Selection bias in observational studies evaluating cancer screening tests and examinations

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Background and purpose

Background In previous analyses of German claims data we found that the groups of self-selected mammography screening participants and nonparticipants are not comparable in terms of 4-year all-cause mortality.

We also found that comorbidity measures determined based on claims data are insufficient to control for this selection bias in observational studies of mammography screening. *(Czwikla et al. J Clin Epidemiol 2018;104:1-7)*

Purpose We aimed to extend these analyses to cervical (Pap smear), prostate (digital rectal exam), colorectal (fecal occult blood test (FOBT)/colonoscopy), and skin cancer (visual whole-body skin examination) screening.

Methods

Data source

- Claims data of the BARMER covering the years 2007-2017

Study populations

1) Mammography
   - Women aged 50-68 years
   - Participation status in 2010-2011
2) Pap smear
   - Women 20+ years
   - Participation status in 2010
3) Digital rectal exam
   - Men 45+ years
   - Participation status in 2010
4) FOBT/colonoscopy
   - Women and men 55 years
   - Participation status in 2010-2011
5) Skin examination
   - Women and men 35+ years
   - Participation status in 2010-2011

Insured persons with a prevalent breast, cervical, prostate, colorectal or skin cancer diagnosis in 2007-2009 were excluded from the respective study population.

Cox proportional hazards regression

- *Outcome:* Death from any cause within ≤ 7 years of follow-up
- *Exposure:* Screening participation
- *Covariates:* Sex (if applicable), age (if applicable), federal state of residence, and the single comorbidities of the Multipurpose Australian Comorbidity Scoring System

Results

Claims data of 5,765,852 persons were analyzed.

Table 1. Numbers of breast, cervical, prostate, colorectal, and skin cancer screening participants and nonparticipants by sex

	Women		Men	
Test/examination	Participants	Nonparticipants	Participants	Nonparticipants
Mammography	700,047 (56.5%)	538,773 (43.5%)	N/A	N/A
Pap smear	1,790,570 (47.4%)	1,987,915 (52.6%)	N/A	N/A
Digital rectal exam	N/A	N/A	376,081 (25.4%)	1,103,873 (74.6%)
FOBT/colonoscopy	30,220 (43.2%)	39,653 (56.8%)	9,535 (22.4%)	32,984 (77.6%)
Skin examination	924,126 (30.7%)	2,084,378 (69.3%)	492,969 (28.8%)	1,221,514 (71.2%)

Table 2. Hazard ratios for death from any cause for participants vs. nonparticipants of the respective cancer screening test/examination

	Hazard ratio (99.9% confidence interval)		
Test/examination	without adjustment	+ (sex), (age), residence	+ comorbidity
Mammography	0,46 (0,45-0,48)	0,45 (0,43-0,46)	0,53 (0,51-0,55)
Pap smear	0,22 (0,22-0,23)	0,55 (0,54-0,55)	0,57 (0,56-0,58)
Digital rectal exam	0,88 (0,86-0,89)	0,63 (0,62-0,64)	0,69 (0,68-0,70)
FOBT/colonoscopy	0,51 (0,45-0,58)	0,58 (0,51-0,65)	0,57 (0,50-0,65)
Skin examination	0,70 (0,70-0,71)	0,68 (0,68-0,69)	0,75 (0,74-0,76)

Discussion and conclusions

Because cancer screening is expected to reduce all-cause mortality by only 1-3% *(Stang et al. Dtsch Arztebl Int 2018;115(29-30):481-6)*, the observed lower mortality among screening participants must be due to selection bias.

The extent of selection bias and the amount of adjustment of selection bias differ considerably between tests and examination for the early detection of breast, cervical, prostate, colorectal, and skin cancer screening.

Observational studies evaluating the effectiveness of cancer screening need to apply appropriate methods for controlling selection bias. Controlling only for sex, age, residence, and comorbidity appears to be insufficient.

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