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Relation between door-to-balloon times and mortality after primary percutaneous coronary intervention over time: a retrospective study

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Abstract

Background—Recent declines in average door-to-balloon (D2B) times at the population-level have not been associated with decreases in mortality. This study investigated this seemingly paradoxical observation by evaluating individual and population-level components of the association simultaneously. Our hypothesis was that the changing population of patients undergoing primary percutaneous coronary intervention (pPCI) contributed to secular trends toward an increasing mortality risk, despite consistently lower mortality among individual patients with shorter D2B times.

Methods—This was a retrospective study of ST-elevation myocardial infarction (STEMI) patients who underwent pPCI between January 2005 and December 2011 in the National

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Statement of Contributions Dr. Nallamothu was responsible for conception and design of the work; the acquisition, analysis and interpretation of data for the work; drafting the work and revising it critically for important intellectual content; and final approval of the version to be published. Dr. Normand was responsible for conception and design of the work; the analysis and interpretation of data for the work; revising the work critically for important intellectual content; and final approval of the version to be published. Mr. Wang was responsible for design of the work; the analysis and interpretation of data for the work; revising the work critically for important intellectual content; and final approval of the version to be published. Dr. Hofer was responsible for design of the work; the interpretation of data for the work; revising the work critically for important intellectual content; and final approval of the version to be published. Dr. Brush was responsible for interpretation of data for the work; revising the work critically for important intellectual content; and final approval of the version to be published. Dr. Bradley was responsible for interpretation of data for the work; revising the work critically for important intellectual content; and final approval of the version to be published. Dr. Rumsfeld was responsible for interpretation of data for the work; revising the work critically for important intellectual content; and final approval of the version to be published. Dr. Krumholz was responsible for conception and design of the work; the acquisition, analysis and interpretation of data for the work; drafting the work and revising it critically for important intellectual content; and final approval of the version to be published.

Cardiovascular Data Registry (NCDR) CathPCI Registry. Multilevel models were constructed to evaluate the relationship between D2B time and in-hospital and 6-month mortality, including both individual and population-level components of this association after adjusting for patient and procedural factors.

Findings—423 hospitals reported data on 150,116 procedures with a 55.4% increase in the number of patients undergoing pPCI between the first and last years of this period at these facilities, as well as numerous changes in patient and procedural factors. Annual D2B times decreased significantly from a median of 86 minutes in 2005 to 63 minutes in 2011 ($p<0.001$) with a concurrent rise in risk-adjusted in-hospital mortality (4.7% to 5.3%; $p=0.06$) and risk-adjusted 6-month mortality (12.9% to 14.4%; $p=0.001$). In multilevel models, shorter patient-specific D2B times were consistently associated at the individual-level with lower in-hospital mortality (adjusted OR for each 10-min decrease, 0.92; 95% CI, 0.91 to 0.93; $p<0.001$) and 6-month mortality (adjusted OR for each 10-min decrease, 0.94; 95% CI, 0.93 to 0.95; $p<0.001$). In contrast, risk-adjusted in-hospital and 6-month mortality at the population-level, independent of patient-specific D2B times, rose in the growing and changing population of patients undergoing pPCI during the study period.

Interpretation—Shorter patient-specific D2B times were consistently correlated with lower mortality within years, while secular trends suggest increased mortality risk over time in the pPCI population. The lack of association of annual D2B time and changes in mortality at the population-level should not be interpreted as an indication of its individual-level relationship in STEMI patients, but more likely reflects higher-risk patients undergoing pPCI in later years.

Door-to-balloon (D2B) time predicts survival in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI).[1–3] This relationship has been thought to be causal, supported by experimental animal models and observational evidence indicating shorter times to reperfusion are linked to less myocardial damage and lower mortality.[4–6] As a result, clinical guidelines and national quality initiatives over the last decade have focused on shortening D2B times, including the large Door-to-Balloon (D2B) Alliance sponsored by the American College of Cardiology (ACC) and the Mission:Lifeline Program led by the American Heart Association (AHA).[7–9] Yet recent studies have reported that contemporary declines in annual D2B times in the population of patients undergoing pPCI have not been associated with temporal improvements in mortality.[10–12] These unexpected results have raised uncertainty about the value of existing quality initiatives and questions about the true relationship between D2B time and mortality.[13]

Results from these recent studies warrant further evaluation. The findings have been interpreted, in some quarters, to suggest that shorter D2B times do not result in better outcomes for individual patients.[14,15] However, for such an assertion to be true it is critical to disentangle the relationship between mortality and patient-specific D2B times (i.e., the D2B time that an individual patient experiences) from secular trends in the overall size, profile and outcomes of the pPCI population that was simultaneously occurring. It is possible that expanded use of the procedure in later years through developing STEMI systems of care led to an overall higher risk group of patients undergoing the procedure (i.e., survivor-cohort effect), which may not be completely captured by traditional variables

collected in clinical registries. Although this possibility could mask the effects of shorter D2B times on outcomes at the population-level, it would not obviate a clinically-meaningful relationship between D2B times and mortality for an individual patient.

Accordingly, the goal of this study was to unravel the relationship between patient-specific D2B time and mortality from secular trends in outcomes for the pPCI population. Our hypothesis was that the changing population of patients undergoing pPCI contributed to secular trends toward an increasing mortality risk, despite consistently lower mortality among individual patients with shorter D2B times. With support from the National Cardiovascular Data Registry (NCDR) CathPCI Registry, we constructed a cohort of patients identical to a prior study,[12] but extended this earlier work by examining both in-hospital and 6-month mortality outcomes, incorporating more recent data, and utilizing multilevel models as a principal part of our methods. Multilevel models are invaluable in this setting as they allow for associations to be examined simultaneously for both annual D2B times and patient-specific D2B times, and thereby, clarify uncertainty about the individual-level relationship of D2B times in the context of broader population-level changes.[16,17] By providing access to the same data sources, this study also represents an "open science" approach by the NCDR program that expands on earlier work.[18]

Methods

Data Sources and Study Sample

Data sources were obtained from the NCDR CathPCI Registry, co-sponsored by the American College of Cardiology (ACC) and the Society for Cardiovascular Angiography and Interventions (SCAI). The NCDR CathPCI Registry is the largest national registry of patients undergoing PCI in the US, with a rapid doubling in participation from approximately 600 hospitals in 2005 to over 1400 by 2011.[19] Hospitals voluntarily participate in the NCDR CathPCI Registry, so it is not population-based. It does employ trained personnel who collect detailed information on patient and hospital characteristics, coronary angiographic and procedural findings, and outcomes using standardized data elements – a process overseen by an established data quality program.[20] The data quality program attempts to ensure that data submitted are complete, consistent, and accurate. Each year, 25 sites also are selected randomly for a comprehensive on-site data audit. Because PCI practices change quickly, several registry modifications have occurred over time, with recent versions including well over 200 data fields. Definitions and specifications for these data fields are available online (https://www.ncdr.com/WebNCDR/cathpci/home). Data in the NCDR CathPCI Registry are collected up to the time of hospital discharge with long-term follow-up unavailable, which is a potential limitation.

For this study, a total of 512,321 catheterization laboratory visits associated with STEMI were identified between January 1, 2005, and December 31, 2011. We excluded patients not undergoing pPCI (n=52,372), transfer patients for pPCI (n=129,579), patients with D2B times less than 15 minutes or more than 3 hours (n=45,391), and patients at hospitals that did not consistently report data across the study period (n=134,863). This selection process created a pPCI population for analysis and was identical to that used to create a cohort from the most recent study to evaluate this question.[12] No patients were excluded for non-system

delays. We did identify variations in these selection criteria over time that correlated with expansion of STEMI systems of care nationally. For example, the number of patients undergoing pPCI as a percentage of total PCIs at a hospital grew from 4.3% in 2005 to 6.8% in 2011 and non-transfer patients grew from 62.3% to 78.3% of all pPCIs. The Institutional Review Board at Yale University granted a waiver of written informed consent and provided authorization for this study.

Study Variables

Patient-specific D2B times were calculated for each case and then used to determine annual D2B times at the population-level for each year. Patient-specific D2B times were based on data from catheterization laboratory visits and defined as the time from hospital arrival to first device use during pPCI (e.g., balloon or thrombectomy catheter). Annual D2B times were determined by calculating the median of patient-specific D2B times during the year the procedure was performed in the pPCI population. We examined both in-hospital and 6-month mortality. All-cause in-hospital mortality was obtained from the NCDR CathPCI Registry, while 6-month mortality was assessed in a group of patients 65 years and older in the NCDR CathPCI Registry who had been successfully matched to fee-for-service (FFS) claims data available from the Centers for Medicare & Medicaid Services (CMS) between 2005 and 2011, consistent with prior work.[12] The process of matching, and its success and generalizability has been previously reported.[21] In general, approximately 75% of eligible procedures can be linked to patients within the CMS claims data, with similar patient characteristics noted between linked and unlinked individuals.

An extensive list of patient and procedural factors related to the pPCI were available from the NCDR Cath PCI Registry for risk-adjustment. These include: age, body mass index, diabetes mellitus, end-stage renal disease on dialysis, cerebrovascular disease, peripheral vascular disease, chronic lung disease, prior congestive heart failure, heart valve disease, prior heart valve surgery, prior PCI, New York Heart Association Classification, cardiogenic shock on admission, intra-aortic balloon pump placement, PCI status of ‘salvage’, lesion location, lesion classification using Society of Coronary Angiography and Intervention (SCAI) criteria, pre-procedure TIMI flow, ejection fraction and glomerular filtration rates. Missing data were rare for most variables (<1%) with the exception of ejection fraction (~25%) and glomerular filtration rate (~8% of pre- or post-procedure creatinine assessments). In both cases, values for these variables were imputed for missing data through a standardized approach used in prior publications involving the NCDR CathPCI Registry.[22]

Statistical Analysis

Baseline demographic and clinical characteristics of patients undergoing pPCI were compared across years. For these analyses, we defined 7 years in the study period: 2005, 2006, 2007, 2008, 2009, 2010, and 2011. Continuous variables across years were compared using analysis of variance and categorical variables with the χ^2-test. We plotted the annual D2B time in the pPCI population against unadjusted in-hospital mortality for each year to examine the population-level relationship across years. Next, we plotted patient-specific D2B times (grouped by deciles) against unadjusted in-hospital mortality within each of the

periods to examine the individual patient-level relationship within years. Fitted linear trend lines were used to aid with visual comparison.

Multilevel logistic regression models were then constructed to estimate both individual and population-level components of the association between D2B time and mortality, after accounting for differences in observed patient and procedural factors. Models simultaneously included patient-specific D2B time (i.e., the D2B time the individual patient experienced) and annual D2B time (i.e., the median D2B time in the year in which the PCI for that patient was performed) as predictors of mortality. Neither of these variables was centered prior to its inclusion. The coefficient estimate for patient-specific D2B time represented the individual-level relationship between D2B time and mortality after accounting for other factors, including annual D2B time. The coefficient estimate for annual D2B time represented the population-level relationship or secular trend between declining average D2B time and mortality after accounting for other factors, *including* patient-specific D2B time. We also constructed models that only included annual D2B time for each patient. The coefficient estimate for annual D2B time obtained from this model represented the aggregate relationship that was comprised of both the individual and population-level relationships of D2B time.

Patient and procedural factors included within the models for risk-adjustment were those from the published NCDR CathPCI mortality risk model for PCI.[22] Random intercepts for each hospital were included to account for the clustering effects of procedures within hospitals. Analogous models were constructed for both in-hospital and 6-month mortality. Odds ratios (ORs) and 95% confidence intervals for mortality were generated for reporting. For patient specific D2B times, these ORs are reported as a change per 10-minute decrease while for annual D2B time they are reported as a change per year. SAS software version 9.2 (Cary, NC) was used for all analyses. We used the SAS GLIMMIX procedure for all analyses related to the multilevel models.

This study was supported by the NCDR, which funded the analysis through an NCDR-contracted data analytic center (Yale University). The authors had access to all the data and are responsible for overall study design, analysis, interpretation, writing of the manuscript and the decision to submit.

Results

Study Sample

There were 150,116 pPCI procedures performed in 146,940 patients at 423 hospitals during the study period; 37,954 procedures in 37,445 patients age 65 years or older at 359 hospitals were also available in the CMS claims data-matched cohort for the assessment of 6-month mortality. Annual D2B times in the pPCI population decreased significantly from a median of 86 minutes in 2005 to 63 minutes in 2011 ($p<0.001$). Overall, unadjusted in-hospital mortality was 4.7% in the total cohort and unadjusted 6-month mortality was 13.5% in the cohort of patients age 65 years or older. During this time period, risk-adjusted in-hospital mortality rose non-significantly (4.7% to 5.3%; $p=0.06$) while risk-adjusted 6-month mortality increased significantly (12.9% to 14.4%; $p=0.001$).

The mean age of patients was 60.9 years (±13.0) and 42,086 (28.0%) were women. A full list of patient and procedural factors is displayed in Table 1, stratified by year. There were significant, but modest differences across years in several demographic (e.g. age >75 years old) and clinical features (e.g. diabetes mellitus, history of PCI, and New York Heart Association [NYHA] Class IV status) in the pPCI population. Treatment patterns associated with pPCI also differed significantly across years of the study period with some large differences noted. We observed a substantial increase in the total number of patients treated each year at these 423 hospitals: overall, 55.4% more patients underwent pPCI in the last year compared with the first year (24,449 versus 15,730 patients). Rates of direct thrombin inhibitor use increased more than four-fold from 9.7% to 42.3% and manual thrombectomy use rose from 11.8% to 39.2%, while glycoprotein IIb/IIIa use dropped from 73.3% to 44.7% and drug eluting stent use dropped from 76.4% to 53.4%.

D2B Time and Risk of Mortality

Figure 1 displays the individual and population-level relationships between D2B time and unadjusted in-hospital mortality. The individual-level relationship shows shorter patient-specific D2B times are consistently associated with lower mortality within each year of the study period. At the same time, the population-level relationship demonstrates little correlation between declines in annual D2B times and mortality across years. In addition, an increase in mortality is observed across years, as the lines are generally higher during later years, and predominately diverge during later deciles of patient-specific D2B times. For example, the last decile of patient-specific D2B times in 2005 was 154 minutes with an unadjusted in-hospital mortality of 8.1% while the last decile of patient-specific D2B times in 2011 was 127 minutes with an unadjusted in-hospital mortality of 11.0%. Lastly, longer delays in patient-specific D2B time were associated with increasing mortality over the years of the study. For example, patients with D2B times >90 minutes had an in-hospital mortality of 6.1% in 2005 and an in-hospital mortality of 10.3% in 2011.

Table 2 displays results of estimates from the multilevel models that simultaneously examined individual patient and population-level associations between D2B time and mortality. (Full model results that include all of the variables accounted for during risk-adjustment are displayed in the online Appendix; the c-statistics for the models for in-hospital mortality and 6-month mortality were 0.893 and 0.812, respectively.) Adjusted for observed patient and procedural factors and population D2B times, shorter patient-specific D2B times over the study period were consistently associated with lower in-hospital mortality (adjusted OR for a 10-minute decrease, 0.92; 95% CI, 0.91 to 0.93; $p<0.001$) and 6-month mortality (adjusted OR for a 10-minute decrease, 0.94; 95% CI, 0.93 to 0.95; $p<0.001$) (Figure 2). However, declines in annual D2B times were associated with higher risk-adjusted in-hospital mortality (adjusted OR per year, 1.12; 95% CI, 1.09 to 1.15; $p<0.001$) and significantly higher 6-month mortality (adjusted OR per year, 1.11; 95% CI, 1.07 to 1.14; $p<0.001$). Figure 3 displays secular trends in-predicted in hospital (upper panel) and 6-month mortality (lower panel) for the pPCI population across years, keeping all other covariates constant, including patient-specific D2B times. In models that only included annual D2B time for each patient, we found that the aggregate relationship comprised of both the individual and population-level relationships of D2B time suggested no association

with either in-hospital mortality (0.99; 95% CI, 0.96 to 1.02; p=0.54) or 6-month mortality (0.99; 95% CI, 0.96 to 1.03; p=0.78).

Discussion

Earlier studies linked shorter patient-specific D2B times with lower mortality after pPCI at the individual-level. However, recent declines in annual D2B times at the population-level have not been associated with decreases in mortality as anticipated. The purpose of this study was to offer additional insights on this seemingly paradoxical observation and its implications for STEMI care. Through multilevel models, which simultaneously estimated both the individual and population-level components of the association of mortality with D2B time, we uncovered several key findings. First, we confirmed that recent declines in annual D2B times at the population-level have occurred during a period in which there was no associated improvement in in-hospital mortality. In fact, using more contemporary data and extended follow-up, we found these changes in annual D2B times occurred during a period of rising risk-adjusted in-hospital and 6-month mortality in the pPCI population. However, we also demonstrated that shorter patient-specific D2B times are strongly and consistently associated with lower risk-adjusted in-hospital and 6-month mortality at the individual-level.

So why have anticipated decreases in mortality over time not occurred in the pPCI population despite declines in annual D2B time and a consistent relationship between patient-specific D2B time and outcomes? The results of this study suggest that the most likely explanation is expanding use of pPCI and the changing population of STEMI patients undergoing the procedure. This is supported by the observation that the number of pPCIs reported within this stable cohort of hospitals increased by more than 50% between the first and last years of the study – a period during which estimates of pPCI use grew from 40% of STEMI patients to 80% in the US[23,24] while STEMI incidence rates declined nationally.[25] Additionally, we found several patient and procedural factors varied across years, with unobserved factors potentially altering patient case-mix as well. For example, manual aspiration thrombectomy and bivalirudin use increased by approximately four-fold in the pPCI population during this study period, and it is uncertain if (or how) these changes impacted on outcomes as recent clinical trials of these therapies have demonstrated mixed results.[26,27] Lastly, we observed increasing mortality over the study period among patients with the longest D2B times. We hypothesize that some of these patients may have not reached the cardiac catheterization laboratory in past years when STEMI systems of care were less common, and a phenomenon Terkelsen et al. have referred to as the survivor-cohort effect.[28] Thus, it is plausible that the increased mortality of this high-risk cohort offset gains among patients with shorter D2B times.

There are several implications of these findings for patients and the cardiology community. Importantly, the results caution against misinterpreting the lack of association between declining annual D2B times and mortality at a population-level as evidence that improvements in patient-specific D2B time have not impacted on mortality at an individual-level. Such an interpretation, as asserted in some recent discussions on the topic,[14,15] conflates “micro-level” and “macro-level” relationships, which is an ecologic fallacy.[29] The

multilevel models employed in this study address these concerns by allowing both types of relationships to be modeled simultaneously to generate better inferences for each. As such, this study helps clarify that shorter patient-specific D2B times are associated with lower mortality at the individual level, after accounting for secular trends toward higher mortality overall in the pPCI population over time (as use of the procedure changed in later years). We believe this finding continues to lend support to ongoing quality improvement initiatives that target minimizing time-to-treatment in the hospital, as well as point toward the importance of reducing total ischemic time through other system delays.

In addition, this study highlights the importance of an "open science" approach and reproducible research, a growing movement in other fields that is also gaining recent traction in medicine.[30] We had the opportunity to conduct these analyses because of access to the same data sources used in a prior study also supported by the NCDR CathPCI Registry.[12] This access allowed us to build on the earlier work using more years of data and long-term outcomes. However, it also eliminated the possibility that differences in the findings we report here merely reflected variability in data collection methods, study populations, or healthcare systems. These same data sources were made available to us from the NCDR CathPCI Registry with funds also provided to perform these additional analyses. The process itself demonstrates the value of a collaborative research framework that is aimed at advancing scientific progress through an iterative process for the ultimate benefit of patients and clinicians.

The study findings should be interpreted in light of the following limitations. Most importantly, the inference of a causal relationship between shorter patient D2B times and lower mortality cannot be proven conclusively by this study, or any other based on observational data. However, the individual-level relationship we observed lends support to the causal hypothesis that ischemia time affects outcomes. Additional work will be needed to examine how this relationship extends to other key parameters of total ischemia time, such as time from symptom onset to first medical contact, as well as use of pre-hospital electrocardiography and emergency medical services. All of these areas are logically becoming the next stage for focus as D2B times have dropped significantly in recent years and recognition of the importance of system delay has grown.[28] Second, there are limitations in the risk-adjustment methods we employed, some of which, in fact, may help explain the seemingly paradoxical results we discuss. We used the NCDR PCI risk model to be consistent with a prior study,[12] but this risk model was developed in a broad population of patients that primarily included non-emergent PCI.[22] It may not capture all the patient and procedural factors that changed in the pPCI population over time, and more recent models have been developed incorporating better variable definitions around high-risk patients. We unfortunately could not use these newer models as such information was inconsistently available over the study period.

Third, these hospitals that consistently participated in the NCDR CathPCI Registry over this study period may not be representative of all hospitals performing PCI either in the US or worldwide, although we have no reason to suspect that the clinical relationship between D2B time and outcomes would differ for patients at these centers. Fourth, we provide data only until 2011 even as the use of pPCI continues to grow. Fifth, there is evidence that the

relationship between time-to-treatment and outcomes in STEMI is non-linear with benefits of reperfusion diminishing over time.[31,32] Estimation of per-minute survival benefits made directly from our data and over a broad range of delays should be done cautiously. Finally, this study cannot determine all of the specific reasons for rises in in-hospital mortality or 6-month mortality for the pPCI population over time. The results indicate, however, expansion in the pPCI population and substantial changes in treatment and patient characteristics over time. The population-level trend in outcomes therefore should not be taken as evidence against the clinical benefits of pPCI, as established in clinical trials.[33] The expanded use of pPCI in later years in a larger number of STEMI patients, particularly in the US, reflects its use in those who would have previously received fibrinolysis or no reperfusion therapy with a potentially higher risk for worse outcomes. However, we cannot comment on whether this policy is appropriate or effective for a population, especially where resources for pPCI may differ and alternative therapeutic options exist (e.g., pharmacoinvasive strategy with fibrinolytic therapy followed by non-emergent PCI).

In conclusion, this study found that shorter D2B times were consistently associated with lower in-hospital and 6-month mortality among patients with STEMI undergoing pPCI. At the same time, mortality has not declined and may be increasing over time at the population-level despite reductions in annual D2B time. This appears to reflect secular trends in the pPCI population toward higher mortality risk in later years that coincides with expansion in the use of the procedure during STEMI, as well as changes in patient and procedural factors. These findings highlight the importance of continued vigilance with D2B times and caution against misinterpreting the lack of association of annual D2B time and changes in mortality at the population-level as an indication of its individual-level relationship in STEMI patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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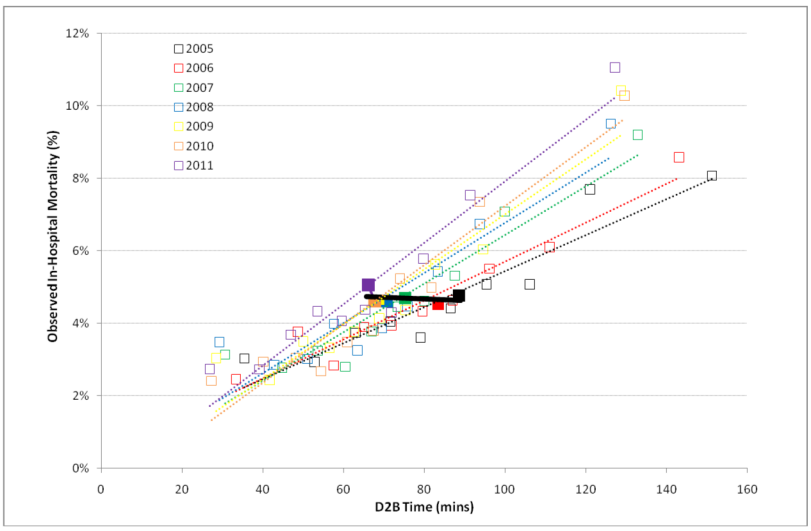

Figure 1.

Relationship between observed in-hospital mortality and annual D2B times across years (solid boxes) and deciles of patient-specific D2B times within years (open boxes). Fitted linear trend lines are represented to aid with visual comparison of these relationships across years and within years.

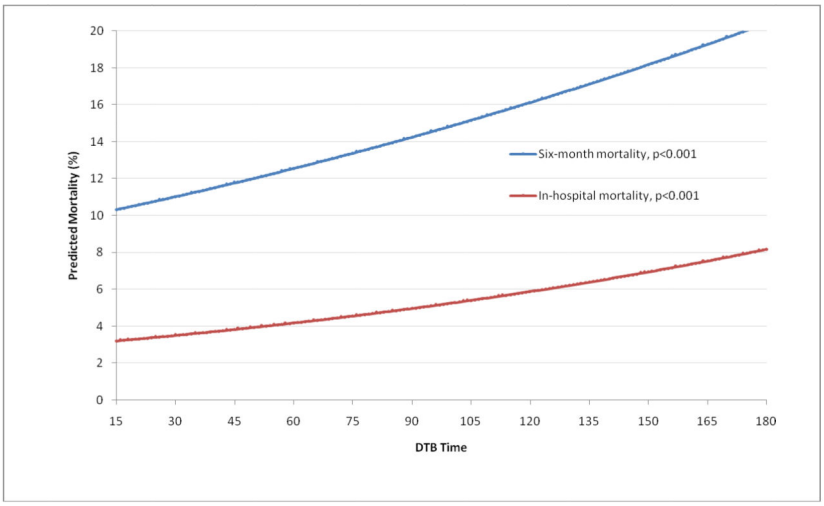

Figure 2.

The blue and red lines show predicted in-hospital and six-month mortality, respectively, from the multilevel model over a range of patient-specific D2B times, holding all other covariates constant including secular trends at the population-level. The figure suggests that mortality decreased with shorter patient-specific D2B times over the study period.

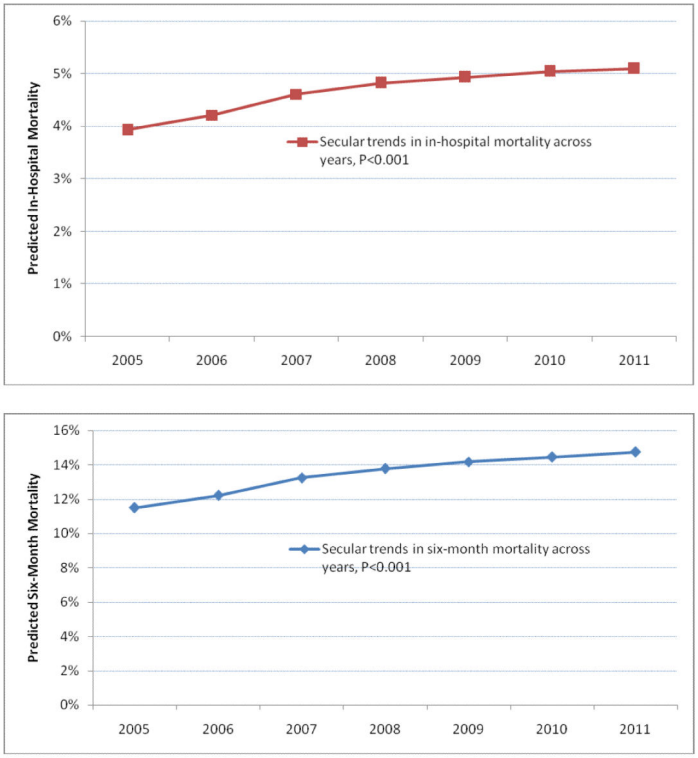

Figure 3.

The red and blue line shows predicted in-hospital (upper panel) and six-month mortality (lower panel) across years related to secular trends at the population-level, holding all other covariates constant including patient-specific D2B time. The figure indicates patients undergoing pPCI were at higher risk in later years.

Table 1

Patients Characteristics Stratified by Calendar Year

Variable	Total (N=150116)	Year 2005 (N=15730)	2006 (N=19612)	2007 (N=21183)	2008 (N=22681)	2009 (N=22550)	2010 (N=23911)	2011 (N=24449)	P
Patient Demographics, History and Cardiac Status									
Patient Age [μ (σ)]	60.9 (13.0)	60.5 (13.1)	60.5 (13.0)	60.7 (13.1)	60.9 (13.2)	61.1 (13.0)	61.2 (12.9)	61.3 (12.9)	<0.0001
Female	42086 (28.0)	4485 (28.5)	5416 (27.6)	6002 (28.3)	6406 (28.2)	6249 (27.7)	6712 (28.1)	6816 (27.9)	0.3804
Hypertension	93089 (62.0)	9019 (57.3)	11565 (59.0)	12741 (60.2)	14046 (61.9)	14277 (63.3)	15475 (64.7)	15966 (65.3)	<0.0001
Diabetes	28660 (19.1)	2732 (17.4)	3498 (17.8)	4023 (19.0)	4310 (19.0)	4366 (19.4)	4678 (19.6)	5053 (20.7)	<0.0001
Current Tobacco	64944 (43.3)	6933 (44.1)	8617 (43.9)	9290 (43.9)	9717 (42.8)	9625 (42.7)	10313 (43.1)	10449 (42.7)	<0.0001
Dyslipidemia	91004 (60.6)	8807 (56.0)	11289 (57.6)	12563 (59.3)	13722 (60.5)	14111 (62.6)	15367 (64.3)	15145 (62.0)	<0.0001
Family History of Early CAD	31178 (20.8)	3869 (24.6)	4290 (21.9)	4414 (20.8)	4574 (20.2)	4439 (19.7)	4625 (19.3)	4967 (20.3)	<0.0001
Body Mass Index [μ (σ)]	28.9 (6.0)	28.6 (5.8)	28.7 (5.9)	28.8 (5.9)	28.9 (6.0)	28.9 (6.0)	29.0 (6.1)	29.1 (6.1)	<0.0001
Previous MI (>7 Days)	28587 (19.0)	2767 (17.6)	3560 (18.2)	3905 (18.4)	4225 (18.6)	4383 (19.4)	4751 (19.9)	4996 (20.4)	<0.0001
CHF – Prior	6208 (4.1)	671 (4.3)	759 (3.9)	827 (3.9)	892 (3.9)	920 (4.1)	1035 (4.3)	1104 (4.5)	0.0021
Previous Valve Surgery	752 (0.5)	72 (0.5)	87 (0.4)	95 (0.5)	105 (0.5)	115 (0.5)	131 (0.6)	147 (0.6)	0.1361
Previous PCI	31632 (21.1)	2776 (17.7)	3795 (19.4)	4357 (20.6)	4865 (21.5)	4987 (22.1)	5282 (22.1)	5570 (22.8)	<0.0001
Previous CABG	8615 (5.7)	827 (5.3)	1063 (5.4)	1206 (5.7)	1270 (5.6)	1379 (6.1)	1420 (5.9)	1450 (5.9)	0.0021
GFR [μ (σ)]	74.6 (29.6)	74.9 (32.6)	73.5 (27.5)	72.9 (30.7)	74.7 (30.3)	74.6 (29.3)	75.5 (29.0)	75.8 (27.9)	<0.0001
Renal Failure - Dialysis	1250 (0.8)	107 (0.7)	134 (0.7)	173 (0.8)	197 (0.9)	209 (0.9)	207 (0.9)	223 (0.9)	0.0223
Cerebrovascular Disease	10007 (6.7)	977 (6.2)	1256 (6.4)	1359 (6.4)	1479 (6.5)	1523 (6.8)	1604 (6.7)	1809 (7.4)	<0.0001
Peripheral Vascular Disease	9143 (6.1)	955 (6.1)	1204 (6.1)	1309 (6.2)	1350 (6.0)	1343 (6.0)	1520 (6.4)	1462 (6.0)	0.4996
Chronic Lung Disease	16218 (10.8)	1815 (11.5)	2212 (11.3)	2341 (11.1)	2645 (11.7)	2345 (10.4)	2365 (9.9)	2495 (10.2)	<0.0001
NYHA Class IV *	54396 (36.2)	8602 (54.7)	11270 (57.5)	12516 (59.1)	13431 (59.2)	7299 (32.4)	615 (2.6)	663 (2.7)	<0.0001
Cardiogenic Shock	13647 (9.1)	1527 (9.7)	1897 (9.7)	2146 (10.1)	2226 (9.8)	1967 (8.7)	1872 (7.8)	2012 (8.2)	<0.0001
Symptom Onset to Admission **									
Unknown	8216 (5.5)	46 (0.3)	102 (0.5)	101 (0.5)	140 (0.6)	1523 (6.8)	3127 (13.1)	3177 (13.0)	<0.0001
<6 hours	123170 (82.1)	13318 (84.7)	16563 (84.5)	18075 (85.3)	19511 (86.0)	18457 (81.9)	18303 (76.6)	18943 (77.5)	
6 to 12 hours	9614 (6.4)	1217 (7.7)	1418 (7.2)	1458 (6.9)	1422 (6.3)	1325 (5.9)	1383 (5.8)	1391 (5.7)	

Variable	Total (N=150116)	Year							P
		2005 (N=15730)	2006 (N=19612)	2007 (N=21183)	2008 (N=22681)	2009 (N=22550)	2010 (N=23911)	2011 (N=24449)	
>12 hours	9116 (6.1)	1149 (7.3)	1529 (7.8)	1549 (7.3)	1608 (7.1)	1245 (5.5)	1098 (4.6)	938 (3.8)	
Treatment Characteristics									
Stent type									<0.0001
DES	80637 (53.7)	12023 (76.4)	13941 (71.1)	8575 (40.5)	9346 (41.2)	11163 (49.5)	12546 (52.5)	13043 (53.4)	
BMS	53649 (35.7)	2336 (14.9)	3798 (19.4)	10218 (48.2)	10776 (47.5)	8873 (39.4)	8786 (36.7)	8862 (36.3)	
No Stent	15830 (10.6)	1371 (8.7)	1873 (9.6)	2390 (11.3)	2559 (11.3)	2514 (11.2)	2579 (10.8)	2544 (10.4)	
Anticoagulation									<0.0001
Direct Thrombin Inhibitors	34405 (22.9)	1524 (9.7)	2317 (11.8)	2699 (12.7)	4209 (18.6)	5499 (24.4)	7811 (32.7)	10346 (42.3)	
Heparin plus GPI IIb/IIIa	88846 (59.2)	10696 (68.0)	13385 (68.3)	14379 (67.9)	14289 (63.0)	13178 (58.4)	12454 (52.1)	10465 (42.8)	
Heparin	14723 (9.8)	1613 (10.3)	1927 (9.8)	2063 (9.7)	2212 (9.8)	2105 (9.3)	2290 (9.6)	2513 (10.3)	
LMWH plus GPI IIb/IIIa	4978 (3.3)	830 (5.3)	893 (4.6)	806 (3.8)	759 (3.4)	685 (3.0)	535 (2.2)	470 (1.9)	
LMWH	746 (0.5)	113 (0.7)	103 (0.5)	144 (0.7)	75 (0.3)	100 (0.4)	97 (0.4)	114 (0.5)	
Other	6418 (4.3)	954 (6.1)	987 (5.0)	1092 (5.2)	1137 (5.0)	983 (4.4)	724 (3.0)	541 (2.2)	
Thrombolytics	1184 (0.8)	257 (1.6)	159 (0.8)	165 (0.8)	141 (0.6)	180 (0.8)	167 (0.7)	115 (0.5)	<0.0001
Thrombectomy catheters	39169 (26.1)	1863 (11.8)	3113 (15.9)	3806 (18.0)	5774 (25.5)	6890 (30.6)	8139 (34.0)	9584 (39.2)	<0.0001
Cath Lab Visit and Coronary Anatomy									
IABP	15917 (10.6)	1727 (11.0)	2166 (11.0)	2408 (11.4)	2464 (10.9)	2299 (10.2)	2406 (10.1)	2447 (10.0)	<0.0001
Ejection Fraction % [μ (σ)]	46.6 (12.6)	46.7 (12.7)	46.6 (12.6)	46.6 (12.6)	46.7 (12.5)	46.8 (12.5)	46.3 (12.5)	46.1 (12.7)	0.0020
Left Main	4687 (3.1)	426 (2.7)	558 (2.9)	632 (3.0)	706 (3.1)	690 (3.1)	822 (3.4)	853 (3.5)	<0.0001
LAD	83895 (55.9)	8622 (54.8)	10833 (55.2)	11776 (55.6)	12589 (55.5)	12726 (56.4)	13538 (56.6)	13811 (56.5)	0.0005
CX	50066 (33.4)	5192 (33.0)	6494 (33.1)	7059 (33.3)	7435 (32.8)	7584 (33.6)	8003 (33.5)	8299 (33.9)	0.1480
RCA	89755 (59.8)	9578 (60.9)	11727 (59.8)	12637 (59.7)	13508 (59.6)	13544 (60.1)	14260 (59.6)	14501 (59.3)	0.0655
Salvage PCI (CPR en route)	2220 (1.5)	199 (1.3)	275 (1.4)	331 (1.6)	353 (1.6)	362 (1.6)	363 (1.5)	337 (1.4)	0.0598
Pre-Procedure TIMI 0 Flow	86164 (57.40)	8384 (53.3)	10709 (54.6)	12138 (57.3)	13025 (57.4)	12984 (57.6)	14071 (58.9)	14853 (60.8)	<0.0001
Radial Access	2616 (1.7)	106 (0.7)	153 (0.8)	186 (0.9)	186 (0.8)	301 (1.3)	536 (2.2)	1148 (4.7)	<0.0001
D2B Time and Outcomes									
D2B Time [med (IQR)]	69 (37.0)	86 (44.0)	80 (41.0)	72 (35.0)	68 (33.0)	66 (33.0)	64 (33.0)	63 (33.0)	<0.0001

Variable	Total (N=150116)	Year							P
		2005 (N=15730)	2006 (N=19612)	2007 (N=21183)	2008 (N=22681)	2009 (N=22550)	2010 (N=23911)	2011 (N=24449)	
In-Hospital Mortality	7062 (4.7)	751 (4.8)	888 (4.5)	996 (4.7)	1045 (4.6)	1047 (4.6)	1103 (4.6)	1232 (5.0)	0.1878
Six-Month Mortality ***	5130 (13.5)	509 (13.3)	596 (13.2)	687 (14.1)	803 (13.6)	818 (13.7)	837 (13.3)	880 (13.4)	0.83

Continuous Variables are reported as [μ (σ)] and categorical variables are reported as [n (%)]. Most variables are categorical.

* Variable definition changed in mid-2009 to reflect only symptom classification within 2 weeks;

** Variable definition changed in mid-2009 to reflect attempt to document symptom onset time for STEMI;

*** Only includes individuals in long-term CMS-matched cohort

Table 2

Relationship between patient-specific D2B times, population D2B times and mortality.

	OR Estimate			
	In-Hospital Mortality		6-Month Mortality	
	Adjusted OR	P-Value	Adjusted OR*	P-Value
Patient-Specific D2B Times (Per 10-Min Decrease)	0.92 (0.91-0.93)	<0.001	0.94 (0.93-0.95)	<0.001
Annual D2B Times (Per 1-Yr Change)	1.12 (1.09-1.15)	<0.001	1.11 (1.07-1.14)	<0.001

*Adjusted for patients characteristics within the NCDR CathPCI Risk Model.