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# The clinical and cost burden of coronary calcification in a Medicare cohort: An economic model to address under-reporting and misclassification☆,☆☆

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ABSTRACT

*Background:* Coronary artery calcification (CAC) is a well-established risk factor for the occurrence of adverse ischemic events. However, the economic impact of the presence of CAC is unknown.
*Objectives:* Through an economic model analysis, we sought to estimate the incremental impact of CAC on medical care costs and patient mortality for *de novo* percutaneous coronary intervention (PCI) patients in the 2012 cohort of the Medicare elderly (≥65) population.
*Methods:* This aggregate burden-of-illness study is incidence-based, focusing on cost and survival outcomes for an annual Medicare cohort based on the recently introduced ICD9 code for CAC. The cost analysis uses a one-year horizon, and the survival analysis considers lost life years and their economic value.
*Results:* For calendar year 2012, an estimated 200,945 index (*de novo*) PCI procedures were performed in this cohort. An estimated 16,000 Medicare beneficiaries (7.9%) were projected to have had severe CAC, generating an additional cost in the first year following their PCI of $3500, on average, or $56 million in total. In terms of mortality, the model projects that an additional 397 deaths would be attributable to severe CAC in 2012, resulting in 3770 lost life years, representing an estimated loss of about $377 million, when valuing lost life years at $100,000 each.
*Conclusions:* These model-based CAC estimates, considering both moderate and severe CAC patients, suggest an annual burden of illness approaching $1.3 billion in this PCI cohort. The potential clinical and cost consequences of CAC warrant additional clinical and economic attention not only on PCI strategies for particular patients but also on reporting and coding to achieve better evidence-based decision-making.


## 1. Introduction

Coronary artery calcification (CAC) is both an established risk factor for poor cardiovascular clinical outcomes and a predictor of additional resource utilization and overall health care costs [1–5]. Although most percutaneous coronary intervention (PCI) trials have excluded patients with either moderately- or severely-calcified coronary lesions, Genereux and colleagues' recent analysis of pooled data from the HORIZONS-AMI [6] and ACUITY [7] trials demonstrates that patients with moderate and severe coronary calcification experience worse ischemic outcomes – stent thrombosis, target lesion revascularization (TLR), and mortality – after PCI compared to patients with no CAC [4].

Less is known about the population-level burden of coronary calcification. Prior to 2011, clinically significant CAC lacked a specific ICD9 diagnosis code, an important administrative data element needed for conducting a population-level, epidemiologically-based analysis. Although a new diagnostic code (ICD9 414.4 for coronary calcification) was introduced late in 2011, actual documentation of CAC via administrative coding practice has lagged. This is the first published analysis to examine the reporting and use of this ICD9 code and to assess the clinical and cost burden of calcification in *de novo* PCI patients in the elderly (age 65 and older) Medicare population. In addition, we estimated the economic burden of CAC in this select Medicare PCI population in

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2012 by addressing this question: What is the estimated incremental impact of CAC – at both the PCI patient-level and in the aggregate – on associated medical care costs and patient mortality in the 2012 cohort of the Medicare elderly population?

## 2. Methods

### 2.1. Study design

The target study population was the Medicare elderly with atherosclerosis in calendar year 2012 experiencing a new (*de novo*) index PCI, defined as a patient receiving a coronary angiogram with no prior coronary revascularization in the preceding six months. This was an aggregate, population-level economic burden study, which is also known as a "cost-of-illness" or "burden-of-disease" study [8,9]. The study design was incidence-based, focusing on cost and survival outcomes for an annual cohort of the target study population. The horizon of the cost analysis was one year because the greatest cost impact tends to occur in the first year post-procedure, and due to the limited data for these patients. The horizon for survival analysis was a patient's lifetime, given that mortality differences at one year can be modeled as life years lost over the remaining expected lifetime.

CAC could potentially adversely affect patients' clinical outcomes for those who underwent PCI, coronary artery bypass graft surgery (CABG), or prescribed medical therapy for severe atherosclerosis deemed not treatable via surgical intervention. Of coronary angiography patients without a revascularization in the last 6 months, 5% underwent CABG (3.1% documented calcification), 31% underwent PCI (1.9% documented calcification), and 64% underwent a medical intervention (1.5% documented calcification). However, the focus of this analysis was on patients receiving PCI, due to the limited number of CABG and medical therapy patients documented with the calcification code in the available Medicare data.

The study design and analysis were influenced by the availability of CAC data. A new diagnostic code for calcification (ICD9 414.4) was introduced in the last quarter of 2011. Because the reporting of new codes can take time to become a part of regular medical documentation practice, there is a high likelihood of under-reporting of CAC in this initial period. This limited reporting affected the ability to do a strict epidemiologically-based comparison of patients with reported calcification versus those with non-calcified coronary lesions, given that such an approach would be subject to misclassification bias in which many patients with severe calcification would be inappropriately classified in the non-CAC group. Therefore, an aggregate estimate was constructed using an economic modeling approach that synthesizes data from multiple sources described below.

The principal data sources for cost and survival analyses were Medicare's Standard Analytic Files (SAFs). The SAFs comprise seven data sets containing detailed claims information about health care services rendered to Medicare beneficiaries in fee-for-service (FFS) Medicare. SAFs are available for institutional (inpatient, outpatient, skilled nursing facility, hospice, or home health agency) and non-institutional (physician and durable medical equipment providers) claim types. Data are organized at the claim level and include basic beneficiary demographic information, date of service, diagnosis and procedure code, provider number, and reimbursement amount. Two SAF databases were used: the Medicare 5% random sample SAF and 100% SAF. The 5% sample of beneficiaries includes all of their claims (inpatient, outpatient, physician, durable medical equipment, etc.) except drugs, which are tracked and reported separately via Medicare Part D. The 100% SAF includes only inpatient and outpatient claims but includes all FFS beneficiaries. In addition, a special sub-sample was defined from the 100% SAF that included all hospitals (n = 17) that coded more than 10% of their PCI patients as having CAC (using code 414.4).

The Medicare SAF analyses were conducted with Limited Data Set (LDS) files, which encrypt beneficiary identifiers, and this research complies with the Centers for Medicare and Medicaid Services Data Use Agreement rules on blinding and data use. Institutional Review Board approval is not required for use of LDS administrative data under the HIPAA Privacy Rule.

To better estimate the degree of calcification and incidence of major adverse cardiovascular events among this target patient group, additional data from the HORIZONS-AMI/ACUITY pooled sample were used, though this dataset does not contain information on costs [4]. Approval for analyses of this pooled sample was obtained from the Institutional Review Boards or Ethics Committees at each of the enrolling sites.

### 2.2. Economic model: cost burden of coronary calcification

A population-level economic model was constructed drawing parameter estimates from both a detailed analysis of the available Medicare claims data and from the published literature. A modeling approach also allowed for assessing the sensitivity of the results to varying assumptions about key parameters.

As depicted in Fig. 1, the economic model had three major components: 1) the estimated annual incidence of elderly Medicare patients receiving an index PCI (typically a drug-eluting stent); 2) the incidence of CAC in these PCI patients, classified as severe, moderate, or mild/none; and 3) the estimated impact of the three levels of CAC on Medicare per-patient costs and health outcomes (viz., mortality).

### 2.3. Incidence of PCI in 2012

The 100% Medicare SAFs of administrative claims data were used to define the index population in 2012, which includes only patients in the Medicare FFS population. The cohort was restricted to elderly patients (i.e., age 65 or older). Although Medicare Advantage (MA) patients represented about 21.7% of the Medicare population in 2012- and rising substantially annually – these data are not included in this database. To account for MA patients, we made a simple, crude adjustment, increasing the aggregate burden estimate for the whole population upward to reflect the inclusion of this subpopulation.

### 2.4. Incidence of calcification in the elderly

We reported incidence of CAC in the Medicare population based on the 414.4 code. However, given the likely under-reporting of CAC in the 2012 Medicare SAF cohort, the estimated incidence of moderate and severe CAC was based on estimates from the HORIZONS-AMI/ACUITY pooled sample [4]. The estimated means for the elderly subsample were used in the base case. The range for the assumption was based on the literature [5,10]. Calcification incidence from the HORIZONS-

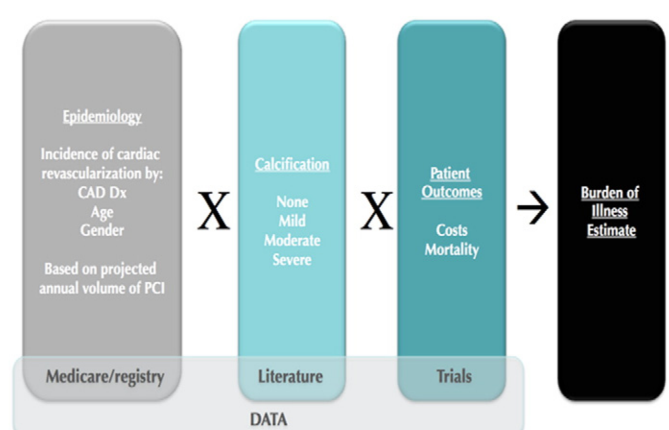


**Fig. 1.** Schematic diagram of the economic burden model. The aggregate burden of illness is the product of PCI incidence, the severity of calcification, and the patient outcomes in terms of costs and outcomes. Abbreviations: CAD = coronary artery disease, Dx = diagnosis, PCI = percutaneous coronary intervention, CABG = coronary bypass graft.

AMI/ACUITY sample was multiplied by the Medicare population to determine population size for CAC.

### 2.5. Medical care cost impact

Estimation of the first-year impact of calcification following index PCI on costs was based on a generalized estimating equation (GEE) regression analysis of data from the Medicare 5% Standard SAFs, which were used because they contain the most complete cost data including physician claims—adjusting for age, gender, and the Charlson comorbidity index [11]. The Charlson index was used rather than individual comorbidities to decrease the effect of correlation and increase power of the models. As previously noted, an adjustment for the MA patients was applied in the aggregate population model. In the aforementioned available data, approximately 20% of patients had one-year of follow-up data. Techniques developed by Lin et al. [12] and Basu et al. [13] were applied to address censoring in order to fully utilize patient cost data up to the point of loss-to-follow-up or death.

### 2.6. Mortality impact

We reported the impact of CAC on mortality using the 100% Medicare SAF. However, given the likely under-reporting of CAC in the 2012 Medicare SAF cohort, the estimated mortality impact of moderate and severe CAC was based on new tabulations from the HORIZONS-AMI/ACUITY pooled sample, an in-depth analysis of cardiac death in the sample studied by Genereux et al. [4]. Cardiac death was used, as all causes of mortality were not available and cardiac death was assumed to be most relevant. A Cox proportional hazards model was used to account for censoring with adjustment for age, gender, the Charlson comorbidity index, and the comorbidities end-stage renal disease and diabetes, which were included explicitly in order to evaluate their specific effects due to their potential key role in the causal framework. The impact of the mortality differential on the health outcomes for the 2012 cohort was assessed both in terms of lost life-years and the associated monetized value of those lost life-years. For the life expectancy calculation, the estimate of lost life years was based on the median age and gender of an elderly PCI patient (i.e., a 74-year-old male) who would normally have an expected lifetime of 11.5 years: this was then adjusted down to 9.5 years after standard discounting at 3% per annum. A sensitivity analysis scenario used a mortality differential 25% higher than the base case as a 'high case' for mortality, and a 'low case' sensitivity analysis conservatively assumed no survival difference between CAC and non-CAC PCI patients.

### 2.7. Aggregate burden-of-illness model

In order to assess the overall burden of CAC, we aimed to include both true economic costs as well as the effects on health. Fig. 1 illustrates how the economic model of the burden of illness integrated each of the components above to produce an aggregate estimate of the economic burden. The first component was the incidence of PCI by age and gender. The second component represented the degree of CAC within these age and gender groups.

The third component was patient outcomes with two dimensions: cost and mortality impacts, which were included in the model in two capacities. First, the attributed medical cost burden was the product of the number of patients with CAC and the expected average attributable annual cost for patients in the 2012 cohort receiving an index PCI procedure. Second, to combine health and economic effects, we converted health impact into a monetary value. We utilized a method valuing life-years according to willingness-to-pay thresholds, as discussed in the recently published ACC/AHA Task Force on value and cost in guideline development [14]. For example, if the societal willingness-to-pay for one year of healthy life is $100,000, we valued a year of healthy survival in the model at that amount. In this way we could report a singular economic impact rather than separate economic and health impacts. The willingness-to-pay threshold has the limitations both of being subject to societal acceptance, as well as being difficult to estimate with a high degree of certainty. Accordingly, we varied the willingness-to-pay threshold at three levels in order to address societal uncertainties in the threshold. Estimates of societal willingness to pay for life year gains were based on the Andersen et al. thresholds for "levels of value"—high, medium, and low [14]: the base case assumed $100,000 per life year gained, while the lower bound was $50,000 and the upper bound was $150,000.

For all inputs, the model was evaluated at a base case, based on the results of the analyses, and at low and high values in the scenario sensitivity analyses based on the expert judgment of the co-authors as to the degree of uncertainty and plausible variation.

## 3. Results

### 3.1. Incidence of index PCI—Medicare cohort

Based on the analysis for the Medicare 100% SAF for calendar year 2012, there were 157,340 index PCI procedures performed, which amounted to an estimated 200,945 when adjusted for the MA patients. Table 1 shows mean Charlson comorbidity scores and ages by gender. The mean age was 73.4 years, 61.8% were males, and 66.4% were between ages 65 and 74.

**Table 1**
Baseline characteristics of Medicare patients with and without coronary artery calcification.

| Characteristic | CAC | No CAC | Total |
|---|---|---|---|
| Age 65–74 | | | |
| Male | | | |
| n | 825 | 65,193 | 66,018 |
| Mean Charlson Score (SD) | 2.5 (2.3) | 2.1 (2.2) | 2.1 (2.2) |
| 95% CI | 2.1–2.3 | 2.0–2.1 | |
| Mean Age (SD) | 69 (3) | 69 (3) | 69 (3) |
| 95% CI | 69–70 | 69–69 | |
| Female | | | |
| n | 427 | 34,874 | 35,301 |
| Mean Charlson Score (SD) | 2.5 (2.4) | 2.3 (2.3) | 2.3 (2.3) |
| 95% CI | 2.3–2.7 | 2.3–2.3 | |
| Mean Age (SD) | 70 (3) | 70 (3) | 70 (3) |
| 95% CI | 69–70 | 70–70 | |
| Age 75–84 | | | |
| Male | | | |
| n | 393 | 25,399 | 25,792 |
| Mean Charlson Score (SD) | 2.8 (2.5) | 2.4 (2.3) | 2.4 (2.3) |
| 95% CI | 2.5–3.0 | 2.4–2.5 | |
| Mean Age (SD) | 79 (3) | 79 (3) | 79 (3) |
| 95% CI | 79–79 | 79–79 | |
| Female | | | |
| n | 267 | 18,798 | 19,065 |
| Mean Charlson Score (SD) | 2.7 (2.4) | 2.3 (2.2) | 2.3 (2.2) |
| 95% CI | 2.5–3.0 | 2.3–2.3 | |
| Mean Age (SD) | 79 (3) | 79 (3) | 79 (3) |
| 95% CI | 79–80 | 79–79 | |
| Age 85 + | | | |
| Male | | | |
| n | 92 | 5392 | 5484 |
| Mean Charlson Score (SD) | 3.1 (2.5) | 2.7 (2.3) | 2.7 (2.3) |
| 95% CI | 2.6–3.6 | 2.6–2.8 | |
| Mean Age (SD) | 87 (2) | 87 (2) | 87 (2) |
| 95% CI | 87–88 | 87–87 | |
| Female | | | |
| n | 80 | 5600 | 5680 |
| Mean Charlson Score (SD) | 2.7 (2.1) | 2.3 (2.1) | 2.3 (2.0) |
| 95% CI | 2.3–3.2 | 2.2–2.3 | |
| Mean Age (SD) | 88 (3) | 88 (3) | 88 (3) |
| 95% CI | 87–88 | 88–88 | |

Values are based on authors' analysis of the Medicare 100% Standard Analytic File for 2012. Presents descriptive data on subgroup characteristics. Abbreviations: CAC = Coronary Artery Calcification, CI = Confidence Interval, SD = Standard Deviation.

**Table 2**
Coronary calcification rates by age.

| | Medicare Patients with CAC from SAF[a] | Genereux et al. estimates for calcification prevalence in the PCI population[b] | Adjusted calcification prevalence in the Medicare Population (n) |
|---|---|---|---|
| Moderate Coronary Calcification | | | |
| 65–74 | N/A | 30.0% | 30,396 |
| 75–84 | N/A | 34.0% | 15,251 |
| 85+ | N/A | 28.6% | 3193 |
| Total | N/A | – | 48,840 (**31.0%**) |
| Severe Coronary Calcification | | | |
| 65–74 | 1252 (1.2%, 95% CI 1.1–1.3) | 7.2% | 7295 |
| 75–84 | 660 (1.5%, 95% CI 1.4–1.6) | 8.8% | 3947 |
| 85+ | 172 (1.5%, 95% CI 1.3–1.8) | 10.5% | 1172 |
| Total | 2084 (1.3%, 95% CI 1.3–1.4) | – | 12,414 (**7.9%**) |

Comparison of age-specific coronary calcification rates by age group and severity level. Abbreviations: CAC = coronary artery calcification, CI = Confidence Interval, PCI = Percutaneous Coronary Intervention, SAF = Standard Analytic Files.
[a] ICD9 code 414.4.
[b] These estimates are based on new tabulations from HORIZONS-AMI/ACUITY pooled sample, as described in Genereux et al. (2014) (Data on file, Cardiovascular Research Foundation, New York, NY, USA).

### 3.2. Incidence of calcification

We estimated that, in the 2012 Medicare SAF data, 1.3% of index PCI and CABG patients were coded as having CAC (Table 2). When compared with estimates from the HORIZONS-AMI/ACUITY pooled analysis of 5.9% severe CAC and 26.1% moderate CAC in a PCI patient population with a mean age of 65 [4], under-reporting seems highly likely. The base case estimates were weighted by the age distribution of the Medicare population (data on file at Cardiovascular Research Foundation, New York, NY, USA) and projected to be 7.9% for severe and 31% for moderate CAC based on a tabulation using HORIZONS-AMI/ACUITY pooled data for the elderly (Table 2). For comparison, within the sub-sample of hospitals that coded more than 10% of their PCI patients as having CAC using code 414.4 (n = 17), 14.1% of PCI patients were coded as calcified in 2012.

### 3.3. Medical cost impact

Based on the adjusted GEE analysis in the Medicare 5% SAF data, elderly PCI patients without CAC incurred an average of $16,800 in costs at the time of index event and a total of $24,700 in the first year, and those with severe CAC incurred an additional $800 in costs at the time of index event for a total of $3500 in additional costs (Table 3) in the first year following the procedure [15]. Based on the assumed 50% differential, the base case patient with moderate CAC incurs $1750 in costs, on average.

**Table 3**
Incremental costs of coronary calcification by time after procedure in the elderly Medicare 5% SAF.

| | Average Cost for Non-Calcified Patient | Incremental Cost of Calcification | |
|---|---|---|---|
| | | Unadjusted | Adjusted for age, gender, and censored costs using Lin et al. method) |
| Time Period | | | |
| Index | $16,800 | $1300 | $800 |
| 1–30 days | $1700 | $1100 | $400 |
| 31–90 days | $2200 | $500 | $1050 |
| 91–180 days | $2350 | $650 | $350 |
| 181–270 days | $1100 | $550 | $550 |
| 271–360 days | $550 | $1800 | $350 |
| **Total** | **$24,700** | **$5900** | **$3500** |

Comparison of costs by period for Medicare 5% SAF patients with reported calcification (n = 221 at index; n = 88 at 360 days) and without reported coronary calcification (n = 11,489 at index; n = 4660 at 360 days), with adjustments for covariates and censoring.

### 3.4. Survival impact

Based on the 100% Medicare SAF, the one-year hazard ratio for mortality for patients with CAC compared to no CAC was 1.08 (9.30% mortality at 1-year vs. 8.6% without CAC), but was not statistically significant at the p = 0.05 level without adjustments for sample differences in age, gender, or the Charlson comorbidities index. The inclusion of comorbidities, such as diabetes and end-stage renal disease, further minimized the effect of CAC. New tabulations using the HORIZONS-AMI/ACUITY pooled sample estimated that one-year cardiac mortality in patients with severe CAC was 5.8%, in patients with moderate CAC was 4.5%, and in patients with no or mild CAC was 3.3% (data on file at Cardiovascular Research Foundation, New York, NY, USA); resulting in an observed 1.2% differential in 1-year mortality between moderate CAC and no/mild CAC, and a 2.5% differential between severe CAC and no/mild CAC. These differentials were used as inputs in the aggregate burden model below.

### 3.5. Aggregate burden

Table 4 summarizes the input assumptions for the aggregate burden in the base case analysis for index PCI patients in 2012, and Table 5 summarizes the results. Of the 2012 cohort of index PCI patients, 15,875 Medicare beneficiaries (7.9%) were projected to have had severe CAC. Based on the estimate of an additional $3500 per patient in the first year following their PCI, these patients were projected to generate an additional $55.6 million in total. The impact on survival (based on these estimates) of patients with severe CAC can be attributed to an additional 397 deaths in 2012, resulting in 3770 lost life years, which when monetized in the base case would represent an estimated loss of about $377 million.

Of the 2012 cohort of index PCI patients, 62,896 Medicare beneficiaries (31%) were projected to have had moderate CAC. Based on the estimate of an additional $1750 per patient in the first year following their PCI, these patients were projected to generate an additional $110 million in medical care costs. This result is driven by the much larger number of patients projected to have had moderately-calcified lesions. In total for 2012, in the base case, the estimated medical cost burden was $166 million and the monetized mortality burden was $1.1 billion for a total of $1.3 billion for this cohort (Fig. 2).

**Table 4**
Model inputs.

| | Low | Base | High | Source |
|---|---|---|---|---|
| **Annual Incidence** | | | | |
| PCI | 157,340 | **157,340** | 157,340 | Medicare 100% SAF estimates |
| Adjustment for Medicare Advantage | 21.70% | **21.70%** | 21.70% | Medicare Program Statistics |
| Total | 200,945 | **200,945** | 200,945 | Calculated (PCI/MA Adjustment) |
| **Coronary Calcification** | | | | |
| Percentage Severe | 6% | **8%** | 10% | Assumption based on [4] |
| Percentage Moderate | 26% | **31%** | 35% | Assumption based on [4] |
| **Annual Cost Impact** | | | | |
| PCI: Moderate Calcification | $1250 | **$1750** | $3750 | Assumption |
| PCI: Severe Calcification | $2500 | **$3500** | $7500 | Medicare 5% SAF |
| **Annual Mortality Impact** | | | | |
| PCI: Moderate Calcification | 0 | **0.012** | 0.015 | Authors' calculation |
| PCI: Severe Calcification | 0 | **0.025** | 0.031 | Authors' calculation |
| **Other** | | | | |
| Patient Age | 73.4 | **73.4** | 73.4 | Cohort Mean in Medicare 100% SAF |
| Mean Remaining Life Expectancy | 8 | **9.5** | 11 | US Life Tables (in years) |
| Value of Lost Life Year | $50,000 | **$100,000** | $150,000 | Assumptions based on [14]. |

Summary of values and ranges for all variables in the economic burden calculation. Abbreviations: MA = Medicare Advantage, PCI = percutaneous coronary intervention, SAF = Standard Analytic Files.

As shown in the low and high scenarios in Fig. 3, these estimates are highly sensitive to the assumptions about the impact of CAC on mortality. If patients with CAC did not experience any additional mortality, then the medical cost alone would be $95 million in the low-cost scenario and $414 million in the high-cost medical scenario. If, however, lost life-years are valued at $150,000 per life year, then the economic burden would be greatly multiplied to over $3 billion for this cohort with moderate or severe CAC in 2012.

## 4. Discussion

To the best of our knowledge, this analysis represents the first estimate of the societal burden of illness due to CAC in the U.S. The aggregate economic burden is substantial, estimated to be over $1 billion in the base case, and up to as much as $3 billion. The burden of illness is much greater when CAC is associated with greater post-PCI morbidity and mortality. Given the lagging documentation of the recently introduced new ICD9 code for coronary calcification (414.4), one might wonder if this attempt to quantify the burden of CAC is premature. Studying the early experience of the use of this code for CAC in the Medicare program highlights the challenges in conducting this kind of analysis. In the future, more refined estimates should be possible, based on more accurate assessments of prevalence of CAC. However, clinical and economic policy decisions are being made – even if implicit – and they cannot necessarily wait for complete or perfect data.

Based on this analysis, CAC is substantially under-reported in the elderly Medicare population, particularly when one appreciates the relationship between advanced age and CAC [4]. Inadequate medical coding of CAC – and likely incomplete medical record documentation of it – also raises concerns about clinician awareness and management of this important element of comorbidity, which is often associated with chronic conditions including advanced age, diabetes mellitus, renal insufficiency, and hypertension [16,17]. Even so, our estimates project that CAC generates a large economic burden in the elderly Medicare population—and perhaps in younger cohorts.

The recent call by the ACC/AHA for the greater use of economic data in guideline development underscores the point that formulating appropriate treatment guidelines depends on the availability of clinical and claims data in which CAC is defined in relevant clinical terms that enable appropriate consistent measurement and reporting [14]. Findings such as these also should have implications for curriculum and training programs for interventional cardiology fellows.

Most analyses in the health economics and outcomes research literature are assessments of either short-term costs or comparative cost-effectiveness of various treatment options. Payers are increasingly interested in the comparative costs as well as the clinical benefits of various therapeutic options. Why should we be concerned about the burden of illness for CAC at a societal level? PCI revascularization technologies now are being developed for improved revascularization strategies in patients with CAC that may positively impact both clinical outcomes along with the cost burden of CAC [18–20]. Since societal costs are estimated to be significant, comparative clinical and economic evaluations of potential improved therapeutic approaches to the management of patients with CAC should be pursued.

### *4.1. Limitations*

This study had several key limitations. First, given the apparent low reporting of CAC in the claims we examined, a standard epidemiologic cohort analysis comparing the costs of patients with and without CAC

**Table 5**
Model results.

| | Low | Base | High |
|---|---|---|---|
| **Estimated 2012 PCI Incidence** | 200,945 | **200,945** | 200,945 |
| **Severe Coronary Calcification** | | | |
| Cost | | | |
| Projected Incidence | 12,057 | **15,875** | 20,095 |
| Estimated Incremental Per Patient Cost | $2500 | **$3500** | $7500 |
| Projected Aggregate Medical Cost (000s) | $30,142 | **$55,561** | $150,709 |
| Mortality | | | |
| Estimated Incremental Deaths | 0 | **397** | 628 |
| Projected Total Life Years Lost | 0 | **3770** | 6907 |
| Aggregate Monetized Mortality Burden (000s) | 0 | **$377,023** | $1,036,123 |
| Severe: Total Economic Burden (000s) | $30,142 | **$432,585** | $1,186,832 |
| **Moderate Coronary Calcification** | | | |
| Cost | | | |
| Projected Incidence | 52,447 | **62,896** | 70,331 |
| Estimated Incremental Per Patient Cost | $1250 | **$1750** | $3750 |
| Projected Aggregate Medical Cost (000s) | $65,558 | **$110,068** | $263,740 |
| Mortality | | | |
| Estimated Incremental Deaths | 0 | **755** | 1055 |
| Projected Total Life Years Lost | 0 | **7170** | 11,605 |
| Aggregate Monetized Mortality Burden (000s) | 0 | **$717,012** | $1,740,687 |
| Moderate: Total Economic Burden (000s) | $65,558 | **$827,080** | $2,004,427 |
| **Grand Totals** | | | |
| Total Medical Cost Burden (000s) | $95,700 | **$165,629** | $414,449 |
| Total Monetized Mortality Burden (000s) | $0 | **$1,094,035** | $2,776,810 |
| Total Economic Burden (000s) | $95,700 | **$1,259,664** | $3,191,259 |

Summary of results for burden of illness for three scenarios with alternative sets of base case, lower burden, and higher burden assumptions. Abbreviations: PCI = percutaneous coronary intervention.

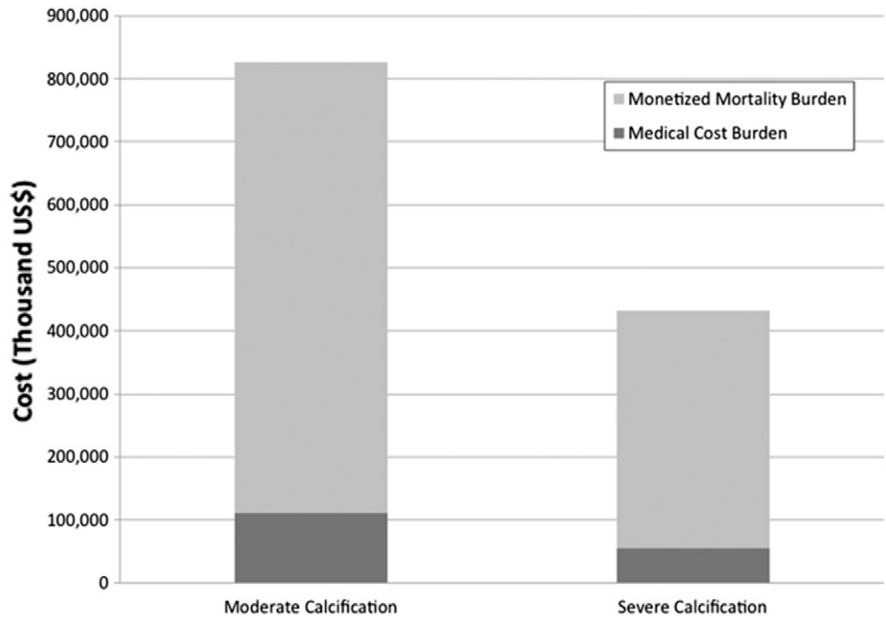


**Fig. 2.** Aggregate economic burden by degree of coronary calcification. This compares the monetized aggregate burden due to moderate vs. severe coronary calcification, the former being larger due to the greater incidence.

would be subject to misclassification bias: the comparison group would be contaminated by patients who actually have CAC. There is no easy or certain way to remove this bias from such an analysis.

Second, a lifetime horizon is preferable to a one-year time horizon for both costs and outcomes; however, no data on cost or mortality differences after year one were available. We assume that patients with CAC would have lower life expectancy and would likely require greater utilization and costs. Thus, our assumptions are conservative in terms of overall burden. Additionally, due to the small sample size, as well as having access only to aggregate data rather than individual patients for the Medicare data, we cannot report rates based on very small numbers of patients, such as repeat PCI and/or bypass surgery for these patients in the follow-up one-year phase, which would be an important and interesting result.

Third, since the 414.4 code for calcification is early in its adoption into standard documentation and clinical practice, it is plausible that the code was used more frequently in cases where calcification was particularly evident or important for the patient's treatment plan. If any misclassification bias did occur, it would likely bias our overall burden estimate downward.

Additionally, basing life expectancy of patients with or without CAC on standard U.S. life tables ignores the effect of cardiovascular disease on life expectancy, and assumes that patients with or without CAC have similar mortality risk. We chose to make this conservative assumption, since we do not have the ability as yet to effectively stratify the CAC population within existing mortality data for cardiovascular disease. There are likely other mechanisms that affect survival as well, specifically myocardial infarction or other revascularizations. For this analysis, data on other mechanisms were not available. We assume that, if anything, the survival outcomes for CAC patients would be worse when additional factors are included. Therefore, our results represent a conservative estimate for burden of the disease.

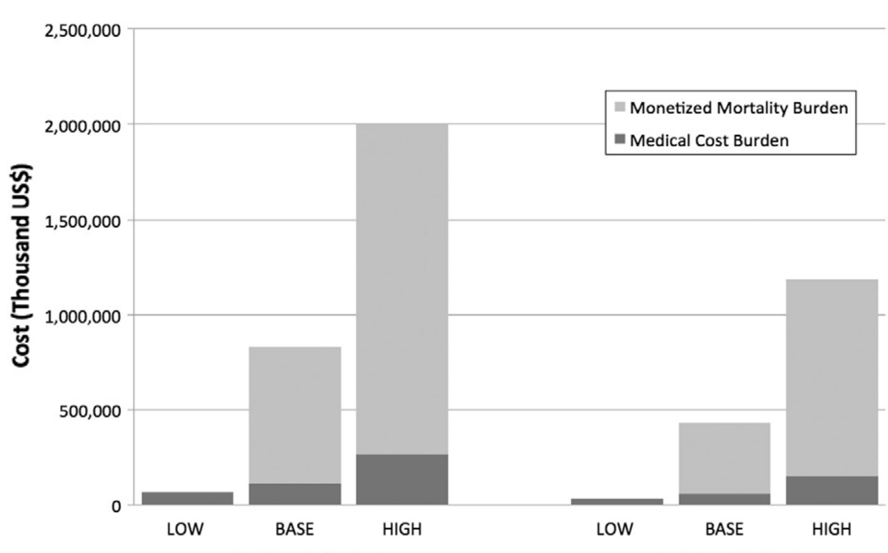


**Fig. 3.** Sensitivity of the economic burden results based on alternative mortality scenarios (low, base, and high). The aggregate economic burden varies widely, depending on assumptions about mortality and cost impact.

Finally, the model focuses on the PCI patient population receiving stents, due to (1) the lack of data on index CABG with CAC in the 5% SAF (fewer than 50 patients); and (2) the inability to measure cost impacts on patients with moderate or severe CAC receiving medical therapy. The incidence of PCI in the 100% SAF may seem low compared to other PCI annual volume estimates in the literature, but these other estimates also include repeat PCIs, patients under the age of 65, and those enrolled in MA. Our Medicare SAF-based estimates suggest that the average cost of CABG is more than twice that of PCI. Other trials – such as the SYNTAX trial [21] – have suggested that CAC can be a reason for the use of (higher cost) CABG rather than lower cost PCI. Furthermore, some patients with severe CAC are likely to be treated medically and not even considered for revascularization, and some of these patients will die before becoming candidates for revascularization. All of these would generate additional burden that is not measured here. Hence, the estimated economic burden, based only on index PCIs, is likely to be conservative.

## 5. Conclusions

While there is clear evidence that the degree of CAC complicates the treatment of CAD, there has been little, if any, previous effort to assess its related economic burden. Analyses relying on aggregate administrative claims alone have been hampered by the lack of routine medical coding for CAC, which results in substantial under-reporting and makes epidemiologic and economic analyses challenging and potentially biased. Despite these limitations, a plausible and conservative economic model was constructed. In the base case, the economic burden in one annual elderly cohort alone is estimated to be $1.3 billion. Although the potential bias and sample size limitations have been noted, the results demonstrate conservatively the significant economic burden of calcification in the population. Although the data available to address the burden of CAC are neither complete nor ideal, it is clearly a significant clinical and economic issue, and this analysis is an important first step to pave the way for future work. At a minimum, this analysis suggests the need for ongoing, periodic reviews to assess the prevalence of CAC in the Medicare population.

Clinical guidelines and economic policies both need to be grounded in reliable evidence to promote substantial health improvement and to seize appropriate cost containment opportunities. Professional medical and other clinical societies should consider initiating a member education campaign on the new standards for appropriate coding of CAC. A greater appreciation of the potential consequences for CAC is warranted, arguing for greater attention not only to its treatment but also its reporting and coding in order to support better evidence-based decision-making in this area.

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