Impact of Prostate Cancer Diagnosis on Noncancer Hospitalizations Among Elderly Medicare Beneficiaries With Incident Prostate Cancer

Amit D. Raval, PhD; Suresh Madhavan, MBA, PhD; Malcolm D. Mattes, MD; Mohamad Salkini, MD; and Usha Sambamoorthi, PhD

Abstract

**Objectives:** The purpose of this study was to analyze the impact of cancer diagnosis on noncancer hospitalizations (NCHs) by comparing these hospitalizations between the precancer and postcancer periods in a cohort of fee-for-service Medicare beneficiaries with incident prostate cancer. **Methods:** A population-based retrospective cohort study was conducted using the SEER-Medicare linked database for 2000 through 2010. The study cohort consisted of 57,489 elderly men (aged ≥67 years) with incident prostate cancer. NCHs were identified in 6 periods (t₁–t₆) before and after the incidence of prostate cancer. Each period consisted of 120 days. For each period, NCHs were defined as inpatient admissions with primary diagnosis codes not related to prostate cancer, prostate cancer–related procedures, or bowel, sexual, and urinary dysfunction. Bivariate and multivariate comparisons on rates of NCHs between the precancer and postcancer periods accounted for the repeated measures design. **Results:** The rate of NCHs was higher during the postcancer period (5.1%) compared with the precancer period (3.2%). In both unadjusted and adjusted models, elderly men were 37% (odds ratio [OR], 1.37; 95% CI, 1.32, 1.41) and 38% (adjusted OR, 1.38; 95% CI, 1.33, 1.46) more likely to have any NCHs during the postcancer period compared with the precancer period. **Conclusions:** Elderly men with prostate cancer had a significant increase in the risk of NCHs after the diagnosis of prostate cancer. This study highlights the need to design interventions for reducing the excess NCHs after prostate cancer diagnosis among elderly men.

Background

The period immediately after cancer diagnosis can be considered a point of turbulence for the management of preexisting chronic conditions. Cancer is often considered a dominant condition that eclipses the management of all other chronic conditions. Among individuals with cancer, the management of chronic conditions that are not related to cancer may be neglected. Undermining the management of chronic conditions in patients with cancer may result in adverse outcomes and poor quality of care for non–cancer-related conditions. For example, among elderly men (age ≥66 years) with localized prostate cancer, the quality of care for acute chronic conditions is neglected. Furthermore, among men of all ages with prostate cancer, many hospitalizations are attributable to chronic conditions other than prostate cancer. For example, using the encounter-level data for 1997 through 2004, Milenkovic et al found that among adults with prostate cancer, 84% of the inpatient encounters were for chronic conditions other than prostate cancer. Although these studies confirm the burden of noncancer hospitalizations (NCHs) among men with prostate cancer, the changes in hospitalizations attributable to noncancer conditions over a period of prostate cancer diagnosis remain unknown because of the use of encounter level data.

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Submitted September 20, 2015; accepted for publication January 5, 2016.

The authors have disclosed that they have no financial interests, arrangements, affiliations, or commercial interests with the manufacturers of any products discussed in this article or their competitors.

This project was supported by the Agency for Healthcare Research and Quality (AHRQ) Grant no: R24HS018622-03 and National Institute of General Medical Sciences Grant (U54GM104942). The content is solely the responsibility of the authors and does not necessarily represent the official views of AHRQ and NIH.

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© JNCCN—Journal of the National Comprehensive Cancer Network | Volume 14 Number 2 | February 2016
An understanding of the risk of NCH in patients diagnosed with incident prostate cancer is critical to better manage their care at the time of the finding. Therefore, the primary objective of the current study is to analyze the impact of cancer diagnosis on NCHs among elderly men with incident prostate cancer by comparing the rates of NCHs in 6 periods before and after the prostate cancer diagnosis. Furthermore, elderly men with prostate cancer have differential rates of chronic conditions. For example, cardometabolic conditions (eg, heart disease and diabetes) are observed in 18.1% of men with prostate cancer, followed by respiratory conditions (eg, chronic obstructive pulmonary disease, 9.8%) and mental health conditions (eg, depression, 8%). Thus, the risk for hospitalizations may differ by the types of chronic conditions. One study, not specific to prostate cancer, reported that adults aged 50 years and older in the United States with cardometabolic conditions had higher rates of annual hospitalizations (40%) compared with those with respiratory conditions (20%). The incidence of prostate cancer can have a varying impact on the risk for NCHs among individuals with different types of chronic conditions. Therefore, the secondary objective of our study is to examine whether the impact of cancer diagnosis on NCHs differs by the types of chronic conditions.

Methods

Study Design
A retrospective longitudinal cohort design with baseline, precancer and postcancer periods were used. Using the date of cancer diagnosis as the index date, a 24-month window before the index date was constructed. This 24-month period was split into two 12-month periods (ie, baseline and precancer period). This was necessary because identification of preexisting chronic conditions and NCHs during the precancer period involved the use of inpatient claims. To avoid circular reasoning, the first 12-month period was used as the baseline period, during which the types of chronic conditions and other independent variables were measured. The 12-month period before the diagnosis of cancer was considered the precancer period and this period was used to derive NCHs. The postcancer period consisted of 12 months after the diagnosis of cancer. To ensure a robust study design, the NCHs were measured repeatedly every 120 days during the precancer and postcancer period, yielding a total 6 repeated measures per individual. Thus, \( t_1 \), \( t_2 \), and \( t_3 \) represented the precancer period and \( t_4 \), \( t_5 \), and \( t_6 \) represented the postcancer period (Figure 1).

Data Sources

SEER-Medicare Linked Data: We used the NCI’s SEER cancer registries data linked with Medicare administrative claims data. As of now, the SEER data represent 28% of the US population from 18 registries and consist of a total of 7,397,159 malignant cancer cases, and most of these cancer cases are diagnosed among the elderly population aged 65 years and older. Medicare is the US Government–mandated insurance program covering 97% of the US population aged 65 years and older. A total of 93% of men aged 65 years and older in SEER has been linked to Medicare enrollment records. In the current study, we used data from the SEER-Medicare linked database of prostate cancer cases diagnosed between 2002 and 2009 and their linked claims between 2000 and 2010. Furthermore, we included elderly men aged 67 years and older because we required at least 2 years of health care utilization data before diagnosis of prostate cancer.

Study Cohort: The study population was based on 289,701 men diagnosed with incident prostate cancer between January 1, 2002, and December 31, 2009. Men with multiple cancers (N=25,785), those diagnosed with prostate cancer during the autopsy (N=2,944), and those younger than 67 years who died during the study period (N=111,643) were excluded. Furthermore, the cohort was further restricted to those with continuous fee-for-service Medicare Part A and Part B enrollment during the entire study period (N=101,302). To reduce the misclassification bias, individuals with newly diagnosed conditions during the precancer and postcancer periods (N=40,544) were excluded. After excluding individuals with missing information on race/ethnicity, county, and in situ, unknown, and advanced cancer stage, the final study cohort comprised 57,589 elderly men with incident prostate cancer (Figure 2).

Key Dependent Variable

Noncancer Hospitalizations: Inpatient admissions during the precancer and postcancer periods were derived from the MEDPAR file. Hospitalizations with the primary diagnosis of prostate cancer were consid-
ered prostate cancer–related hospitalizations and were excluded from the analysis. Although this approach is commonly used in published studies to identify disease-specific hospitalizations, the challenges in measuring the NCH should also be noted. Elderly men with prostate cancer may have hospitalizations due to cancer-related complications such as bowel, sexual, or urinary dysfunction or cancer-related procedures such as surgery. Therefore, NCHs were considered any admission to an inpatient facility with a principal diagnosis for conditions other than prostate cancer or hospitalizations for causes other than cancer-related complications, such as bowel, sexual, and urinary dysfunctions or primary or treatment-related procedure codes for cancer-related procedures. The details of the codes used to identify the cancer-related complications and procedures are listed in eAppendices 1 and 2 (available with this article at JNCCN.org).

Independent Variables: Our study used the widely known Andersen’s Behavioral Model of Health Services Use (ABM) to identify the potential independent factors associated with NCHs in our study population. The ABM and adapted versions of this model have been extensively used in health services research to study the factors associated with health care service use and health care outcomes. The ABM states that the use of health care services is determined by individual and contextual determinants, which can be categorized into 4 groups: (1) predisposing factors, (2) enabling factors, (3) external environment factors, and (4) need factors (Figure 3).

Predisposing Factors: These factors represent the unique feature of individuals who tend to engage more or less use of health care services. Age, race/ethnicity, and marital status were the predisposing characteristics. Age at the time of diagnosis (67–74 years, ≥75 years), race/ethnicity (White, African American, Hispanic, and other), and marital status (married, divorced/separated, unmarried, and others) were identified from the Patient Entitlement and Diagnosis Summary File (PEDSF).

Enabling Factors: These factors serve as conditions that enable individuals to use health care services. Income, education, access to care, and the initial cancer treatment were the enabling factors. The PEDSF file provides 2000 Census information on education level and median income. Access to care was measured with at least one visit to a primary care provider during the baseline period. Receipt of active treatment was identified using inpatient, outpatient, and carrier files with appropriate International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic and procedure codes; Current Procedural Terminology (CPT) or Healthcare Common Procedure Coding System (HCPCS) codes; or revenue center code within the 6 months after the index date (eAppendix 1). We classified the cancer treatment into 4 groups based on a hierarchy: (1) radical prostatectomy (RP), (2) radiation therapy (RT), (3) hormone therapy, and (4) none of these therapies.

External Environment Factors: These factors facilitate the use of health care services related to the structure of services in the geographic areas near the individuals. External environment characteristics comprised the individual’s region (Northeast, South, North-Central, and West) and county-level health care resources, such as radiation oncology units and urology units. County-level health care resources were measured by the number of radiation oncology and urology units, which were derived from the Area Health Resource Files (AHRF). For the purposes of our analyses, we cat-
Noncancer Hospitalization After Prostate Cancer

Original Research

Figure 2. Study cohort development chart for study population of elderly Medicare beneficiaries diagnosed with prostate cancer.

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**Figure 2. Study cohort development chart for study population of elderly Medicare beneficiaries diagnosed with prostate cancer.**

Need Factors: These factors require the need to use health care services at the individual level. We classified the common types of chronic conditions using the organ domains. We selected this approach because of the synergism in treatment and self-management approaches. For example, the management of cardiometabolic conditions, such as diabetes and heart disease, have similar treatment and self-management strategies. Among men with prostate cancer, cardiometabolic diseases, respiratory diseases (eg, chronic obstructive pulmonary disease, asthma), and mental health conditions (eg, depression, other mental conditions) are commonly reported. These common chronic conditions were classified into 7 mutually exclusive categories: (1) cardiometabolic conditions only, (2) mental health conditions only, (3) respiratory conditions only, (4) cardiometabolic and mental health conditions, (5) cardiometabolic and respiratory conditions, (6) all 3 chronic conditions, and (7) none of these chronic conditions. However, because of insufficient numbers for the category “respiratory and mental health conditions,” this category was excluded from analysis.

All of the chronic conditions were identified during the baseline period using 1 inpatient claim or 2 outpatient claims for each of the chronic conditions listed. A very small percentage of men (<5%) had chronic conditions other than the cardiometabolic, mental health, and respira-
tory conditions; 42 other conditions were derived using the list of chronic conditions from published literature. We calculated the total number of other chronic conditions during the baseline period and categorized these as “zero or one condition” and “two or more conditions.” The AJCC TNM classification system was used for prostate cancer staging. The cohort was restricted to elderly men with no-node-positive or nonmetastatic prostate cancer. Three groups of cancer stage at diagnosis were defined as T1 or less, T2, and T3 or T4.

**Statistical Analyses**

Because the NCHs were measured repeatedly during each of the 6 periods, the observations were no longer independent and were correlated. To account for correlated data, we used a statistical approach suggested by Liang et al, which involves using the generalized estimating equations (GEE) with the specific correlation matrix. The general form of the model is given in the following equation:

$$\ln \left( \frac{p_{ij}}{1-p_{ij}} \right) = \beta_0 + \beta_1 \left( \text{time}_{ij} \right) + \beta_2 \left( \text{CC}_j \right) + \cdots + \beta_n \left( \text{NCh Variable}_i \right),$$

where $p_{ij}$ denotes the probability of NCHs for individual $i$, in period $j$. $\text{Time}_j$ denotes a specific period $j$ for individual, $i$. $\text{CC}_j$ denotes presence of particular types of chronic conditions at baseline period for individual, $i$. The model also included other independent variables, such as predisposing, enabling, need, and external environment characteristics measured for individual, $i$. $\beta$s are the regression coefficients to be estimated. We specified 3 types of correlation structures—exchangeable, autoregressive, and unstructured—to control for correlations between repeated observations.

Because the parameter estimates of the association between NCH and types of chronic conditions remained the same under different correlation structures, only the results from GEE models with exchangeable correlation structures are reported. For ease of interpretation, the predicted probabilities of NCHs between the precancer and postcancer periods were compared. These probabilities were calculated using the parameter estimates from the GEE models, assuming an additive effect.

Statistical analyses using GEE models were performed using STATA Statistical Software: Release 13 (STATA-13; StataCorp LP, College Station, TX). The predicted probabilities were derived using the “margins” command in STATA-13. The term “risk” is used to describe the results associated with odds ratios (OR). Although the risk ratio and OR will yield different estimates, for events with low prevalence (≤10%), such as NCHs, these 2 measures will produce similar results.

**Results**

**Study Population**

The study cohort (N=57,489) was primarily white (82.4%), within the age group of 67 to 74 years (58.3%; mean age, 74.6 years; SD, 5.1), and married (68.5%). Most men in the study cohort (80.5%) received treatment for cancer (Table 1).

**NCHs During the Precancer and Postcancer Periods**

Table 2 reports the rates of NCHs during each of the periods. The rates of NCHs were the highest during the postcancer period ($t_p$; ie, 120 days immediately after the cancer diagnosis) at 5.1% and lowest during the precancer period ($t_c$) at 3.2%, representing an increase of 1.9 percentage points. Among the categories of chronic conditions, the rates of NCHs during the postcancer period were significantly higher compared with the precancer period. Among elderly men with all 3 types of types of chronic conditions, the rates were 20.8% during the postcancer period ($t_p$) and 14.3% during the precancer period ($t_c$), an increase of 6.5 percentage points. Among elderly men with none of the chronic conditions, the rates were 2.6% during the postcancer period ($t_p$) and 1.3% during the precancer period ($t_c$), an increase of 1.3 percentage points. Similar increases were seen for other chronic condition categories.

Table 3 displays the ORs and adjusted ORs and 95% CI using the unadjusted (model 1) and adjusted GEE models (models 2 and 3) on NCHs with exchangeable correlation structures. Model 1 revealed that elderly men were 37% more likely to have NCHs during the postcancer period compared with the precancer period (OR, 1.37; 95% CI, 1.32, 1.41). In model 2, with adjustments for only the types of chronic conditions, elderly men were 38% more likely to have NCHs during the postcancer period (adjusted OR, 1.38; 95% CI, 1.33, 1.42) compared with the precancer period. In model 3, which controlled for all the independent variables, elderly men were 38% more likely to have NCHs during the postcancer period compared with the precancer period.
Probabilities of NCHs by Precancer and Postcancer Period

Table 4 displays the probabilities of NCHs in the precancer and postcancer periods for the types of chronic conditions. Based on the fully adjusted model (model 3), an increase in the probability of NCHs was observed for the postcancer period (\(P = .027\)) compared with the precancer period (probabilities: \(P = .028\) vs .036; change in \(P = .009\)). Elderly men with all 3 types of chronic conditions had the greatest increase in the probabilities of NCHs during the postcancer period (\(P = .141\)) compared with the precancer period (\(P = .107\)), whereas elderly men with none of the types of chronic conditions had the lowest change in the probability of NCHs (\(P = .021\)) during the postcancer period compared with the precancer period (\(P = .016\)).
Discussion

To date, this is the only large population-based cohort study to examine the risk of NCHs among elderly men before and after the diagnosis of incident prostate cancer. We observed many noteworthy findings, which have implications for improving management of preexisting chronic conditions among men with incident prostate cancer.

Elderly men with incident prostate cancer had a higher risk of NCHs during the postcancer period compared with the precancer period, even after controlling for a comprehensive list of risk factors. A closer examination of the rates of hospitalizations over 6 periods suggested that the highest rates of NCHs occurred during first 4 months after the cancer diagnosis. There are several plausible explanations for this increased risk. It has been documented that the diagnosis of prostate cancer can trigger psychological distress, anxiety, and suicidal ideations. This increase in psychological stress may increase blood levels of epinephrine and norepinephrine, resulting in increased heart rate, blood pressure, and blood sugar levels. In fact, studies have shown that acute psychological stress may stimulate inflammatory markers, such as interleukins, sex hormones, and cortisol levels, which may develop into serious conditions such as heart disease. Our findings based on types of chronic conditions showed that patients with cardiometabolic conditions alone or cardio-

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precancer</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postcancer</td>
<td>1.37</td>
<td>[1.32, 1.41]</td>
<td>b</td>
</tr>
</tbody>
</table>

Model 2, adjusting for precancer and postcancer period + types of chronic conditions

<table>
<thead>
<tr>
<th>Variable</th>
<th>AOR</th>
<th>95% CI</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precancer</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postcancer</td>
<td>1.38</td>
<td>[1.33, 1.42]</td>
<td>b</td>
</tr>
</tbody>
</table>

Model 3, adjusting for precancer and postcancer period + types of chronic conditions + predisposing, enabling, need, and external environment characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>AOR</th>
<th>95% CI</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precancer</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postcancer</td>
<td>1.38</td>
<td>[1.33, 1.43]</td>
<td>b</td>
</tr>
</tbody>
</table>

Abbreviations: AOR, adjusted odds ratio; GEE, generalized estimating equation; OR, odds ratio; Ref, referent; Sig, level of significance.

aBased on 57,489 elderly men, aged ≥67 years, diagnosed with incident prostate cancer between 2002 and 2009 and alive throughout the observation period. Significant differences in noncancer hospitalizations (NCHs) over time were tested with Wald chi-square, after accounting for correlations due to repeated measures. Red highlighted values suggest high and low percentages of NCH during precancer and postcancer periods.

bP<.001.

c.001≤P<.01.
metabolic conditions combined with respiratory or mental health conditions had a greater increase in the risk of NCHs during the postcancer period compared with the precancer period. Previous literature suggests that acute emotional or psychological stress experienced by elderly men with preexisting cardiometabolic conditions may trigger the incidence of another heart failure episode,\(^{26,27}\) leading to hospitalization. It must be noted that the present study did not include newly diagnosed chronic conditions, and therefore increased hospitalizations during the postcancer period for this group may suggest the worsening of preexisting cardiometabolic conditions as a result of prostate cancer diagnosis.

This is one of very few studies to explore the trajectory of noncancer outcomes (ie, hospitalizations) during the precancer and postcancer period among fee-for-service Medicare beneficiaries with incident localized prostate cancer using the cancer registry–linked administrative claims data. The study findings reinforce the need for intervention to reduce NCHs among elderly men with incident prostate cancer. Among elderly men with prostate cancer, the risk of NCH was higher during the year after prostate cancer diagnosis compared with the year before. These findings highlight the need for targeted research, program, policy, and intervention efforts to reduce the excess NCHs in this group.

### Table 4. Predicted Probabilities With 95% CIs for Types of Chronic Conditions From GEE Analysis on Noncancer Hospitalizations in Elderly Medicare Beneficiaries With Incident Prostate Cancer: SEER-Medicare Linked Database, 2000–2010\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>Precancer</th>
<th>Postcancer</th>
<th>Changes in Probabilities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P Value</td>
<td>95% CI</td>
<td>P Value</td>
</tr>
<tr>
<td>Overall(^b)</td>
<td>.035</td>
<td>[0.034, 0.036]</td>
<td>.047</td>
</tr>
<tr>
<td>Model 2, adjusted for precancer and postcancer period + types of chronic conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall(^b)</td>
<td>.028</td>
<td>[0.027, 0.029]</td>
<td>.038</td>
</tr>
<tr>
<td>Types of chronic conditions(^b)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>.018</td>
<td>[0.017, 0.018]</td>
<td>.031</td>
</tr>
<tr>
<td>CM only</td>
<td>.044</td>
<td>[0.043, 0.046]</td>
<td>.077</td>
</tr>
<tr>
<td>MH only</td>
<td>.032</td>
<td>[0.027, 0.037]</td>
<td>.055</td>
</tr>
<tr>
<td>RSP only</td>
<td>.029</td>
<td>[0.026, 0.031]</td>
<td>.05</td>
</tr>
<tr>
<td>CM + MH</td>
<td>.075</td>
<td>[0.069, 0.081]</td>
<td>.127</td>
</tr>
<tr>
<td>CM + RSP</td>
<td>.087</td>
<td>[0.084, 0.091]</td>
<td>.146</td>
</tr>
<tr>
<td>All 3</td>
<td>.150</td>
<td>[0.138, 0.162]</td>
<td>.239</td>
</tr>
<tr>
<td>Model 3 adjusted for precancer and postcancer period + types of chronic conditions + predisposing, enabling, need, and external environment characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall(^b)</td>
<td>.027</td>
<td>[0.026, 0.028]</td>
<td>.036</td>
</tr>
<tr>
<td>Types of chronic conditions(^b)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>.016</td>
<td>[0.015, 0.016]</td>
<td>.021</td>
</tr>
<tr>
<td>CM only</td>
<td>.039</td>
<td>[0.038, 0.041]</td>
<td>.053</td>
</tr>
<tr>
<td>MH only</td>
<td>.026</td>
<td>[0.022, 0.030]</td>
<td>.036</td>
</tr>
<tr>
<td>RSP only</td>
<td>.021</td>
<td>[0.019, 0.023]</td>
<td>.029</td>
</tr>
<tr>
<td>CM + MH</td>
<td>.056</td>
<td>[0.051, 0.061]</td>
<td>.075</td>
</tr>
<tr>
<td>CM + RSP</td>
<td>.066</td>
<td>[0.062, 0.069]</td>
<td>.088</td>
</tr>
<tr>
<td>All 3</td>
<td>.107</td>
<td>[0.097, 0.116]</td>
<td>.141</td>
</tr>
</tbody>
</table>

Abbreviations: CM, cardiometabolic conditions; MH, mental health conditions; Ref, referent; RSP, respiratory conditions; Sig, level of significance. 
\(^a\)Based on 57,489 elderly men, aged ≥67 years, diagnosed with incident prostate cancer between 2002 and 2009 and alive throughout the observation period. Significant differences are based on the log-likelihood test using a repeated measure generalized estimating equations. Model 3 adjusted for predisposing (age, race, and marital status), enabling status (quartile of median census 2000 income, quartile of median census 2000 education, and cancer treatment), external environment (region, quartile of radiation oncology, and quartile of urology centers), and need characteristics (number of other chronic conditions and T stage). 
\(^b\)P < 0.001.
Because appropriate management of preexisting chronic conditions is key to reducing the risk of NCH, effective communication between oncologists and primary care physicians should be facilitated in order to implement an individualized care plan and provide patient education. Elderly men with cardiometabolic conditions alone and those with a combination of cardiometabolic and respiratory or mental health conditions were most vulnerable to an increased risk of NCH. In this regard, optimizing care in the clinical settings by focusing on the “ABCS” (aspirin when appropriate, blood pressure control, cholesterol management, and smoking cessation) can help reduce the risk of NCH. A mid-year review by the national Million Hearts initiative, which was launched in 2012, suggests this program has had some success in reducing the risk of NCHs. However, the current study’s findings need to be interpreted in the context of its limitations. Although due diligence was given in measuring NCHs based on previously published studies, one cannot rule out the possibility that some NCHs may be due to cancer treatment (e.g., sepsis due to surgery).

Conclusions
Diagnosis of incident prostate cancer was associated with an increase in the risk of NCHs among elderly men with incident localized prostate cancer. Future research is warranted to examine whether better management strategies for cardiometabolic and other chronic conditions can reduce the increased risk for NCHs after the diagnosis of prostate cancer.

References