# Cumulative risk of adverse events inside and outside an organized breast cancer screening program

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## INTRODUCTION

- After 10 screening rounds for women aged 50-69 years old, the reported cumulative risk of false-positive mammography (20%-63%) or benign biopsy (2%-19%) were highly variable
- Such adverse effects among participating women are never compared to those in non-pariticpating women although such women can have mammogram or biopsy outside the program

## QUEBEC BREAST CANCER SCREENING PROGRAM

- Established in 1998
- Offers a bilateral mammogram every 2 years for women aged 50 to 69 years
- About 1,200,000 eligible women and 340,000 screening mammograms per year
- Participation rate increases between 2000 and 2013: 42 % to 58 %

## OBJECTIVES

To compare the cumulative risk of having an adverse event (**false-positive mammogram** or **benign biopsy**) over a 20-year periods among women aged 50-69 who were screened every 2 years in the Quebec breast cancer screening program to the cumulative risk among women who did not participate in the program.

## METHODS

### Program participants

**Data sources**

Information system of the program (1998-2006)

Provincial administrative databases (Physician claim's and hospitalizations database , 1998-2006)

| Available informations for women with screening mammogram in the program between 1998 and 2006 (n = 1,267,111) |
|---|
| Age of women |
| Date of screening mammogram in the program |
| Result of mammogram (normal or abnormal) |
| Symptoms (mass, nipple inversion or discharge) |
| Previous mammography (self-reported) |
| Previous biopsy (self-reported) |
| Date of breast cancer diagnostic |
| Date of biopsy (core or open) |

**Statistical model**

$$P(at\ least\ one\ event\ among\ 10\ screening\ rounds) = 1 - \prod_{j=1}^{10} q_j$$

$$q_j = \mathbb{P}\ (round\ j\ with\ no\ event | no\ event\ in\ j-1\ previous\ round)$$

Log-binomial regression is used for smoothing and projecting the probability $q_j$ from observed probability in Quebec Breast Cancer Screening Program.

| Age group | Round 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| 50 – 51 | $q_1$ | × | × | × | × | × | × | × | × | × |
| 52 – 53 | | $q_2$ | × | × | × | × | × | × | × | × |
| 54 – 55 | | | $q_3$ | × | × | × | × | × | × | × |
| 56 – 57 | | | | $q_4$ | × | × | × | × | × | × |
| 58 – 59 | | | | | $q_5$ | × | × | × | × | × |
| 60 – 61 | | | | | | $q_6$ | × | × | × | × |
| 62 – 63 | | | | | | | $q_7$ | × | × | × |
| 64 – 65 | | | | | | | | $q_8$ | × | × |
| 66 – 67 | | | | | | | | | $q_9$ | × |
| 68 – 69 | | | | | | | | | | $q_{10}$ |

Observed probability (Program data, 1998-2006)

Predicted probability by modeling

Factors considered for modeling:
- Round of screening (linear)
- Initial mammogram in the program (yes/no) previous mammography (yes/no)
- Age group (10 groups)
- Year (1998, 1999, …, 2006)
- Previous breast biopsy (for the benign biopsy event)

### Non-participants

**Data sources**

Information system of the program (1998-2003)

Physician claim's database(1987-2003)

Tumor registry (1998-2004)

Death registry (1998-2003)

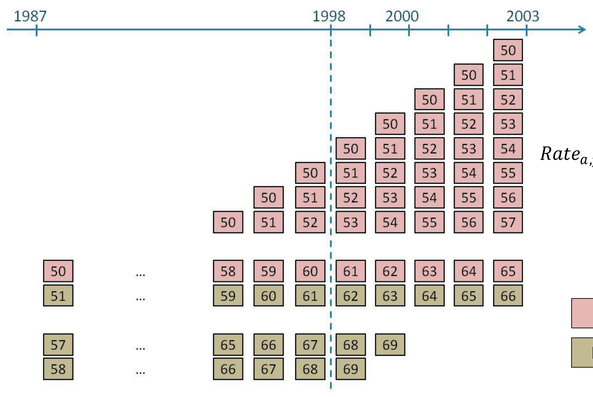
| Available informations for eligible women to the program between 1998 and 2003 (n=1,054,120) |
|---|
| Age of women |
| Date of any medical act related to breasts (imaging, core or open biopsy) |
| Date of screening mammogram in the program |
| Date of breast cancer diagnostic |
| Date of death |

**Statistical model**

$$P(at\ least\ one\ event\ between\ 50\ and\ 69\ years) = 1 - \prod_{a=50}^{69} (1 - p_a)$$

$$p_a = P\ (Event\ at\ age\ a | no\ event\ between\ age\ 50\ and\ a-1)$$ (calculated for the year 2003)

Log-Poisson model is used to smooth the probability from observed data in the non-participants.




Factors considered into modeling:
- Age of women (50, 51,…, 69)
- Calendar years (1998, 1999,…, 2003)

$$Rate_{a,y} = \frac{Number\ of\ women\ with\ the\ first\ event\ at\ age\ a\ and\ year\ y}{Total\ person-years\ at\ risk\ at\ age\ a\ and\ year\ y}$$

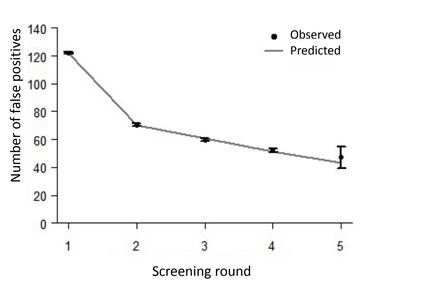
$$P_{a,y} = e^{-Rate_{a,y}}$$

## RESULTS

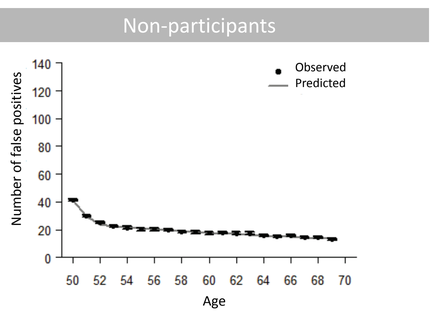
### FALSE POSITIVES

Observed and predicted false positives among 1,000 women

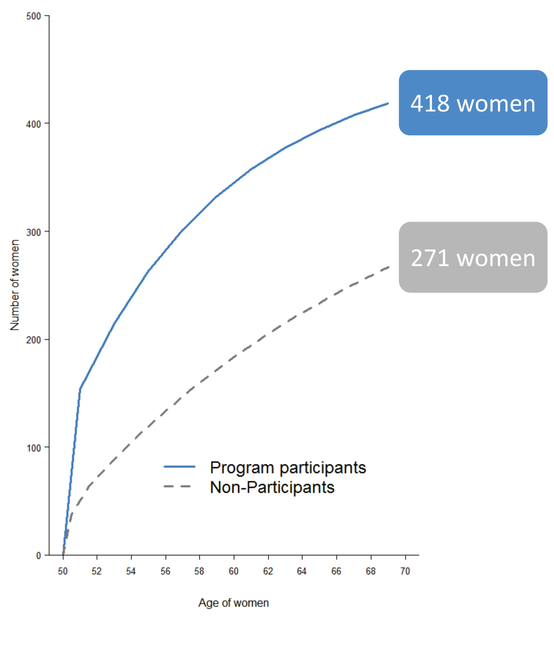
Program participants




Non-participants



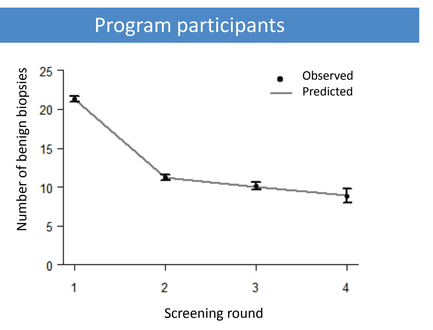

Cumulative number of false positives among 1,000 women



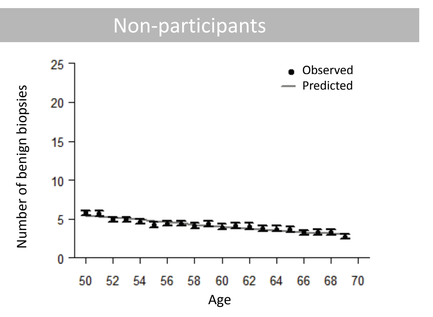

### BENIGN BIOPSIES

Observed and predicted benign biopsies among 1,000 women

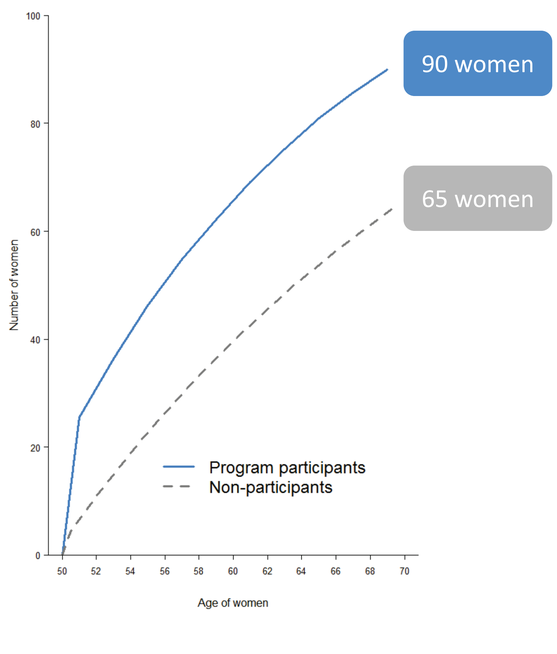
Program participants




Non-participants




Cumulative number of benign biopsies among 1,000 women




## DISCUSSION

- Compared to a hypothetical cohort of 1,000 women who did not participate in the organized screening program, a cohort of 1,000 women who participated in a screening program biennially during 20 years have an excess of 147 women with a false-positive result and an excess of 25 women with a benign biopsy
- Non-participants have a non negligeable risk of false positive mammography or benign biopsy
- Comparing cumulative risk of participants to non-participants allows a better assessment of the absolute excess of these outcomes reported by many screening programs to inform women about harms of participation

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