortality and predictors of complications in the field of model development and risk estimation.[1] In the age of value-based payment programs with Centers for Medicaid Service (CMS), public reporting measures that risk adjust for patients' inherent clinical risk and hospital case-mix is common place.[2] Risk adjusting for social factors such as race in hospital reporting is a broader health equity concern and inextricably intertwined with the healthcare payment system. However, adjusting for social factors such as race, has been a topic of discussion and review for the National Quality Forum which oversees databases and reporting of quality measures in healthcare.[3 4] Presently, The STS functions as both a database for a public reporting tool with star-graded composite reports as well as an individual patient risk of mortality calculator for cardiac surgeons.[5] The calculated STS (PROM)Predicted risk of short term-30-day mortality is documented on informed consent forms before performing surgeries such as CABG (Coronary Artery Bypass graft), AVR (aortic valve replacement), MVR (mitral valve replacement) and more recently CABG+ AVR and CABG+MVR. The STS calculator is one of many tools used by the heart team make shared decisions about surgery.

Research in context

Evidence before this study

The STS maintains that risk adjustment for social risk factors in its model has aimed to avoid high-risk patient aversion rather than cause it.[6] High risk patient aversion and the effects of public reporting have been modestly studied. In 2005, Werner and colleagues studied the effects of public reporting of CABG in NYC on racial disparities in access to care, and found an increase in racial and ethnic disparities in CABG use by 2.0 percentage points (95% CI 0.7 to 3.4, $P<0.006$) in White versus Black patients in the year after beginning the use of report cards.[7] On the other hand, in a report on risk aversion and public reporting, the STS stated that a potential unintentional benefit of public report cards is matching of highest risk patients to providers with lower observed to expected mortality rates.[6] This conclusion came from a study by Glance and colleagues that looked at CABG's performed in New York between 1997 and 1999 and found that patients at higher risk were more likely to be referred and transferred to higher performing providers.[8] Dranove (2003) studied CABG patients in New York and Pennsylvania from 1987-1994 which included the years in which statewide public CABG reporting was

introduced. They found that after report cards were published, a shift occurred in CABG demographics in New York and Pennsylvania toward healthier patients (3.7% to 5.3% decrease in illness severity relative to all other states), putatively as a result of risk aversion. However, CABG illness severity was maintained at New York and Pennsylvania teaching hospitals analyzed alone, which the authors used as a proxy for high-quality institutions. This suggests that teaching hospitals were being sent the sickest CABG patients, who might previously have been cared for at other institutions. [9] A study on risk aversion in cardiac surgery that observed 15-year trends showed the rate of high-risk cases decreased from 17.9% in 2002 to 12.6% in 2016. Significant risk aversion was seen in 39% of hospitals. These risk averse hospitals had a 59% decrease in high-risk volume vs a 16% decrease at non-risk-averse hospitals. However, this study also concluded that non-risk-averse hospitals are high-performing with better-than-expected outcomes, particularly in high-risk cases. [10] A study by Engum in 2015 also showed equal or better outcomes and hospital rankings for centers that accept high risk patients than centers with predominantly low risk patients, which dispels beliefs that accepting high risk cases impacts hospital performance scores, grading, or financial reimbursement. [11]

The above studies suggest that public reporting has had effects on referral patterns and institutional behaviors with a potential benefit being that the sickest patients are referred to the most capable centers. However, a potential concern arises if transfer of care becomes a delay in care and the "high-risk patient" could potentially have been served at their original institution. Studies have found that because high risk patients are often transferred for care, outcomes are worse for patients who live further from a tertiary cardiac center.[12] In addition, while it may be believed that patients are better served at tertiary care centers, a study by Kurlanksy found that even after adjustment for Society of Thoracic Surgeons risk score, no association was found for either hospital or surgeon volume with mortality or morbidity. However, a lack of compliance with National Quality Forum measures was highly predictive of morbidity regardless of volume, indicating that excellent surgical results can also be obtained in low-volume centers.[13] Additionally, mortality after a long CABG waiting list in elective surgeries has been modestly studied. [14] A study published in the Journal of Society of Thoracic Surgeons found the risk of death increases significantly with waiting time. Other impacts of long waiting times for patients undergoing elective CABG in the form of increased patient anxiety and worse quality of life outcomes. [15] [16] [17]

It is worth noting that the STS is aware of concerns of using race in database models and estimation calculators. In an STS report, studies that found better proxies than race for predicting outcomes were cited, such as an expansive study of all isolated CABG patients in the STS Adult Cardiac Surgery Database (ACSD) between 2011 and 2018. Mehaffey and colleagues studied 575,900 patients who could be assigned a 7-indicator Distressed Communities Index (DCI) score which measured impact of SDS/SES. Patients from communities with high (worse) DCI scores had increased STS predicted risk of mortality (1.97% vs 1.85%, $P < .0001$) and composite morbidity or mortality (12.8% vs 11.7%, $P < .0001$).[18] In a study by Koch and colleagues, DCI was a stronger predictor of outcomes than race.[19] Furthermore, another study found that using SES census-tract data to risk adjust patients modestly improved the C-statistic (AUC) of the STS model.[20] Another study found that adding institutional specific risk factors to

risk prediction such as BUN, egfr, albumin, or CRP improved risk prediction compared to the STS PROM calculator alone. [21] Markers of inflammation may also be informative in predicting risk. [22] The STS is aware of better proxies for health differences than race, however the professional society holds a view of indifference in regard to continuing to use race as a proxy as their report states: "The effects (of using SES) on model performance were modest, perhaps because race was already in the model." [23] If race is confounded by socioeconomic deprivation, then it would make logical sense to update models to eliminate variables with confounders rather than stick to the tradition of using race as a variable.

Further health equity concern surrounds the fact that CABG may be underutilized. A 2016 review of papers studying outcomes of PCI vs CABG in various risk groups found that CABG is still underutilized in the United States.[24]Another study by Epstein Et al found a substantial decrease in CABG surgery utilization rates in US hospitals between 2001 and 2008.[25] Underutilization of CABG may or may not be related to clinical decision making and risk prediction. Underutilization of CABG could also be a result of provider volume, surgical volume, or reliance on percutaneous interventions. Performing CABG is beneficial in specific groups such as – those with three vessel disease, 2 vessel disease with significant L proximal artery calcification, and diabetics with three vessel disease.

The STS individual risk estimation tool for CABG should not include a social factor such as race to avoid conflation of a social construct with a biological, clinical factor. Concerns for algorithmic bias are being explored in many fields of medicine ranging from cardiology, nephrology, to gynecology. [4] For example, the Get With the Guidelines Heart Failure In Hospital Mortality (GWTG) calculator creators recently added a disclaimer note in regard to utilizing race in their risk algorithm stating that using the variable may not lead to more accurate predictions. More notably, a study by Vasan and Huevel assessed the 10-year cardiovascular risk calculator for Black and White patients and found divergent calculations of predicted risk that were not biologically plausible considering the identical clinical profiles. They concluded a potential consequence was that Black patients might be more ill before receiving cardiac interventions such as statin medication initiation, because they were differentially labeled as lower risk for developing cardiovascular disease. [26]

Added value of this study

The scope of this study is to look at STS calculator estimated risk scores in *individual* patient assessment and explore the potential for differential surgical decision making based on race. It is unknown if the STS calculator might produce different risk scores for identical risk profiles in Black and White patients eligible for elective CABG surgery. Although this calculator is one of many tools to guide clinical decision making for cardiac surgery, STS predicted mortality at the critical threshold above 5% and above 8% risk used in this study, the patient may be referred to a better performing cardiac center leading to delay in care, or referred for PCI and medical management over CABG. Differential risk scores may impact shared decision making between patient and provider. For example, a patient and their family may deny surgery or opt for PCI if stratified into the high-risk category above 5% or if stratified into very high risk above 8%. Overall, if a patient is deemed to be high risk and unable to be appropriately cared for at a

certain hospital, this risk profile could cause the patient to be transferred for care at a tertiary center, delaying healthcare to those who may benefit the most. The patient could also potentially be denied surgery and given medical management with or without PCI instead of CABG.[27] Studies have shown the benefits of CABG are greater than PCI in terms of long-term mortality. Therefore, underutilization of CABG and overuse of PCI in intermediate to high-risk patients presents a large health equity concern that has been quantified in many investigations.[28-30]

The STS surgical risk scores for 30-day mortality are stratified as low (<2%), intermediate (2-5%), high risk (> 5%), and very high-risk >8%.[31-33] Although surgeons have increasingly taken on higher risk patients with predicted risk as high as 15% in the recent years due to advances in overall outcomes, there is no study assessing possible differential risk stratification between Black and White elective CABG patients using the STS calculator.

Implications of all available evidence

The use of race in medical decision making and prediction algorithms deserves to be reexamined. [4] [34] Elimination of race as a variable will allow for deeper and more thoughtful pre-surgical evaluations and discussions that include investigation into other causal factors that may confer higher risk such as- nutritional status, proximity to care, SES, education level, comorbid conditions, and stress.

Using the STS calculator, patients may be differentially referred to PCI versus CABG, differentially referred to other cardiac centers-further delaying care, or the higher predicted risk may dissuade the patient from receiving surgery altogether in the context of shared decision-making. It is important to explore the possibility for differential risk prediction using the STS calculator between Black and White patients with identical risk profiles to examine the potential for algorithmic bias. We aimed to evaluate this premise by comparing differences between Black and White individuals in STS estimated risk of mortality across various plausible risk factor combinations using an in-silico approach.

Methods

Creation of risk factor categories and their combinations

We used hypothetical data for an in-silico analysis. The hypothetical risk profiles were created to mirror patients that would qualify for isolated CABG in a healthcare setting. As specified by the ACC/AHA guidelines for coronary artery bypass graft, we considered a wide range of permissible and realistic values for risk factor variables. Per guidelines, this study included hypothetical patients without acute coronary syndromes who were candidates for elective CABG with 2 or 3 vessel disease, significant stenosis >50% and were in NYHA class 3. All data was publicly available and the Institutional Review Board at Yale University Medical center approved the study protocol.

We created risk profiles by combining risk factors as follows: age, 60 to 70 in ten year increments (two categories); sex, M versus F, (two categories), weight, 50 kg, 80kg 130kg (three categories, each paired with a height of 170cm to make BMI categories of underweight (17.3), normal weight(27.7), and obese(45); ejection fraction,30-40 in 5% intervals (three categories); hematocrit, 25-40% in 15% intervals (two categories); creatinine values 0.8, 1, 1.3,

1.7, 2 (five categories); insurance status-commercial, Medicaid, and Medicare only if above age 65 (two categories); diabetes on insulin, yes versus no (two categories); moderate lung disease, yes versus no (two categories); and number of diseased vessels two versus three (two categories). If a patient risk profile had 2 vessel disease, the profile included >70% proximal LAD stenosis per guideline recommendations for elective CABG. Certain variables for all risk profiles were the same such as presence of hypertension, medicated with ACE's/ARBs, nonsmoker status, height of 170cm, white blood cell count of 10,000, platelet count 210,000, alcohol use less than 1 time a week, chronic NYHA class 3 heart failure with stable angina, presence of aortic stenosis and mitral stenosis, moderate aortic insufficiency, trace mitral and tricuspid insufficiency, elective surgery status, and first-time surgery. All other variable inputs were not used and the value was NO for all risk profiles. For each of the two strata (Black versus White individuals) we created 11,520 possible risk profile combinations (also referred to as risk profiles).

Study Population

In this exploratory study, the chosen variables and ranges of continuous data were chosen based on clinical relevance to risk and ability to represent realistic characteristics of an intermediate to high-risk patient in which elective CABG is indicated. Main criteria in selection of patients for CABG vs PCI include disease stability, procedural risk (as measured by risk calculators-STS, SYNTAX and EURO score), patient comorbidities, atherosclerotic burden in vessels, and lesion complexity. This study will examine plausible risk profiles that are aligned with choosing CABG over PCI. [31] Input variables, inclusion and exclusion criteria are listed in Supplementary Table 3.

Estimation of 10-year cardiovascular disease risk for risk factor combinations with STS calculator

We calculated the STS predicted risk of short term (30day) mortality for each of the 11,520 risk factor combinations by inputting values into the published STS risk functions (2018 STS Adult Cardiac Surgery Risk models). We excluded risk profiles that yielded a predicted risk of mortality estimates that were below 2% and above 10% as recommended by AHA risk stratification guidelines and to focus on describing intermediate to high-risk cases.

Differences in risk for Black versus White individuals with the identical risk factor combinations

All analysis were sex specific. A total of 5,041 risk profiles were analyzed for men and 4,768 risk profiles were analyzed for women after excluding scores that were below 2% and above 8%. Profiles were excluded to create a hypothetical cohort of predominantly intermediate-to high-risk patients. First, we calculated differences in the STS-based estimates of short-term mortality and composite morbidity/mortality after CABG for Black versus White individuals with identical risk factor combinations. Next, we evaluated two possible scenarios (for each sex) in which the STS PROM estimate for the two races were on opposite sides of the critical 5% threshold that triggers clinical and patient decisions when exceeded (ie: discussions about transfer of care to larger facility, risk benefit analysis of procedure, patient and patients' family opting for PCI instead of CABG). This analysis was repeated at the 8% threshold. We identified the risk factor

combinations that yielded divergent estimates of PROM for Black versus White individuals at the 5% and 8% threshold. For each scenario, we plotted histograms to describe the sex-specific distributions of the differences in absolute and relative risks (of short-term mortality/PROM) for Black versus White individuals. We described the clinical features of the divergent risk profiles.

Statistical Analysis

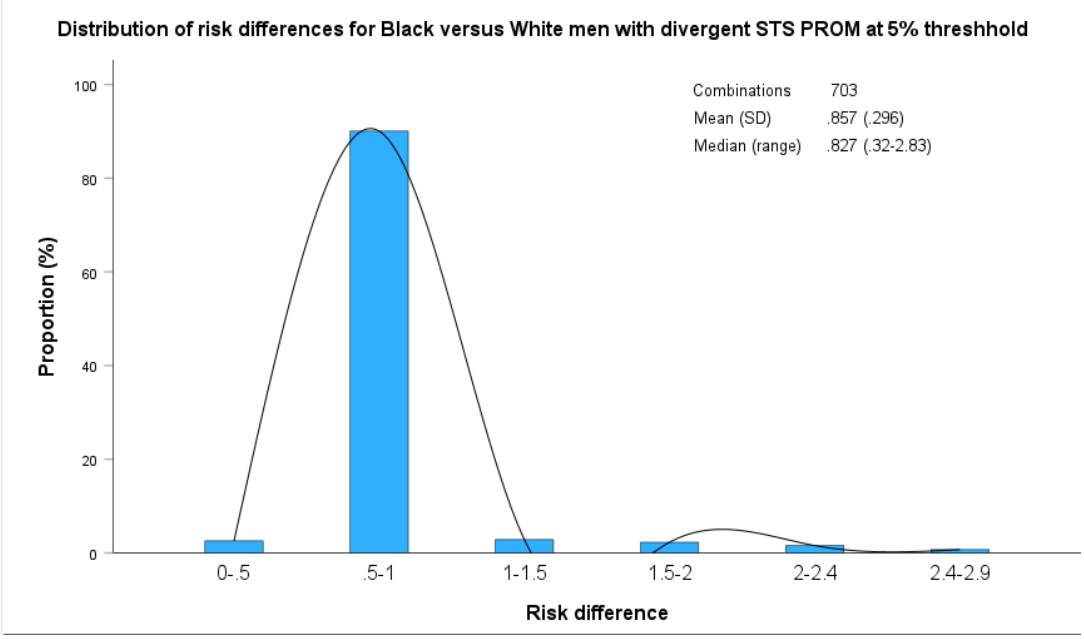
All analyses were sex specific. For the in-silico analysis, first we created a dataset of risk factor profiles for which we calculated the predicated risk of mortality for Black and White individuals. Next, we created two new dataset, one where Black individuals have an STS score exceeding 5% but White individuals do not, and another dataset where the converse was true. For each data set, we calculated the STS estimated risk difference and the relative risk (where the race with the lower risk was the referent). For the divergent profiles, we calculated the secondary outcome- total morbidity/mortality absolute risk difference and total morbidity/mortality relative risk for each sex. All analysis of these dataset were descriptive, using means, medians, SD's, ranges, and related visualizations for risk differences and relative risks.

Results

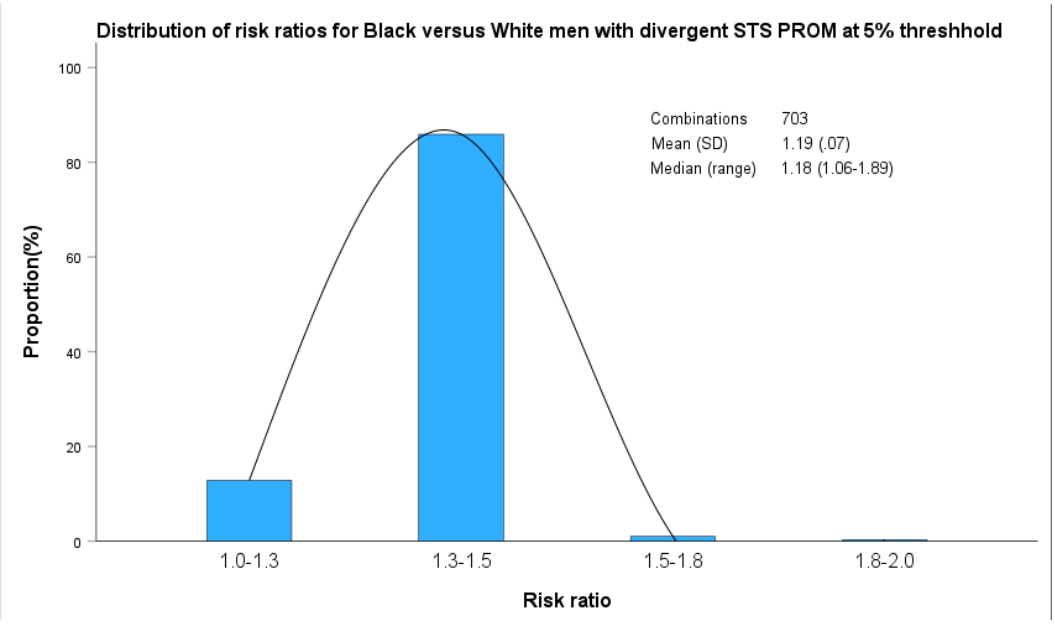
For our in-silico analysis, we evaluated 5,041 risk factor combinations for men and 4,768 risk factor combinations for women after excluding profiles that generated PROM estimates below 2% or above 10%. We evaluated the extent of divergence in STS-estimated PROM in Black versus White individuals with identical risk factor profiles. There were 703 risk profiles where a Black man had an estimated 30-day risk of mortality (STS PROM) exceeding 5% but a White man with an identical risk profile had an estimated risk below that threshold. There were 189 risk profiles associated with STS PROM score above 8% for Black men but not for White men with identical risk factor profiles. Differences between Black and White males in STS PROM scores for these risk factor combinations are shown in Figure1.

Differences in absolute short term mortality risk between Black and White individuals at the 5% threshold can be as large as 2.83% (median 0.827%; Figure1A), and the Black versus white relative risk can be as large as 1.89 (median 1.18; Figure1B). Differences in absolute short term mortality risk between Black and White individuals opposite the 8% threshold can be as large as 3.24% (median 0.81% ; Figure1C), and the Black versus White relative risk can be as large as 1.54 (median 1.11 ;Figure1D)

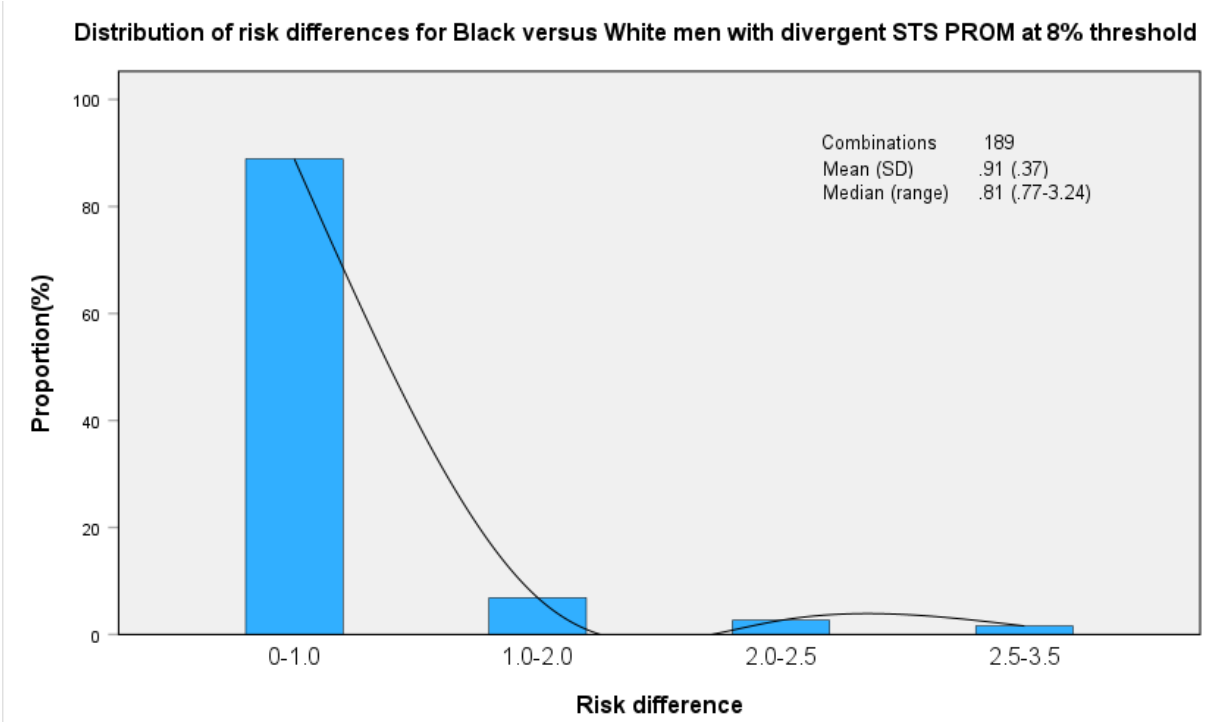
A.


Distribution of risk differences for Black versus White men with divergent STS PROM at 5% threshhold
Combinations 703
Mean (SD) .857 (.296)
Median (range) .827 (.32-2.83)
Proportion (%)
100
80
60
40
20
0
0-.5
.5-1
1-1.5
1.5-2
2-2.4
2.4-2.9
Risk difference

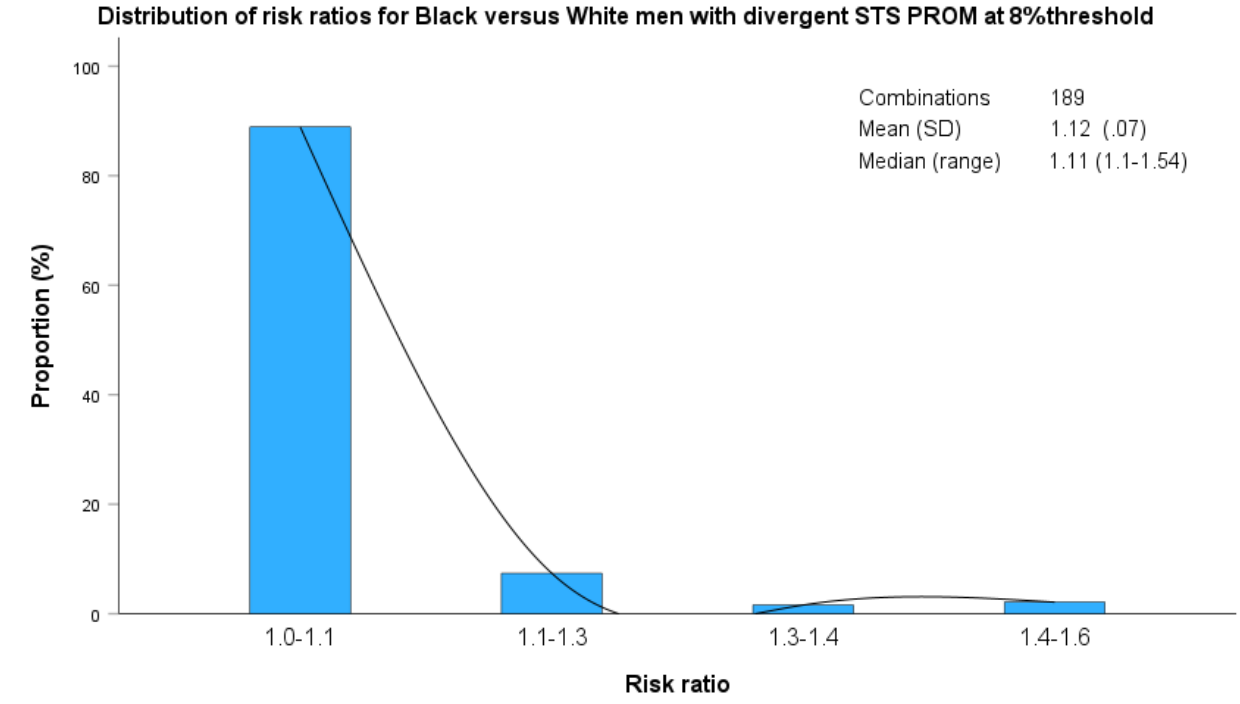
B


Distribution of risk ratios for Black versus White men with divergent STS PROM at 5% threshhold
Combinations 703
Mean (SD) 1.19 (.07)
Median (range) 1.18 (1.06-1.89)
Proportion(%)
100
80
60
40
20
0
1.0-1.3
1.3-1.5
1.5-1.8
1.8-2.0
Risk ratio

C

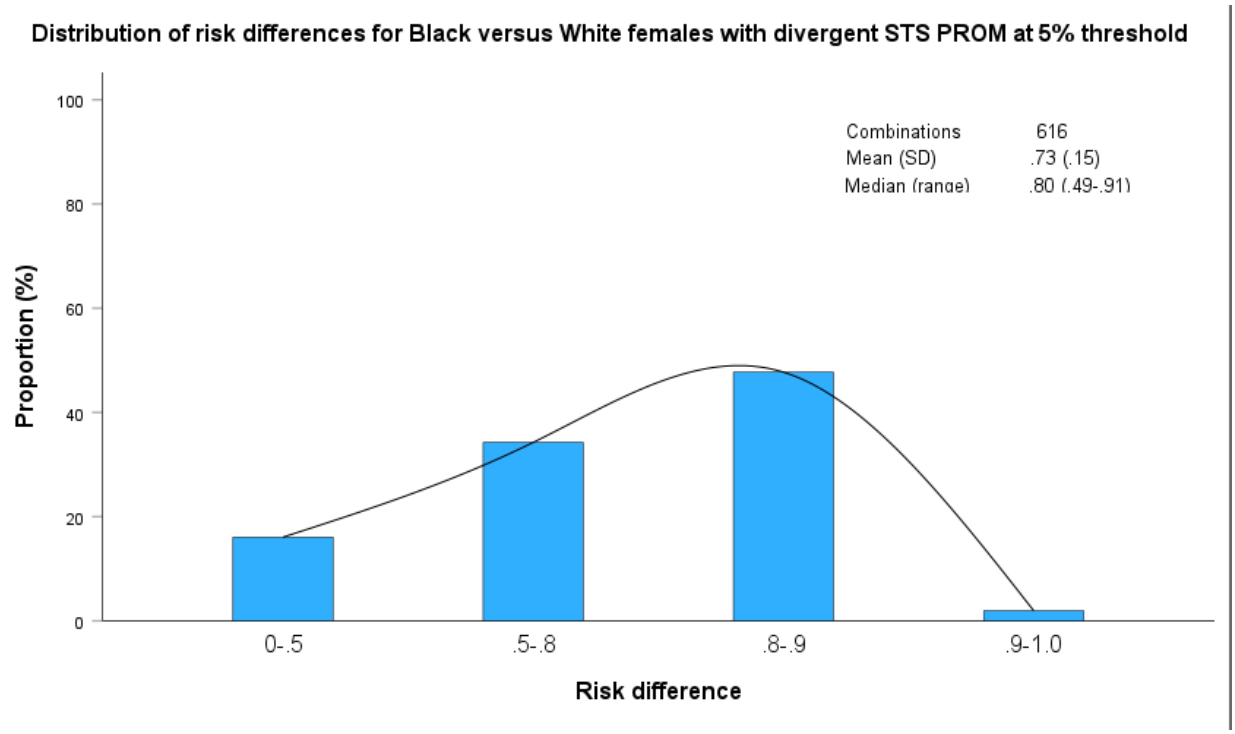

Distribution of risk differences for Black versus White men with divergent STS PROM at 8% threshold
Combinations 189
Mean (SD) .91 (.37)
Median (range) .81 (.77-3.24)
Proportion(%)
100
80
60
40
20
0
0-1.0
1.0-2.0
2.0-2.5
2.5-3.5
Risk difference

D

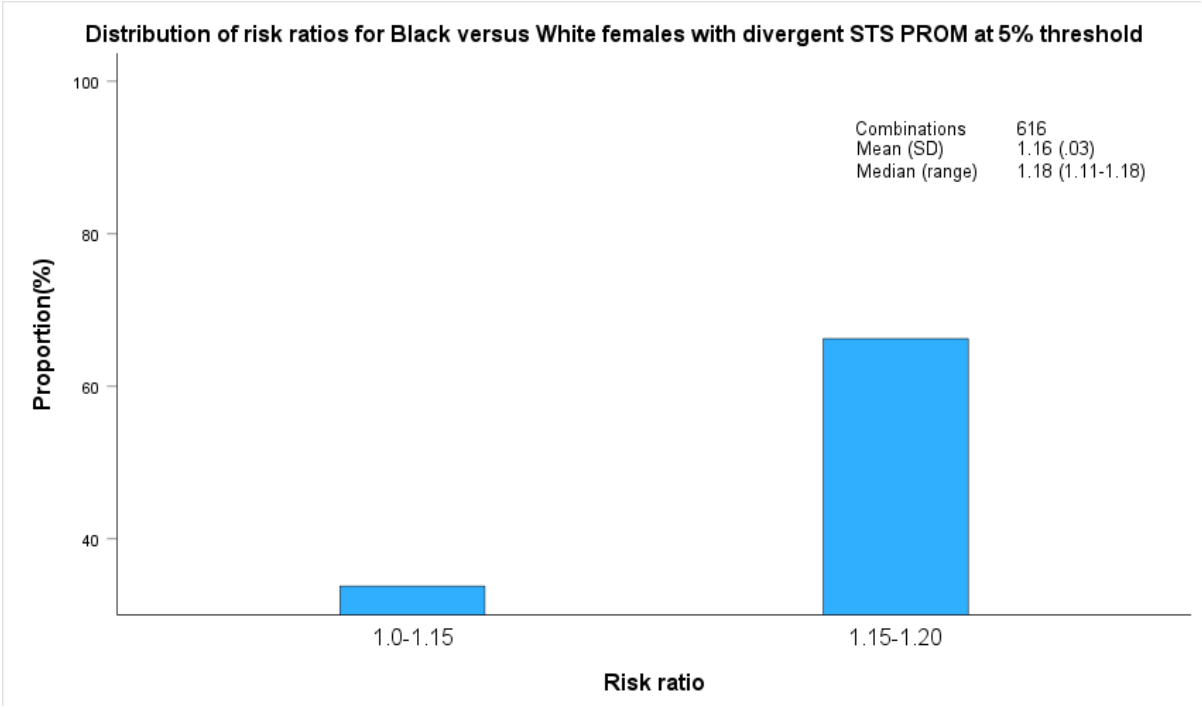

Distribution of risk ratios for Black versus White men with divergent STS PROM at 8%threshold
Combinations 189
Mean (SD) 1.12 (.07)
Median (range) 1.11 (1.1-1.54)
Proportion (%)
100
80
60
40
20
0
1.0-1.1
1.1-1.3
1.3-1.4
1.4-1.6
Risk ratio

There were 616 risk profiles where a Black woman had an STS PROM exceeding 5% but a White woman with an identical risk profile did not. There were 347 risk profiles associated with STS PROM greater than 8% for Black women but not for White women with identical an risk factor profile. Differences between Black and White women in STS PROM for these risk factor combinations are shown in Figure2. The difference in absolute short term mortality risk between Black and White individuals on the opposite side of the 5% threshold can be as large as 0.91% (median 0.80%; Figure2A), and the difference in relative risk of short-term mortality can be as large as 1.18 (median 1.18; Figure2B). The difference in absolute short term mortality risk between Black and White women at opposite side of the 8% threshold can be as large as 2.81% (median 0.81%; Figure2C), and difference in relative risk of short-term mortality can be as large as 1.5 (median 1.11; Figure2D)

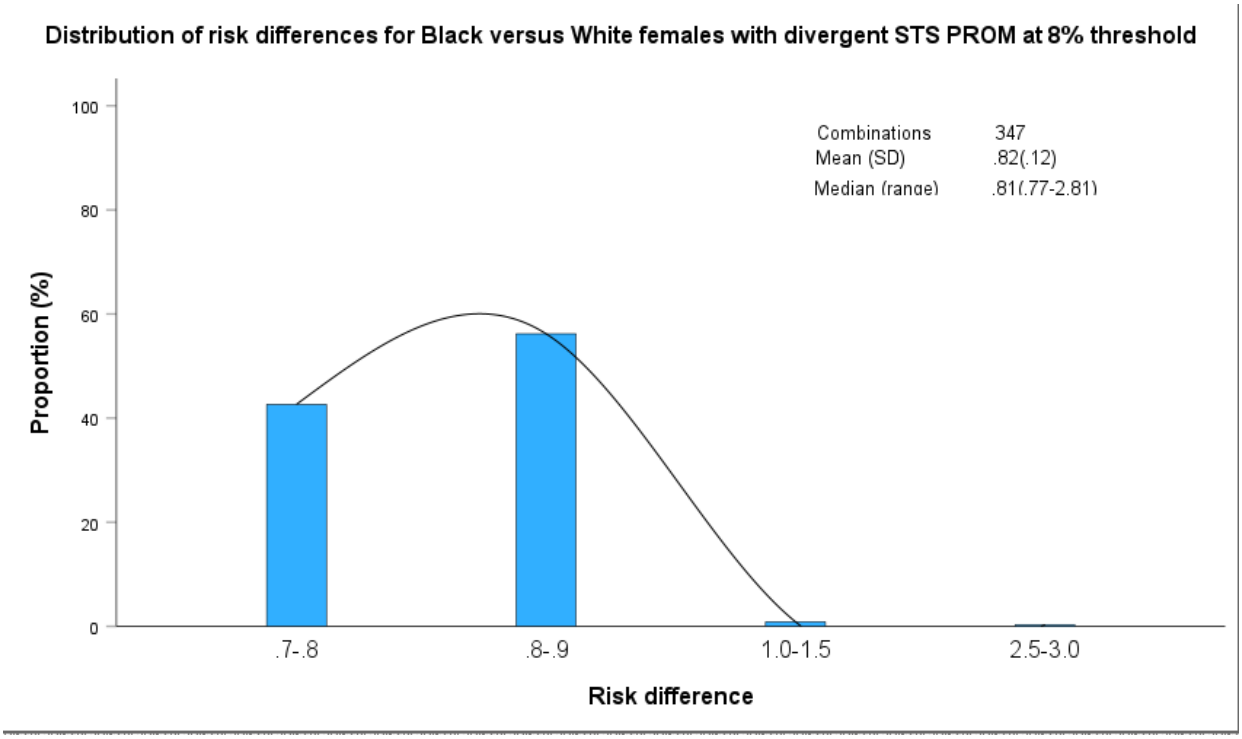
A



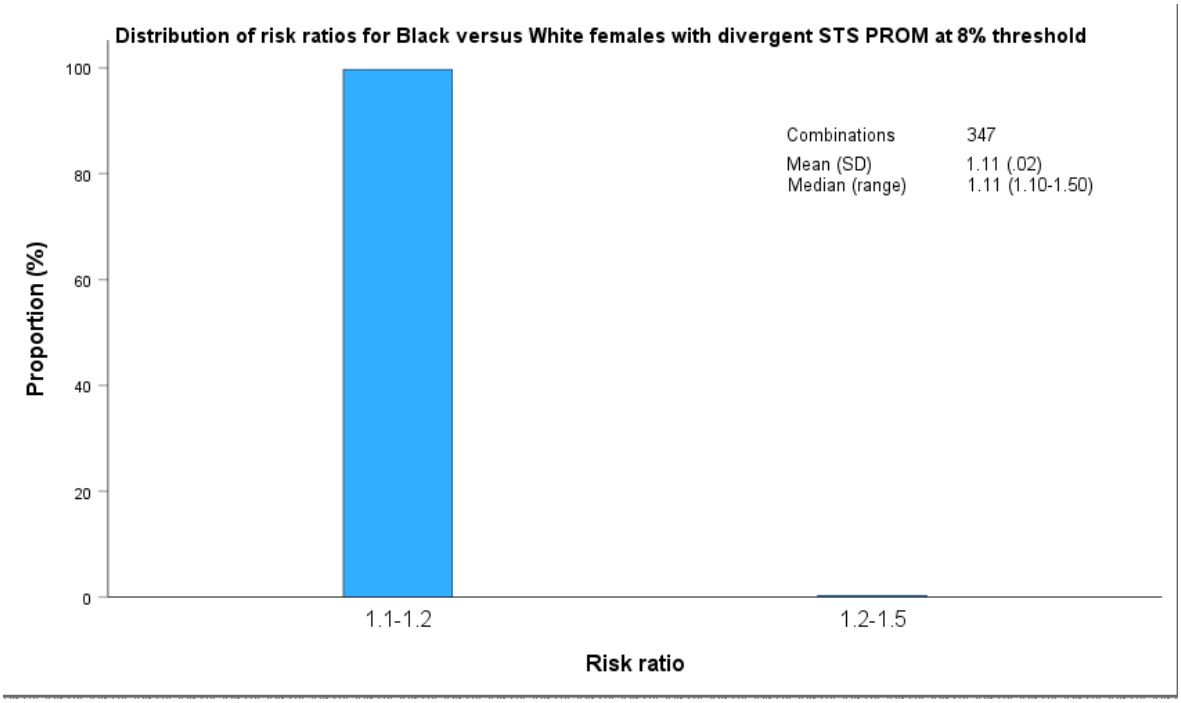
B


Distribution of risk ratios for Black versus White females with divergent STS PROM at 5% threshold
Combinations 616
Mean (SD) 1.16 (.03)
Median (range) 1.18 (1.11-1.18)
Proportion(%)
100
80
60
40
1.0-1.15
1.15-1.20
Risk ratio

C.


Distribution of risk differences for Black versus White females with divergent STS PROM at 8% threshold
Combinations 347
Mean (SD) .82(.12)
Median (range) .81(.77-2.81)
Proportion (%)
100
80
60
40
20
0
.7-.8
.8-.9
1.0-1.5
2.5-3.0
Risk difference

D.

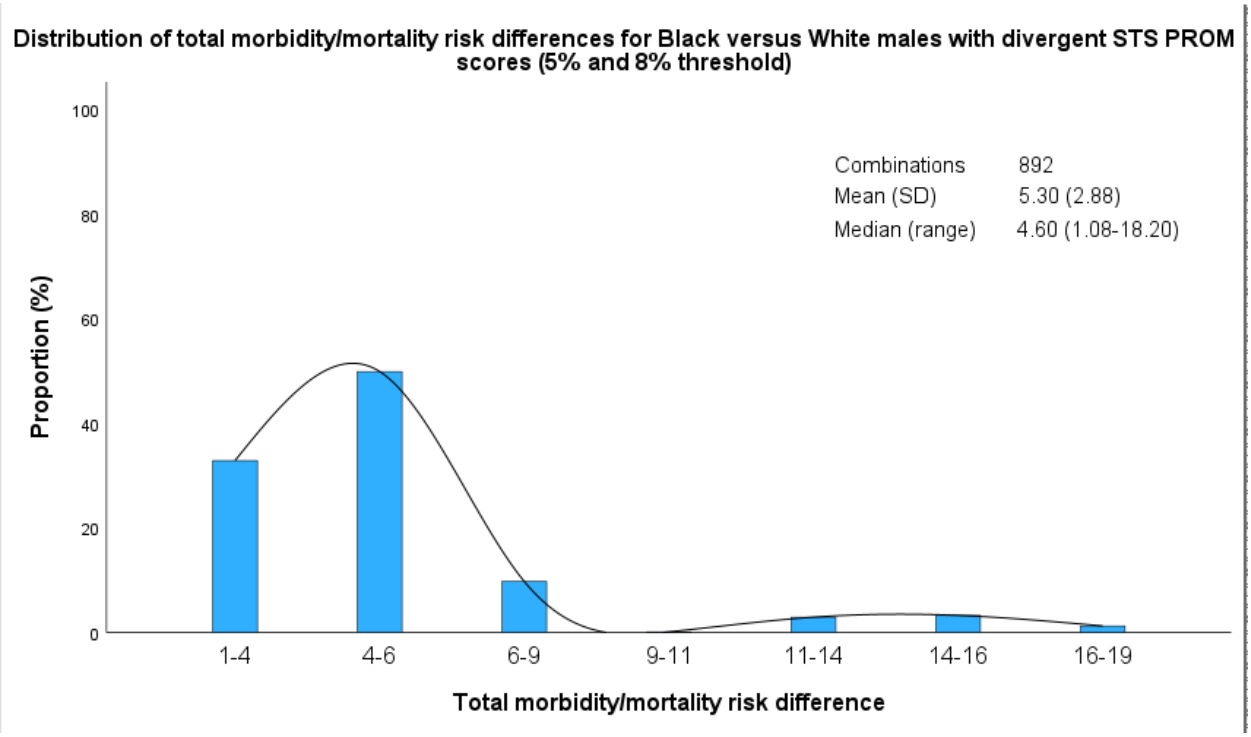


There were no risk profiles using the STS in which PROM for White individuals was above 5% risk and PROM for Black individuals was below 5%. nor any risk profiles, which PROM for White individuals was above 8% risk and PROM for Black individuals was below 8%.

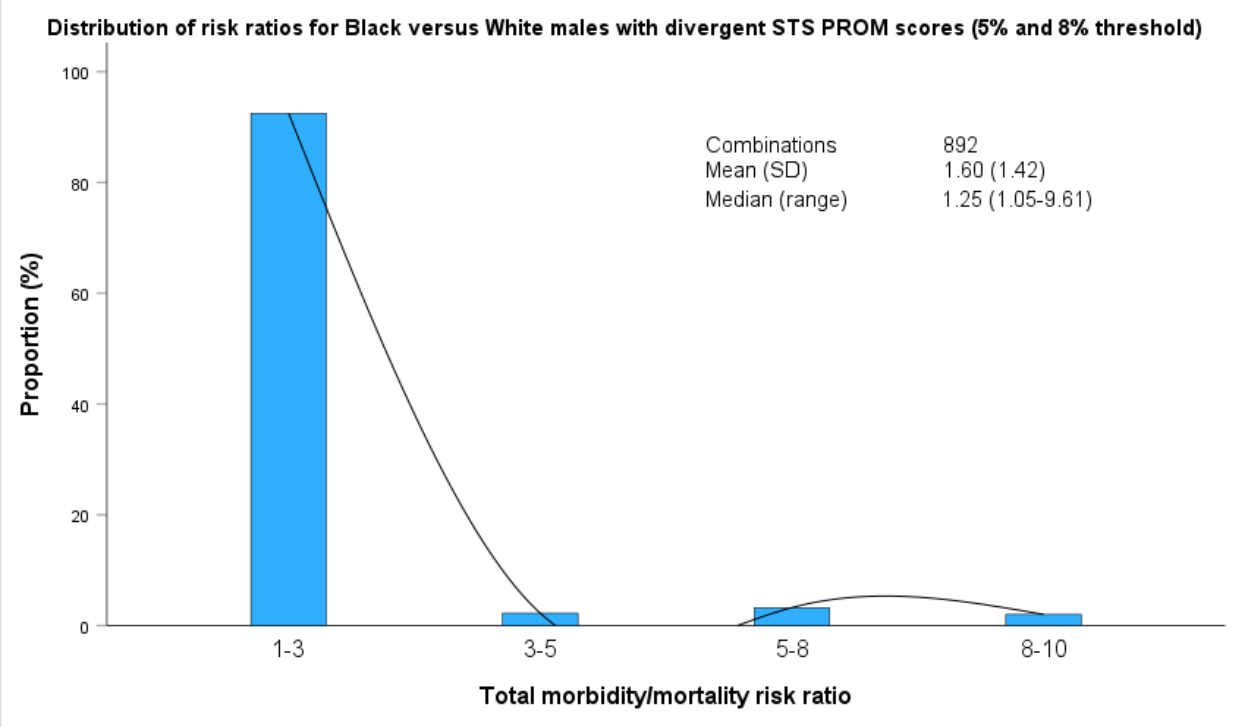
We also analyzed the secondary outcome, composite or total morbidity/mortality, for the divergent risk factor profiles. This STS reported outcome is a composite predicted risk which includes total risk of operative mortality, stroke, renal failure, reoperation, prolonged ventilation and deep sternal wound infection combined. We visually represented distributions of total morbidity risk differences and total morbidity relative risk for male and female risk profiles. The distributions include divergent risk profiles for both thresholds (5% and 8%).

Of the total 892 divergent risk profiles for men at both the 5% and 8% threshold, the difference in absolute total morbidity/mortality was as large as 18.20% (median 4.60%; Figure3A), and total morbidity/mortality relative risk was as large as 9.61 (median 1.25; Figure3B). Of the 963 divergent risk profiles for women at the 5% and 8% threshold, the difference in absolute total morbidity/mortality was as large as 7% (median 3.60%; Figure3C) and the total morbidity/mortality relative risk was as large as 1.30 (median 1.18)

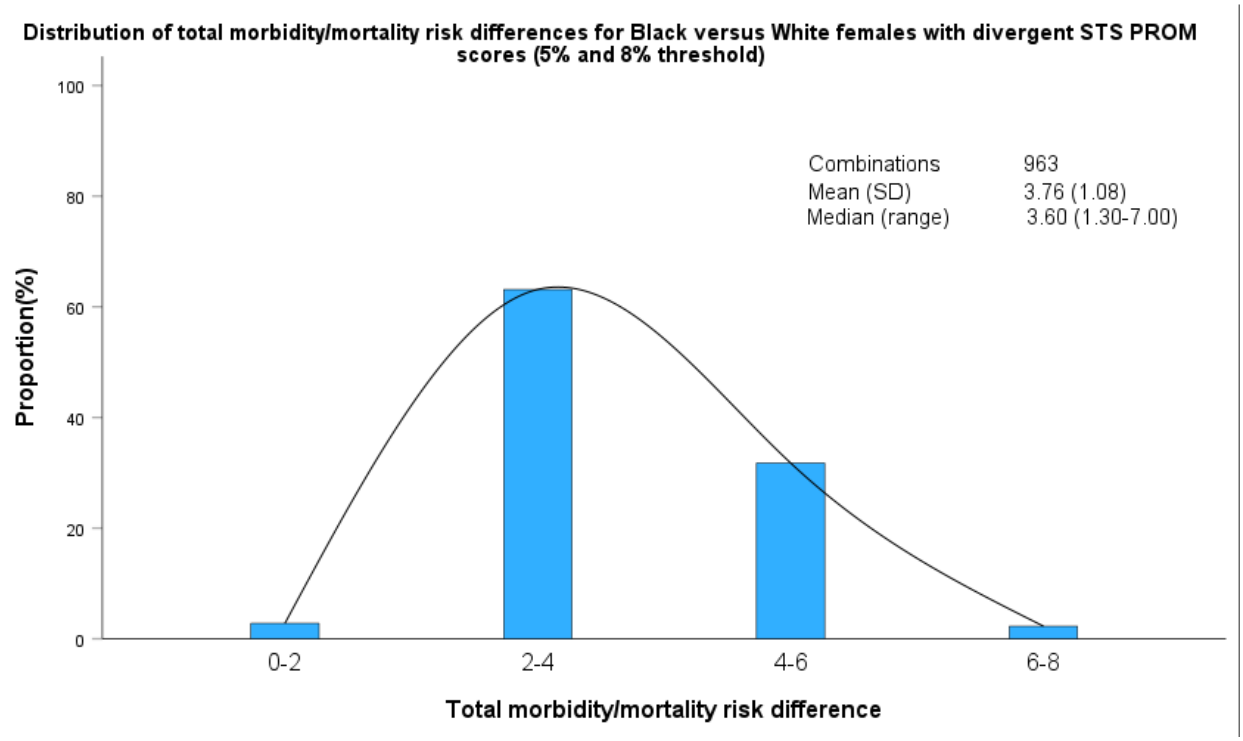
A.


Distribution of total morbidity/mortality risk differences for Black versus White males with divergent STS PROM scores (5% and 8% threshold)
Combinations 892
Mean (SD) 5.30 (2.88)
Median (range) 4.60 (1.08-18.20)
Proportion (%)
100
80
60
40
20
0
1-4
4-6
6-9
9-11
11-14
14-16
16-19
Total morbidity/mortality risk difference

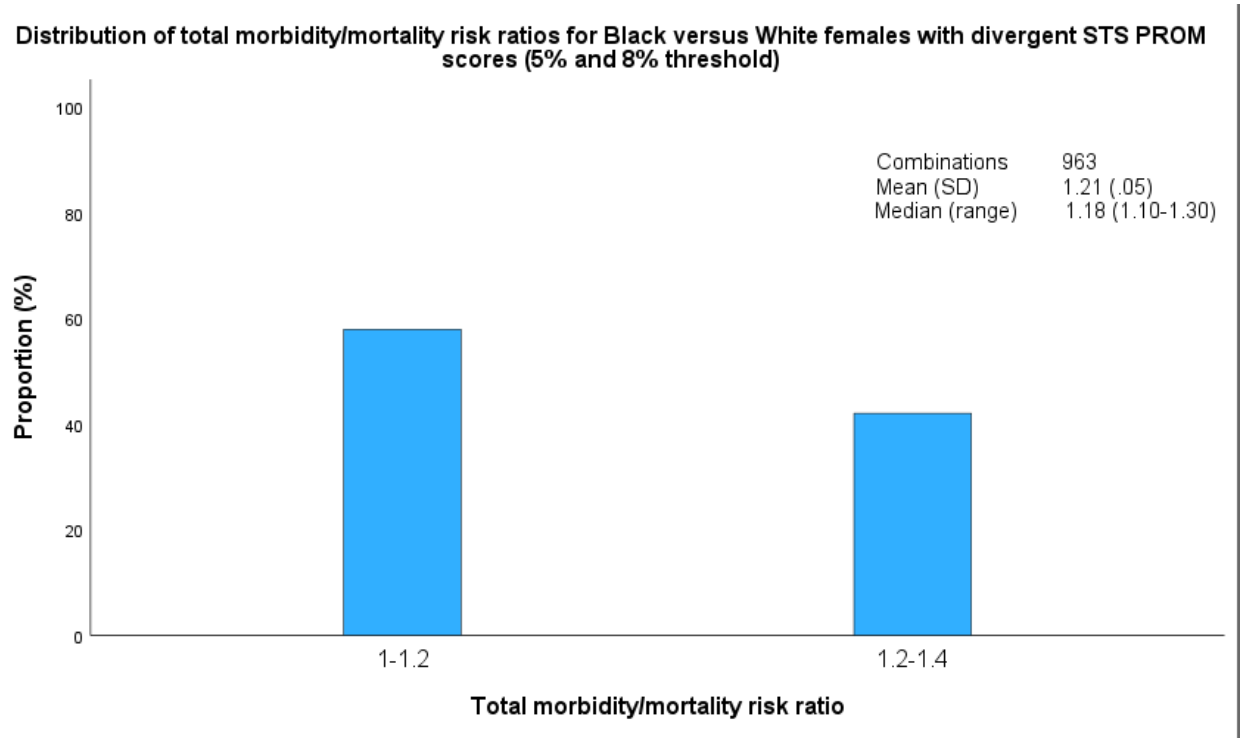
B


Distribution of risk ratios for Black versus White males with divergent STS PROM scores (5% and 8% threshold)
Combinations 892
Mean (SD) 1.60 (1.42)
Median (range) 1.25 (1.05-9.61)
Proportion (%)
100
80
60
40
20
0
1-3
3-5
5-8
8-10
Total morbidity/mortality risk ratio

C.



D.



Of the 892 divergent risk profiles for men at the 5% and 8% threshold, 57% were age 70, 46% had Commercial insurance, 49% weighed 50kg (BMI 17.3), 53% had hematocrit of 25%, 27% of

profiles had creatinine of 2, 58% had peripheral arterial disease, 53% had IDDM, 60% had moderate lung disease, 53% had 3 vessel disease, and 37% had ejection fraction of 30%. Secondary outcomes measured included stroke risk difference (median RD 0.83%, range .02%-3.12%), renal failure risk difference (median RD 3.22%, range 0.64%-11.47%), risk of prolonged ventilation risk difference (median RD 3.00% range 0.32%-5.59%), and risk of long stay >14days (median RD 6.10% range 1.50%-8.70%) (Supplementary Table1)

Of the 963 divergent risk profiles for women at the 5% and 8% threshold, 54% were age 60, 48% had commercial insurance, 42% weighed 50kg (BMI 17.3), 50% had a hematocrit of 25%, 27% had creatinine of 1.3, 53% had peripheral arterial disease, 52% had IDDM, 53% had moderate lung disease, 50% had 3 vessel disease, 35% had ejection fraction of 35%. Secondary outcomes measured included stroke risk difference (median RD 1.35% range 0.23%-6.58%), renal failure risk difference (median RD 0% range 0%-8%), risk of prolonged ventilation (median RD 0%, range 0%-5.63%), and risk of a long stay >14days (median RD 3%, range 1.60%-8.40%) (Supplementary Table2)

For the most divergent risk profile for women, with maximum absolute PROM risk difference of 2.81%, clinical characteristics are described in (Table1).
For the most divergent risk profile for men, with maximum absolute PROM risk difference of 3.24%, clinical characteristics are described in (Table1).

Table1

Sex	Maximum Risk Difference	Age	Insurance status	Weight	Hematocrit (%)	Creatinine	Peripheral arterial disease	Diabetes on insulin	Lung disease	Number of diseased vessels	Ejection Fraction (%)
F	2.81%	60	Medicaid	130kg (BMI 45)	40%	1.00	Yes	Yes	Moderate	2 vessels	30%
M	3.24%	60	Medicaid	130kg (BMI 45)	25%	1.70	Yes	No	No	3 vessels	30%

Discussion:

Our analysis yielded four main findings. First, the STS calculator for short term mortality, total morbidity, and selected adverse outcomes can result in differential risk stratification for Black versus White individuals who have identical risk profiles. In this study, 703 Black male risk profiles were stratified as high risk with STS PROM greater than 5%, while the identical White male risk profile was stratified in to intermediate risk below 5%. additionally, 189 Black male risk profiles were stratified as very high risk >8%, while the identical White male counterfactual risk profile was stratified as high risk<8%. For women, 616 risk profiles stratified Black women as high risk of mortality above 5% while the identical White risk profile counterfactual was stratified into the intermediate risk category below 5%. Lastly, 347 Black female risk profiles were stratified into the very high-risk category above 8%, while the White counterpart was stratified as high risk below 8%.

Second, specific risk factor combinations with multiple comorbidities and severe clinical features might exacerbate differences between Black and White individuals in STS PROM. In both sexes, the most divergent profile, with maximum absolute difference, was more likely to have moderate lung disease, insulin dependent diabetes, peripheral arterial disease, or 3 vessel disease.

Third, the race-related differences in STS PROM might be clinically meaningful- ie they could result in differential surgical decisions, treatment plans (PCI over CABG), and timing of surgeries in individuals with identical risk profiles based solely on their race. Although the surgery is elective, and delays should not affect cardiac outcome, being labeled as high risk may dissuade patient's from pursuing the surgery referral elsewhere, may lead them to opt for PCI over CABG despite guidelines, or may lead to logistic delays in accessing care. It is important that patients who are receiving elective CABG's receive their surgeries in a timely manner because timing of intervention, even if elective, can effect long term outcomes.

Fourth, if the differences between Black and White individuals for predicted risk of short-term mortality are considered to be miniscule and would not affect clinical/surgical decision-making, it is ethically prudent to remove the race variable from the short-term risk calculator altogether. The STS may discover that removing the race variable from their algorithm, does not alter the C statistic of the STS model. The Observed to Expected (O/E) values for large institutions would likely be the same even with a larger portion of "higher risk individuals." Black patients who would previously be expected to have minimally higher risk, would have the same predicted risk as White individuals. If National Quality Forum guidelines are met, it is unlikely that the Observed to Expected mortality ratio of Black patients would suffer (in the form of higher-than-expected mortality). Engem's 2015 **s**tudy revealed that hospitals that take "high risk" individuals often have better risk adjusted mortality rankings, therefore, removing the race variable from risk adjustments would likely not change hospital performance scores or financial reimbursement. [11]

Limitations of the study are that these results may be seen as theoretical in nature because of the in-silico design. An additional study with a community-based cohort may be helpful to look

at differential risk prediction in intermediate to high-risk patients. Further exploration is needed in order to address potential algorithmic bias in the age of big data modeling.[35] The consequence of differential STS estimated risk scores may mean a potential delay in care if being transferred to a tertiary center. It could also mean a delay in care from increased waiting time if patients are placed at lower risk for their elective procedure, presenting a healthcare utilization concern for both White and Black patients. Differential scores could also lead to differential treatment plans such as medical management or PCI over CABG. Lastly, differential scores based on race could lead to patient refusal of surgery if their interpretation of their own STS PROM dissuades them. Epidemiologists, population geneticists, and medical researchers have the responsibility to structure research about race with a socio-politically informed lens in order to propel anti-racist science forward. Medical researchers and algorithm makers have the option to lead by example and end the use of biologically useless categorizations in risk predictions.[36] The legacy of medicine, race, and statistics are heavily intertwined in a racist history, furthering the need for a consensus about how to ethically move forward.[37,38] Furthering anti-racism in academia will take a collaborative effort from medical professionals, population geneticists, researchers, public health experts, journals, and institutions.

Comment – not included in final manuscript

STS PRESIDENT RESPONDS TO LETTER FROM CONGRESS ABOUT RACE AS A VARIABLE:

Separate from the issue of adjusting for race in hospital reporting of outcomes in larger populations, race adjustments should certainly not be made on an individual level. The STS president seems unconcerned for this potential health equity concern due to the general landscape of risk adjustment in reporting. However, the continuation of race as a biological variable has implications for personalized medicine, shared decision-making, and equity. Chairman Richard E. Neal of the US House of Representatives wrote a letter to the president of the STS and asked whether the use of race as a variable would be investigated for possible health equity concerns. The STS president's response was that race correction would not lead to health equity concerns because using race as a variable would help surgeons feel comfortable about the predictions of the calculator and limit high risk patient aversion in low SES groups and Black patients. The STS response letter also states race will continue to be a variable in the calculator due to its strong empiric association with outcomes regardless of the etiology/mechanism of the association. The STS calculator currently has over 65 clinically relevant variables with a C-statistic (AUC) of .804 for operative mortality after CABG. C-statistics for other morbidities after CABG range from .681 for deep sternal wound infection to .826 for renal failure.[39] It is unknown whether removing and replacing race from the model would lessen the C statistic for CABG outcomes. It is also possible that the STS model currently overfits for individual risk assessment and a descriptive SES variable may improve the calibration more than a race variable. Overfitting is a common issue with non-parsimonious models with many variables such as the STS model. [40] There are potentially other variables that could replace race whether they be inflammatory markers such as CRP, DCI/ADI deprivation indices, cytokine markers, or proxies of stress.[41] [42] STS states they will avoid the philosophical objections to including race and continue to develop the model using the "strongest empiric associations."

In addition, the STS president shows pitfalls in his understanding of genetics stating that race will always remain a predictor of cardiac outcomes whether the relationship be "genetic, environmental, social, political, or consist of other non-heritable factors." The president goes on to refute that even though race has been defined as a social construct "population geneticists have published numerous large studies showing that genetic clustering, consistent with continentally-based racial ancestry persists in the modern era, and that differences in human genetic structure are highly correlated with self-identified racial classification." Lastly, the president purports that just because race is a social construct, "these facts should not be construed to imply that socially-defined racial groups do not differ biologically or genetically, including their risk for certain diseases, better or worse outcomes with certain diseases, and differential responsiveness to certain medications". Unfortunately, the STS president shows pitfalls in genetics knowledge. In fact, racial categories do not correlate to pharmacogenomics or SNP's that confer risk of drug reactions despite what medical curriculums continue to propogate.[43] Medical curriculums should understand that high prevalence of an SNP in a specific geographic population does not mean it is related and co-inherited with ancestry markers. In addition, having a certain SNP does not necessarily confer risk of disease because there is widely variable penetrance of these genetic mutations. Lastly, SNP's may have high prevalence in certain places, but that does not mean it cannot exist in a geographic location very far away from its high prevalence. There is no single SNP that solely exists in one racial group and not the other, nor is there an SNP that exists solely in one geographic group and not the other. Human variation represents clinal rather than discrete variation. Therefore, the pharmacogenomics of drug reactions are still under study in the age of molecular genetics and large data collection. Published genetics studies also make spurious associations between SNP's and disease risk without having cellular biological evidence for the claim. Often genetics studies are done stochastically and probabilistically using programs such as STRUCTURE and FRAPPE. If data from ancestral populations are missing, which is often the case when studying "African ancestry", researchers will use present day population proxies rather than true ancestral genetic data, and STRUCTURE or FRAPPE will force the results into a composite of the reference samples used. Therefore, results can be skewed simply because of how the algorithms work. As Royal aptly describes in her review of present-day genomics: "‘"ancestral populations'' are not directly observed—although in many applications, samples from related populations are used as a proxy. For example, present-day Yoruba are the most frequently used proxy for inferring African American ancestry, despite the fact that most African Americans derive their ancestry from diverse West African (and other African) populations that existed over a span of several centuries which might not be well represented by present-day proxy populations".[36] In addition, different parts of the human genome can have differing ancestries- meaning different marker systems used by researchers can provide different information about individual and population history. The emphasis of admixture estimation on differences over similarities can be misleading about the overall genetic structure of the human species. For this reason, it is very necessary for the field of genetics to come to a consensus on how to ethically publish papers regarding ancestry, race, and disease.[36] This type of categorical, historical, and commercialized thinking is why the drug Bi-Dil was approved from a study without a control group as it marketed itself as the world's first "Black hypertension drug".[44] Many cardiologists

also believed the clever marketing as shown in Royal's qualitative study in 2019, highlighting the need for a better understanding of genetics and population structure within the medical and scientific community.[45] This type of thinking will continue to have ripple effects about how surgeons, patients, and the public think about biology and race. The President of the STS's response highlights the general concern when continuing to allow race as variable in clinical models. The president really believes there may be an undetermined genetic basis for which Black race continues to be a predictor of poor outcomes-a core tenet of modern eugenics. Racism is the sole reason for differential outcomes regarding Black health. The philosophical implications for keeping race in clinical algorithms are huge despite what the president of the STS believes. In critiquing Vyas' Hidden in Plain Sight, the STS president refutes that even a difference between a Black and white patient at high risk of 12% vs 10% mortality on the calculator could never dissuade a patient or surgeon out of surgery. While it may be true that high risk scores will not cause a *denial* of surgery especially in the era of risk adjustment in reporting, patient transfers, and tertiary cardiac centers, it still holds true that a risk score above 5% may stratify a patient as high risk making them ineligible to receive surgery at their community hospital- requiring a transfer and *delay of care* or it may influence risk-benefit discussions on PCI over CABG. Evidence discussed earlier displays how long waiting times, transfers of care, and logistic delay can lead to worse outcomes. While it may be in the patient's best interest to receive surgery care from a large institution that is equipped for high-risk patients, this still raises a potential equity concern for those at intermediate and not yet severely high risk. Patients could differentially be referred out of centers despite truly being a candidate for surgery at their community hospital or differentially referred to PCI over CABG, especially at smaller hospitals**.** It is well studied that higher risk patients often benefit from CABG over PCI especially in the setting of diabetes. In regard to shared-decision making, patients may also differentially opt for PCI rather than CABG dependent on their interpretation of their own STS risk score.

Supplementary Tables

Males divergent risk profiles at 5%and 8 % thresholds- 892 divergent profiles

		Stroke RiskDiff	Renal failure RiskDiff	Prolonged ventilation RiskDiff	Long stay>14days RiskDiff
N	Valid	892	892	891	257
Mean		.9292	3.4963	3.2585	5.9818
Median		.8345	3.2200	2.9980	6.1000
Std. Deviation		.45208	1.80887	.96736	1.29189
Minimum		.02	.64	.32	1.50
Maximum		3.12	11.47	5.59	8.70

Females divergent risk profiles at 5% and 8% threshold-963 divergent profiles

		Stroke RiskDiff	Renal failure RiskDiff	Prolonged Ventilation RiskDiff	Longstay> 14days RiskDiff
N	Valid	963	963	963	963
Mean		1.7744	1.3337	1.0008	3.7641
Median		1.3490	.0000	.0000	3.0000
Std. Deviation		1.27308	2.03565	1.40036	1.66645
Minimum		.23	.00	.00	1.60
Maximum		6.58	8.00	5.63	8.40

Supplementary Table3: STS Input Variables

Input Variables STS	Chosen variables *(rational for variables based on clin.relevance+ guidelines)*	
Age	(Value 1-110) chosen= 60,70	2 variables
Gender	M/F (separate analysis)	2 variables
Race	Black/White	2 variables
Primary Payor	(none, **Medicare, Medicaid**, **commercial** , HMO)	2 variables
Secondary Payor	Same as 1st payor * *above age 65 risk profiles will have Medicare as first payor Medicaid as second payor for all Medicaid risk profiles. Risk profiles below 70 will only have Medicaid and commercial risk profiles.*	-
Date of Surg	-leave blank	-
Weight	Value 10-250(50 kg, 80kg 130kg) paired with height for BMI range: underweight BMI =17.3, Normal/overweight BMI=27.7, obese BMI=45)	3 variables
Height	Value (20-251)= 170cm	-*paired with weight for BMI categorization
Hematocrit	Value 1-99 chosen= low or normal=25%,40%,	2 variables
WBC	Value (.1-99)= normal=4,500 to 11,000 WBCs per microliter	-Pick 1 avg value =10 (x10^3 wbc/mm3)
Platelets	Value (1,000-900,000) =210,000	-pick 1 avg value =210,000
Last Cr	Value (.1-30) chosen= .8, 1, 1.3, 1.7, 2	-5 variables
Dialysis	(y/n) NO	-
HTN	(**y**/n) YES	-yes , likely comorbidity
Immunocompromised	(y/n) NO	-
Peripheral artery disease	(y/n)	-2 variables

Cerebrovascular disease	(y/n) NO	-
Mediastinal radiation	(y/n) NO	-
Cancer within 5yr	(y/n) NO	-
Fhx premature CAD	(y/n) NO	-
Sleep apnea	(y/n) NO	-
Liver dz	(y/n) NO	-
Unresponsive state	(y/n) NO	-
Syncope	(y/n) NO	-
Diabetes	(y/n) *YES = + click insulin controlled	-2 variables
Endocarditis	(y/n) NO	-
Chronic lung disease	**(no**, mild, **moderate,** severe, unknown)	-2 variables (none or moderate)
Severity of stenosis on right carotid	Value (50-79, 80-99, 100)	-no click
Severity of stenosis on left carotid	Value (50-79, 80-99, 100)	-no click
Illicit drug use	(y/n) NO	-
Etoh use	(**<1/week**, 2-7/week, >8/week, none)	-choose <1/week
PNA	(recent, remote, **NO,** unknown)	-
Tobacco	(**Never,** current everyday, somedays, unknown, former)	-
Home 02	(Yes prn, yes 02 dep, **no**)	-
Previous cardiac interventions	Do not click	-
MI when	(<6hrs, 6-24 hrs, 1-7 days ago, 8-21 days, >21 days, or **no click**)	-
HF timing	(acute, **chronic,** both)	-choose chronic
NYHA class	(1,2,**3**,4)	-choose 3
At time of admit	(no sx**, stable angina**, STEMI, angina equivalent, unstable angina, NSTEMI)	-stable angina (refractory to med therapy-by guideline indication CABG)
Cardiogenic shock	(yes during procedure, yes within 24 hrs not procedure, **no**)	-
A fib	(y/n)= NO	-
A flutter	(y/n)= NO	-
3rd deg Heart block	(y/n)= NO	-
2nd deg Heart block	(y/n)= NO	-
Sick sinus	(y/n)= NO	-
Vtach/vfib	(y/n)= NO	-
Ionotropic IV	(y/n)= NO	-
ADP inhibitors(p2y12)	(y/n)= NO	-
ACE or ARB	(**y**/n)= YES	-
BB	(**y**/n)= YES	-
Steroids	(y/n)= NO	-

Glycoprotein2b/3a	(y/n)= NO	-
Resuscitation	(within 1 hr procedure, >1hr into surg less than 24hrs, **no**)	-
# diseased vessels	(1,**2,3**) **2 vessel must also click prox LAD >70% stenosis (+1 major artery) by guideline indication)*	-2 variables (3 vessel disease or 2 vessel
Left main artery stenosis >=50%	(yes,no,n/a) **NO**	-
LAD distribution stenosis %	**(**50-69, >70) **choose >70% for 2 vessel disease profiles by guideline indication*	- choose >70% for 2 vessel disease profiles
Ejection fraction	Value (1-99) chosen: 30, 35, 40	-3 variables
Aortic stenosis	(y/n)= YES	-choose yes
Mitral stenosis	(y/n)=YES	-choose yes
Aortic insufficiency	(trace, mild, **mod**, severe)	-choose moderate
Mitral insufficiency	(**trace,** mild, mod, severe)	-choose trace
Tricuspid insufficiency	(**trace,** mild, mod, severe)	-choose trace
AV disease etiology	primary aortic dz,	-no click
Incidence	**(1st surg,** 1st reop,2nd reop, 3rd reop, 4th more reop)	-
Status	**(elective**, urgent, emergent salvage)	-choose all elective
IABP insertion	(pre op, intra op, post op)	-no click
Catheter based assist device used	(pre op, intra op, post op)	- no click
ECMO	(pre op, Intra op, post op)	-no click

Inclusion criteria: First time elective CABG patients with**:** Diffuse 3 vessel disease or 2 vessel disease with >50% LAD stenosis, 50-70 years old, commercially or Medicare/Medicaid insured, moderate COPD or no COPD, ejection fraction/left ventricular dysfunction 30-40%, NYHA class 3, left main artery stenosis >50%, Syntax score >33(high risk for PCI), on beta blockers, on ace/arbs, first time CABG, creatinine range .8- 2, hematocrit 25-40%, Platelets >150000, WBC <20, Diabetes on insulin ok.
Exclusion criteria: STEMI, ACS, NSTEMI, cardiogenic shock, emergent and salvage CABG, Reoperation/2nd revascularization, STS PROM >10% or <2% risk, less than 2 diseased vessels, <50% stenosis of left main artery, ejection fraction <30% or above 50%. Cancer <5yrs diagnosis, on dialysis, immunocompromised, Cerebrovascular disease, mediastinal radiation, sleep apnea, liver disease, endocarditis, illicit drug use, pneumonia, tobacco use/smokers, home oxygen, previous cardiac interventions, acute HF presentation, afib, aflutter, 3rd degree heart block, 2nd degree heart block, sick sinus patients, vtach/vfib, patients on ADP inhibitors, steroids, glycoprotein2b/3a inhibitors, unresponsive/syncope/patients in need of resuscitation.

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