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ORIGINAL ARTICLE

A cohort study of mammography screening finds that comorbidity measures are insufficient for controlling selection bias

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Abstract

Objective: To examine the potential of claims-based comorbidity measures for controlling selection bias in observational studies of mammography screening.

Study Design and Setting: Based on claims data of a large German Statutory Health Insurance fund, the single comorbidities considered by the Charlson, Elixhauser, Multipurpose Australian Comorbidity Scoring System, and M3 comorbidity measures were identified for mammography screening participants and nonparticipants. Total death rates within 4 years after screening invitation were compared. Cox proportional hazards regressions were performed unadjusted and adjusted for age, federal state of residence, and comorbidity.

Results: Among 1,247,919 insured women aged 50−68 years (56.2% participants), 10,311 participants (death rate 375.8/100,000 person-years) and 18,113 nonparticipants (death rate 854.8/100,000 person-years) died from any cause during the follow-up. The unadjusted hazard ratio (HR) for death from any cause for participants vs. nonparticipants was 0.44 (99.9% confidence interval 0.42−0.46). Adjustments attenuated the HR to a maximum of 0.52 (0.50−0.54).

Conclusion: The lower short-term all-cause mortality among participants cannot be explained by mammography screening effects and should be interpreted as selection bias. Adjusting for comorbidities only slightly attenuated this bias. Future studies should examine whether claims data include further information that is beneficial to adequately control selection bias in observational studies of mammography screening.

Keywords: Mammography screening; Selection bias; Observational studies; Comorbidity; All-cause mortality; Claims data

1. Introduction

Organized population-based cancer screening programs need to be monitored and evaluated continuously to ensure process and outcome objectives are achieved [1−3]. Randomized controlled trials (RCTs) are the gold standard for the evaluation of screening programs before their nationwide implementation. After program implementation, however, RCTs are usually not feasible, and observational studies are the main study design for monitoring and evaluation [4]. In these studies, addressing selection bias has been recognized as one of the most challenging methodological tasks [5−12].

In Germany, a nationwide Mammography Screening Program (MSP) for the early detection of breast cancer was implemented between 2005 and 2009. Women aged 50−69 years are now invited biennially for MSP participation, which consists of a two-dimensional, digital, full-field mammography with two views per breast [13,14].

For examining selection bias, the comparison of all-cause mortality between MSP participants and nonparticipants appears useful. Different death rates among participants and nonparticipants within a fairly short period of

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What is new?

Key findings

- In terms of short-term all-cause mortality, the groups of self-selected mammography screening participants and nonparticipants are not comparable.
- The potential of claims-based comorbidity measures for controlling selection bias in observational studies of mammography screening is limited.

What this adds to what was known?

- Addressing selection bias in observational studies of mammography screening is one of the most challenging methodological tasks.
- Using the single comorbidities considered by the Charlson, Elixhauser, Multipurpose Australian Comorbidity Scoring System, or M3 comorbidity measure for controlling selection bias is insufficient.

What is the implication and what should change now?

- Future studies should examine whether the additional consideration of further information included in claims data is sufficient to adequately control selection bias in observational studies of mammography screening.

time should at least partly be explained by differences in health status, particularly by a higher frequency of severe comorbidities among nonparticipants. This would be consistent with nonparticipants' decision to not participate, or their inability to participate, in mammography screening. We thus hypothesized that adjusting for comorbidities prevalent at the time of invitation is beneficial for controlling selection bias, as determined by all-cause mortality.

Statutory Health Insurance (SHI) claims data represent the most comprehensive data source to test this hypothesis in the context of the German MSP. Unlike any other data source, they allow the identification of individual MSP participants and nonparticipants among all women covered by the SHI (i.e., 90% of all women; 10% are privately insured). Furthermore, they capture a broad spectrum of diagnoses present at the time of MSP invitation and provide a comprehensive longitudinal mortality perspective.

Conventionally, studies based on claims data have identified comorbidities using the Charlson [15] or Elixhauser [16] measure [17,18]. More recently, new comorbidity measures such as the updated Multipurpose Australian Comorbidity Scoring System (MACSS) [19] or the M3 index [20] have been published. To date, however, the potential of such comorbidity measures for controlling selection bias in the mortality evaluation of organized population-based cancer screening programs has not been systematically investigated. The purpose of this study was to examine the potential of claims-based comorbidity measures for controlling selection bias in observational studies of mammography screening using the single comorbidities considered by the Charlson, Elixhauser, MACSS, and M3 comorbidity measures.

2. Materials and methods

2.1. Data source

This study was based on pseudonymous SHI claims data covering the years from 2007−2015. The data were provided by the BARMER, one of the two largest German SHI funds insuring more than 9 million people across Germany. Data on demographic characteristics, insurance periods, inpatient and outpatient diagnoses, as well as outpatient therapeutic and diagnostic procedures were available. All diagnoses were coded according to the International Classification of Diseases, 10th Revision, German Modification (ICD-10-GM). With respect to the inpatient setting, main and secondary hospital discharge diagnoses were considered, while admission diagnoses were omitted. In Germany, for the outpatient setting, additional coding for diagnostic certainty is mandatory. This coding differentiates between confirmed diagnosis, suspected diagnosis, status-post diagnosis after a previous diagnosis, and excluded diagnosis. In the present study, only confirmed and status-post outpatient diagnoses were considered. Outpatient procedures were coded according to the doctor's fee scale (Einheitlicher Bewertungsmaßstab [EBM]). Since dates of outpatient diagnoses were only available on a quarterly basis, inpatient diagnoses as well as outpatient procedures were also assigned quarterly.

2.2. Study design and population

In this retrospective cohort study, we identified MSP participants and nonparticipants over a 2-year period covering the invitation years 2010 and 2011. Women with the specific EBM code 01750 for screening mammography were classified as MSP participants. Women without this EBM code were classified as nonparticipants.

For the main analysis (cohort I), inclusion criteria were:

- Age 50−68 years in 2010 (i.e., age was defined in the first invitation year and women aged 69 years in 2010 were not considered to allow all insured women to be eligible for MSP invitation in 2010 and 2011).
- Continuous insurance with no insurance gaps of more than 28 days between January 1, 2007 and December 31, 2011.
- No inpatient or outpatient breast cancer diagnosis of a malignant neoplasm of breast (ICD-10-GM C50) or