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ORIGINAL PAPER

Trends in mammography, hormone replacement therapy, and breast cancer incidence and mortality in Canadian women

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Abstract

Purpose The purpose of the study is to examine relationships between long-term trends of region- and age-specific rates of mammography, hormone replacement therapy (HRT), and breast cancer incidence and mortality in Canadian women aged 35 years and older.

Methods Population-based complex surveys were used to estimate mammography use in the past 2 years and ever, and HRT use in the past month. National population-based administrative data were used to estimate breast cancer incidence and mortality. Joinpoint analyses were used to estimate trends in rates and years where trend changed.

Results No consistent relationship between mammography use and breast cancer incidence was observed across age groups. Opportunistic screening occurred prior to the establishment of organized screening programs in Canada and prior to substantial declines in breast cancer mortality observed around 1990. Women aged 35–39 years demonstrated a 62.8% relative decrease in breast cancer mortality between 1950 and 2015 despite lower rates of mammography use in the past 2 years (range 9.4–15.9%) reinforcing important treatment advances. A substantial proportion of women in their 40s report mammography use in the past 2 years (range 35.8–42.2%) and regional variation exists reflecting inconsistencies in guidelines across Canada.

Conclusion Rates of mammography use over time do not necessarily reflect national guideline releases or establishment of organized screening programs.

Keywords Mammography · Hormone replacement therapy · Breast cancer · Incidence · Mortality

Introduction

Breast cancer is the most commonly diagnosed cancer and second leading cause of cancer deaths in Canadian women. One in 8 Canadian females will develop breast cancer in their lifetime and 1 in 31 will die of the disease [1]. To reduce the burden of breast cancer in Canada, mammography screening recommendations were first published in 1979 (Table 1) and organized programs have gradually been introduced (Table 2). Breast cancer screening, hormone replacement therapy (HRT), and other risk factors (e.g., alcohol consumption, obesity, reproductive factors) have been implicated as potential causes for changes in breast cancer incidence over time [8–12] while breast cancer screening and improvements in breast cancer awareness and treatments have all been reported as contributing to the decline in breast cancer mortality [8, 13–19]. Although Canadian studies have examined regional trends in mammography use [20] and the relationship between trends in HRT and breast cancer incidence at the national level [10], no published work to date has examined all three in conjunction with breast cancer mortality at a region- and age-specific level. Our research updates and expands past work by examining the relationships between long-term trends in region- and age-specific rates of mammography, HRT, and breast cancer incidence and mortality in Canadian women aged 35 years and older.

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Table 1 Canadian guidelines for breast cancer screening using mammography, 1979 to 2011

Year	Age group (years)	Guideline
1979	50–59	Good evidence for annual mammography and clinical examination of the breast [2]
1986	40–49	Insufficient evidence to make firm recommendations. Suggest physicians perform annual clinical examinations of the breast on grounds of clinical prudence
	50–59	Good evidence to support the recommendation for annual mammography and clinical examination of the breast
	≥ 60	Fair evidence to support the recommendation for annual mammography and clinical examination of the breast [3]
1994	40–49	Fair evidence to support the recommendation that asymptomatic women be excluded from screening
	50–69	Good evidence to support the recommendation for annual mammography and clinical examination of the breast [4]
2001	40–49	Current evidence regarding the effectiveness of screening mammography does not suggest its inclusion or exclusion from the periodic health examination of women at average risk of breast cancer. At the age of 40 years, women should be informed regarding the potential benefits and risks of screening mammography and assisted in deciding the age to initiate screening mammography [5]
2011	40–49	Recommend not routinely screening with mammography (weak recommendation based on moderate-quality evidence)
	50–69	Recommend routinely screening with mammography every two to three years (weak recommendation based on moderate-quality evidence)
	70–74	Recommend routinely screening with mammography every two to three years (weak recommendation based on low-quality evidence) [6]

Table 2 The introduction of organized breast cancer screening programs in Canada

Region	Year initiated
British Columbia (BC)	1988
Yukon (YT)	1990
Alberta (AB)	1990
Saskatchewan (SK)	1990
Ontario (ON)	1990
Nova Scotia (NS)	1991
Manitoba (MB)	1995
New Brunswick (NB)	1995
Newfoundland and Labrador (NL)	1996
Quebec (QC)	1998
Prince Edward Island (PE)	1998
Northwest Territories (NT)	2003

Canadian Partnership Against Cancer [7]

Nunavut does not have an organized breast cancer screening program but provides limited opportunistic screening

Methods

Data sources

Mammography

Several population-based surveys were used to estimate mammography use over time: Health Promotion Survey (HPS) for 1990, National Population Health Survey (NPHS) for 1994–1995, 1996–1997, and 1998–1999, and Canadian Community Health Survey (CCHS) for 2001 to 2014.

The HPS was a cross-sectional telephone survey of the Canadian provincial household population aged 15 years and older excluding households without telephones (< 3% of the total population) and residents of institutions. The overall survey response rate was 78% (http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3828).

The NPHS was a biennial cross-sectional and longitudinal survey of the Canadian provincial household population aged 12 years and older excluding people living on Indian Reserves and Crown Lands, full-time members of the Canadian forces, and residents of health institutions and some remote regions in Ontario and Quebec. Interviews occurred in-person or by telephone. We used the first three cycles (1994–1995, 1996–1997, and 1998–1999) because in 2000–2001, the survey became strictly longitudinal and the cross-sectional CCHS data were available. Overall response rates for the three cycles were 85.2%, 79.0%, and 86.3%, respectively (http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3225&lang=en&db=imdb&adm=8&dis=2).

The CCHS is a cross-sectional survey of the Canadian household population aged 12 years and older with exclusions similar to the NPHS representing less than 3% of the Canadian population. The CCHS transitioned from a biennial to annual collection cycle in 2007. Interviews are completed in-person or by telephone. The overall response rate has declined over time from 84.7% in the 2001 cycle to 65.6% in the 2014 cycle. The most recent cycles (2015 and 2016) were excluded because of a substantial

redesign (http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3226).

All three surveys asked females, aged 35 years and older, if they had ever had a mammogram and those responding yes were asked regarding recency. Based on responses, two outcomes were defined: ever having a mammogram and having a mammogram within the past 2 years—a time frame used for screening purposes [6]. By necessity, mammography use includes both screening and diagnostic procedures [20].

Hormone replacement therapy (HRT)

HRT use was estimated using a cross-sectional analysis of the NPHS 1994–1995 to 2010–2011 cycles. Women aged 30 years and older were asked if they had taken hormones over the past month for menopause or aging symptoms and, from the 1996–1997 cycle onward, additional questions about type of hormones used were asked. For the 1994–1995 cycle, women were classified as either using or not using HRT. For the 1996–1997 cycle onward, women using estrogen only, progesterone only, both estrogen and progesterone, or not knowing the type of hormone (5.0% of self-reported HRT users) were classified as using HRT and all others as not. The overall response rates for cycles 2000–2001 to 2010–2011 decreased over time from 84.9 to 69.7%. The CCHS was not used to monitor HRT use because of limited capture across regions and over time.

Breast cancer incidence

Statistics Canada's National Cancer Incidence Reporting System (NCIRS) and Canadian Cancer Registry (CCR) were used to estimate breast cancer incidence over time. The NCIRS contains cases diagnosed between 1969 and 1991 while the CCR contains new cases diagnosed since 1992 (http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&lang=en&db=imdb&adm=8&dis=2&SDDS=3207). Both databases are based on data collected from provincial and territorial cancer registries. Estimates for 1992 to 2015 are based on the Nov 2017 CCR tabulation file compiled using International Rules for Multiple Primary Cancers [21]. Between 1969 and 1991, breast cancer was defined using the International Classification of Diseases Ninth Revision (ICD-9) [22] code 174. From 1992 onward, the International Classification of Diseases for Oncology Third Edition [23] was used to extract all invasive tumors (behaviour = 3) with a topography of breast (C50.0 to C50.9), excluding specific histologies (mesothelial 9050–9055, Kaposi sarcoma 9140, and hematopoietic and lymphoid 9590–9992).

Breast cancer mortality

Statistics Canada's Vital Statistics Death Database, an administrative survey collecting demographic and cause of death information on all deaths in Canada from all provincial and territorial vital statistics registries, was used to estimate breast cancer mortality over time (1950 to 2015) (http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&lang=en&db=imdb&adm=8&dis=2&SDDS=3233). Breast cancer deaths were defined as follows: 1950–1957 ICD-6 code 170; 1958–1968 ICD-7 code 170; 1969–1978 ICDA-8 code 174; 1979–1999 ICD-9 code 174; and 2000–2015 ICD-10 code C50 [24].

Population estimates

Population estimates were based on census data adjusted for census net undercoverage [25].

Regional exclusions

Quebec is excluded from all analyses due to lack of data sharing agreements for cancer incidence and mortality data. The territories are excluded due to inconsistent capture of mammography use over time and no capture of HRT use. Consequently, estimates for Canada exclude Quebec and the territories but, for brevity, are hereafter referred to as estimates for Canada.

Analyses

Specific rates

Year-, province-, and age-specific (35–39, 40–49, 50–59, 60–69, 70–79, and 80+ years) rates of mammography and HRT use acknowledged sampling design. We weighted all estimates and, except for the HPS, obtained corresponding variance estimates using balanced repeated replication with the provided replicate weights. For the HPS, variance estimates were obtained using provided approximate sampling variability tables. Year-, province-, and age-specific breast cancer incidence and mortality rates were estimated over time using standard methods [26]. For disclosure control, presented age-specific rates are based on unbiased random rounding of numerators using a base of 5.

Trend analyses

To objectively quantify trends in the actual rates, piecewise exponential functions were fit using a statistical algorithm that identifies the optimal number and location of points where the trend changes (i.e., joinpoints) [27]. The estimated slope(s) from the joinpoint model were used to obtain the

annual percent change (APC) for each segment of the joinpoint model, and the average annual percent change (AAPC) summarized trends over the complete time period. Joinpoint analyses were performed using Joinpoint Regression Program (version 4.2.0.2, June 2015 release) [28] with default settings that preclude the identification of short-term fluctuations. When communicating trend results, we use the terms "increase" or "decrease" when APCs significantly differ from zero ($p < 0.05$) and "stable" when APCs do not significantly differ from zero ($p \geq 0.05$).

Time periods examined using trend analysis vary by outcome and, for mammography use, by region because of optional provincial capture of mammography use after the 2005 cycle. We focus on results for Canada and highlight important regional variations.

Results

Women aged 35–39 years

Rates of breast cancer incidence and mammography use in the past 2 years (range 9.4–15.9%) were stable in Canadian women aged 35 to 39 years (Fig. 1a; Table 3). Breast cancer mortality, however, decreased 0.4% per year between 1950 and 1989 and then decreased 2.9% per year thereafter. Overall, the breast cancer mortality rate decreased 62.8% between 1950 and 2015 (Table 4).

Women aged 40–49 years

In Canadian women aged 40 to 49 years, rates of breast cancer incidence increased 0.2% per year between 1979 and 2015 while rates of mammography use within the past 2 years remained stable between 1990 and 2012, ranging from a low of 35.8% (95% CI 30.9–40.7%) in 1990 to a high of 42.2% (95% CI 39.2–45.1%) in 2008 (Fig. 1b; Table 3). Rates of HRT use were relatively low overall and decreased 13.7% per year between 2000 and 2010 with the majority of the decline actually occurring between 2002 and 2004. After being stable for 18 years, breast cancer mortality rates began to decrease in 1967 with an overall decline of 55.2% between 1950 and 2015 (Table 4).

Excepting BC, in 1990 mammography use in the past 2 years ranged from a low of 24.0% (95% CI 13.9–34.1%) in NL to a high of 34.8% (95% CI 22.4–47.1%) in NB; in BC an estimated 50.2% (95% CI 38.9–61.5%) of women in their 40s reported having a mammogram in the past 2 years. Trends thereafter varied by province: in BC, SK, MB, ON, and NB mammography use was stable; in AB, NS, and NL mammography use rose until 2010, 2003, and 2009, respectively, and then plateaued; and, in PE mammography use has been increasing 2.4% per year since 1990. As of 2012, mammography use within the past 2 years ranged from a low of 30.2% (95% CI 20.4–39.9%) in SK to a high of 59.0% (95% CI 39.3–78.8%) in PE.

Women aged 50–59 years

A few years after Canadian guidelines recommended annual mammography for women aged 50 to 59 years, breast cancer incidence rates increased 1.8% per year until 1999 and then decreased 2.3% per year before plateauing in 2005 (Fig. 1c; Table 3). There was a temporary spike in breast cancer incidence in 2002: the rate increased 6.9% between 2001 and 2002 and then decreased 11.0% between 2002 and 2003. From 1990 to 1998, mammography use within the past 2 years increased 5.0% per year and then declined 0.4% per year. In 1999, the breast cancer incidence rate demonstrated the characteristic peak associated with the stabilization of mammography use. The rate of HRT use decreased 51.9% between 2002 (26.4%, 95% CI 22.1–30.6%) and 2004 (12.7%, 95% CI 9.6–15.7%). Breast cancer mortality rates increased 1.4% per year between 1950 and 1968 before starting a downward decline until 2015. Overall, the mortality rate decreased 50.3% between 1950 and 2015 (Table 4).

Women aged 60–69 years

In Canadian women aged 60 to 69 years, breast cancer incidence rates increased 1.0% per year between 1969 and 1986 (Fig. 1d; Table 3), the year in which annual mammography was recommended for women aged 60 years and older; thereafter, a brief non-significant increasing trend of 5.3% (95% CI −5.5 to 17.2%) was noted until a plateau in 1989. Again, there was a temporary spike in breast cancer incidence in 2002: the rate increased 8.4% between 2001 and 2002 and then decreased 7.8% between 2002 and 2003. Although the rate of mammography use within the past 2 years increased 6.7% per year prior to plateauing in 1998, there was no consistent corresponding rise in breast cancer incidence rates as seen for women aged 50 to 59 years. The rate of HRT use dropped 65.0% between 2002 (24.3%, 95% CI 19.4–29.3%) and 2004 (8.5%, 95% CI 5.9–11.1%). After being stable for 17 years, breast cancer mortality rates increased 0.9% per year between 1966 and 1988, and then decreased by 2.5% per year until 2015. Overall, the mortality rate decreased 39.6% between 1950 and 2015 (Table 4).

Women aged 70–79 years

For Canadian women aged 70 to 79 years, breast cancer incidence rates have oscillated over time: increasing at 3.1% per year between 1980 and 1991; decreasing 1.1% per year between 1991 and 2004; and then increasing again at 0.8% per year to 2015 (Fig. 1e; Table 3). The decline

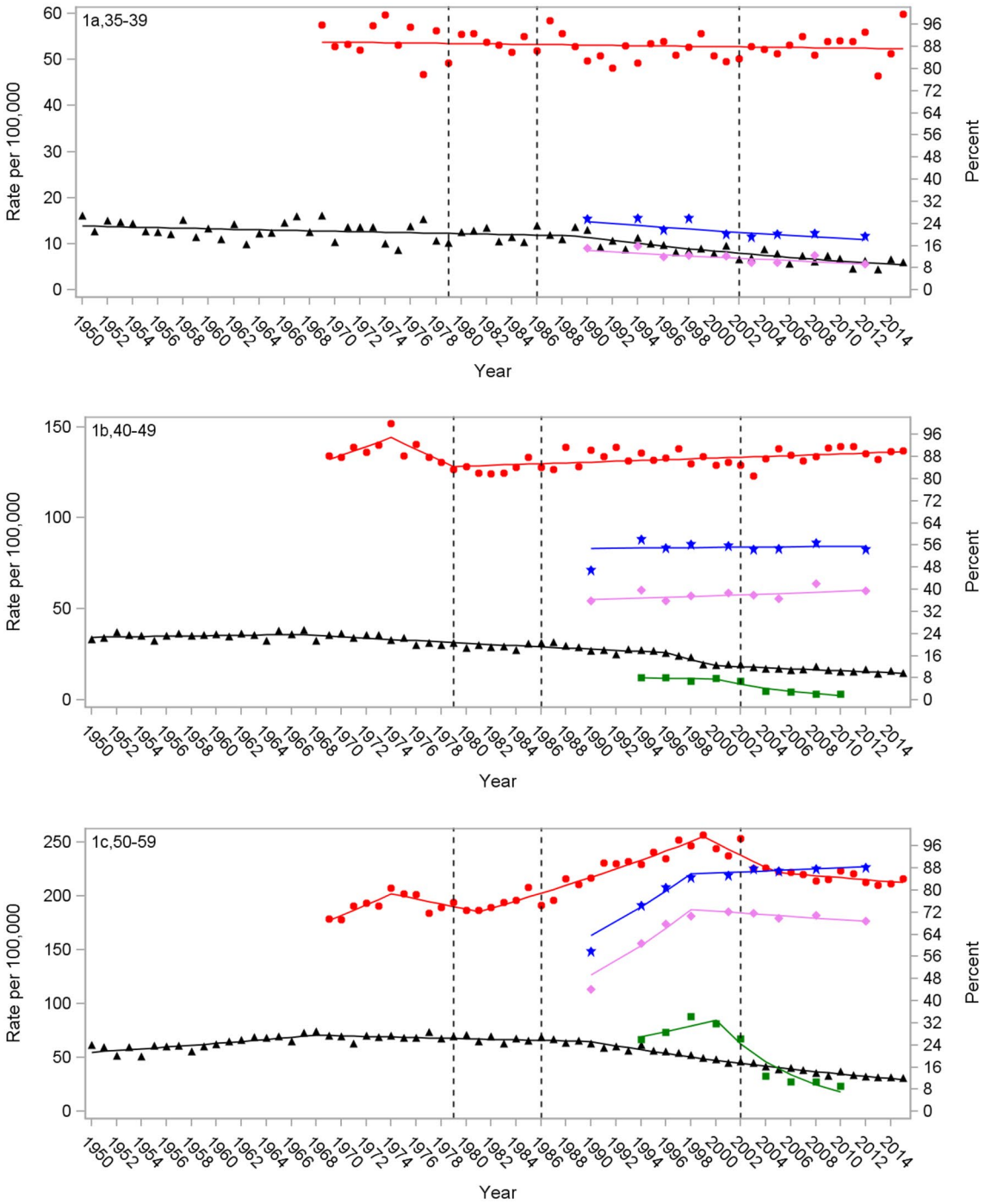

Fig. 1 **a**–**f** Age-specific rates of mammography (%), HRT (%), breast cancer incidence (per 100,000), and breast cancer mortality (per 100,000) for Canadian women (excluding Quebec and the territories). Model estimates are based on joinpoint analysis. Vertical reference lines indicate the release of mammography screening guidelines for women aged 50 to 59 (1979) and 60 to 69 years (1986) and the release of findings from the Women's Health Initiative study (2002) indicating HRT increases the risk of breast cancer [29]. Rates of HRT use were too unstable to report for women aged 35–39, 70–79, and 80+ years. *HRT* hormone replacement therapy. *Source* Mammography use from the Health Promotion Survey (1990), National Population Health Survey (1994 to 1998), and Canadian Community Health Survey (2001 to 2012); HRT use from the National Population Health Survey (1994 to 2010); breast cancer incidence from the National Cancer Incidence Reporting System (1969 to 1991) and Canadian Cancer Registry (1992 to 2015); and breast cancer mortality from the Canadian Vital Statistics Death Database (1950 to 2015)

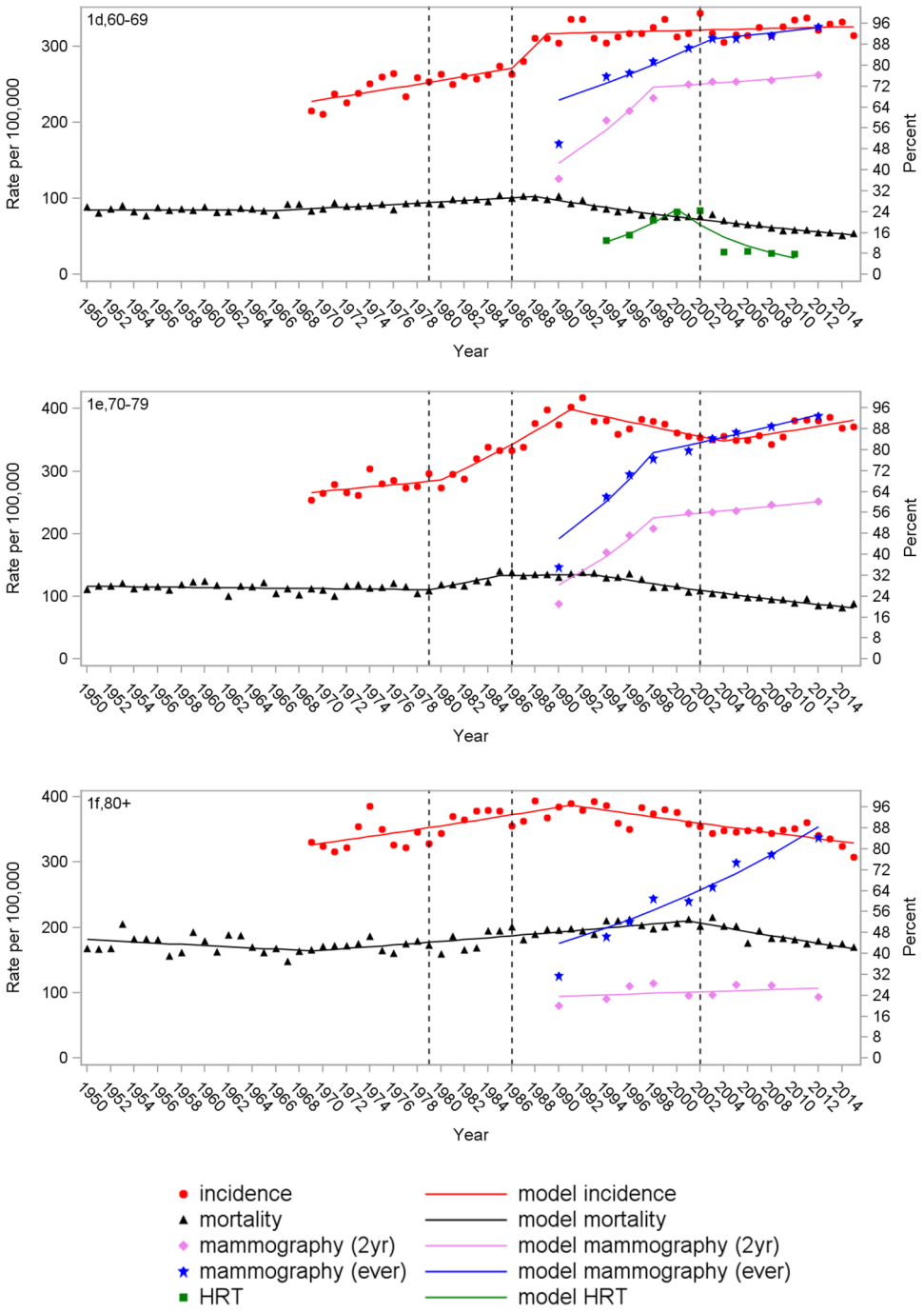

Fig. 1 (continued)

in breast cancer incidence occurred as mammography use in the past 2 years was steeply increasing (8.5% per year). After being stable for 30 years, breast cancer mortality began to increase at 3.2% per year in 1979 and then stabilized between 1985 and 1993 before beginning a downward trend (− 2.3% per year) until 2015.

Women aged 80+ years

In Canadian women aged 80 years and older, breast cancer incidence rates rose 0.8% per year until 1991 and then decreased 0.7% per year until 2015 at which point the breast cancer incidence rate was comparable to that in

Table 3 Trends in mammography, hormone replacement therapy, and breast cancer incidence and mortality rates in Canadian women by age group

Age group	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		Year	AAPC
	Start	APC	Joinpoint	APC	Joinpoint	APC	Joinpoint	APC	Joinpoint	APC		
Mammography use within past 2 years (%)												
35–39	1990	−1.8									1990–2012	−1.8
40–49	1990	0.4									1990–2012	0.4
50–59	1990	5.0*	1998	−0.4*							1990–2012	1.5*
60–69	1990	6.7*	1998	0.5							1990–2012	2.7*
70–79	1990	8.5*	1998	0.8*							1990–2012	3.5*
80+	1990	0.6									1990–2012	0.6
Mammography use ever (%)												
35–39	1990	−1.4*									1990–2012	−1.4*
40–49	1990	0.1									1990–2012	0.1
50–59	1990	3.8*	1998	0.2							1990–2012	1.5*
60–69	1990	2.4*	2003	0.5							1990–2012	1.6*
70–79	1990	7.0	1998	1.2*							1990–2012	3.3*
80+	1990	3.2*									1990–2012	3.2*
Hormone replacement therapy use (%)												
35–39[a]											1994–2010	
40–49	1994	−0.8	2000	−13.7*							1994–2010	−9.1*
50–59	1994	3.4	2000	−14.2*							1994–2010	−8.0*
60–69	1994	12.2	2000	−12.9							1994–2010	−4.2
70–79	1994	13.1	2000	−18.4*							1994–2010	−7.8*
80+[a]											1994–2010	
Breast cancer incidence (per 100,000)[b]												
35–39	1969	−0.1									1969–2015	−0.1
40–49	1969	1.7	1974	−2.3	1979	0.2*					1969–2015	0.1
50–59	1969	2.6*	1974	−1.2	1981	1.8*	1999	−2.3*	2005	−0.4	1969–2015	0.4
60–69	1969	1.0*	1986	5.3	1989	0.1					1969–2015	0.8*
70–79	1969	0.6	1980	3.1*	1991	−1.1*	2004	0.8*			1969–2015	0.8*
80+	1969	0.8*	1991	−0.7*							1969–2015	0.0
Breast cancer mortality (per 100,000)[b]												
35–39	1950	−0.4*	1989	−2.9*							1950–2015	−1.4*
40–49	1950	0.2	1967	−1.1*	1996	−7.6*	2000	−1.7*			1950–2015	−1.3*
50–59	1950	1.4*	1968	−0.4*	1990	−3.1*					1950–2015	−0.9*
60–69	1950	−0.1	1966	0.9*	1988	−2.5*					1950–2015	−0.8*
70–79	1950	−0.2	1979	3.2*	1985	0.1	1993	−2.3*			1950–2015	−0.5*
80+	1950	−0.5	1969	0.8*	2001	−1.6*					1950–2015	−0.1

Mammography use from the Health Promotion Survey (1990), National Population Health Survey (1994 to 1998), and Canadian Community Health Survey (2001 to 2012); hormone replacement therapy use from the National Population Health Survey (1994 to 2010); breast cancer incidence from the National Cancer Incidence Reporting System (1969 to 1991) and Canadian Cancer Registry (1992 to 2015); and breast cancer mortality from the Canadian Vital Statistics Death Database (1950 to 2015)

APC annual percent change, *AAPC* average annual percent change

Excludes Quebec and the territories

[a]Age-specific rates too unstable to perform joinpoint analysis

[b]Joinpoint analysis used actual age-specific rates

*Statistically significant ($p < 0.05$)

Table 4 Long-term changes in age-specific rates of mammography, hormone replacement therapy, and breast cancer incidence and mortality for Canadian women

Age in years						
	35–39	40–49	50–59	60–69	70–79	80+
Mammography use within past 2 years (%)						
1990	15.1 (10.4–19.8)	35.8 (30.9–40.7)	44.3 (38.0–50.5)	36.7 (30.4–43.0)	21.2 (14.8–27.6)	20.0 (15.0–25.0)
2012	9.4 (7.0–11.8)	39.4 (36.2–42.7)	68.9 (66.1–71.7)	76.4 (73.9–78.8)	60.3 (57.6–63.1)	23.5 (20.0–27.1)
%ch[a]	−37.5	10.2	55.7	108.2	184.5	17.6
Mammography use ever (%)						
1990	25.9 (20.5–31.3)	47.1 (42.0–52.2)	57.8 (51.3–64.4)	50.0 (44.1–56.0)	35.0 (28.2–41.8)	31.6 (25.2–37.9)
2012	19.5 (16.2–22.8)	54.6 (51.3–57.9)	88.2 (86.2–90.2)	94.8 (93.8–95.8)	93.1 (91.6–94.6)	84.4 (81.1–87.7)
%ch	−24.6	15.9	52.6	89.4	166.0	167.5
Hormone replacement therapy use (%)						
1994	1.5 (0.7–2.4)	8.0 (6.1–9.9)	26.1 (22.3–29.9)	13.1 (10.2–15.9)	5.3 (3.3–7.4)	X[b]
2010	X	2.3 (1.0–3.5)	9.1 (6.5–11.7)	8.0 (5.3–10.7)	X	X
%ch	–[c]	−71.7	−65.1	−39.0	–	–
Breast cancer incidence rate (per 100,000)						
1969	57.4 (50.5–65.0)	134.0 (126.5–141.9)	178.9 (169.2–189.1)	215.5 (202.7–228.9)	254.3 (237.1–272.5)	330.4 (301.5–361.3)
2015	59.9 (55.0–65.1)	136.7 (131.4–142.1)	216.2 (209.9–222.7)	314.5 (305.8–323.3)	371.2 (359.0–383.7)	308.0 (295.0–321.4)
%ch	4.3	2.0	20.8	45.9	46.0	−6.8
Breast cancer mortality rate (per 100,000)						
1950	16.1 (12.1–21.0)	33.0 (28.4–38.2)	61.5 (54.3–69.2)	88.5 (78.7–99.2)	110.3 (95.7–126.5)	167.5 (137.0–202.7)
2015	6.0 (4.5–7.8)	14.8 (13.1–16.7)	30.6 (28.2–33.1)	53.5 (49.9–57.2)	87.6 (81.7–93.8)	169.7 (160.1–179.7)
%ch	−62.8	−55.2	−50.3	−39.6	−20.6	1.3

Mammography use from the Health Promotion Survey (1990), National Population Health Survey (1994 to 1998), and Canadian Community Health Survey (2001 to 2012); hormone replacement therapy use from the National Population Health Survey (1994 to 2010); breast cancer incidence from the National Cancer Incidence Reporting System (1969 to 1991) and Canadian Cancer Registry (1992 to 2015); and breast cancer mortality from the Canadian Vital Statistics Death Database (1950 to 2015)

Excludes Quebec and the territories

[a]Percent change = (End year estimate − Start year estimate)/(Start year estimate)*100. Percent change was calculated prior to rounding the start and end year estimates

[b]Rate too unstable to report

[c]Not applicable

1969 (Fig. 1f; Tables 3, 4). During the decline in breast cancer incidence, mammography use within the past 2 years remained stable ranging from a low of 20.0% (95% CI 15.0–25.0%) in 1990 to a high of 28.6% (95% CI 21.5–35.7%) in 1998. After being stable for 20 years, breast cancer mortality rates began to increase 0.8% per year in 1969, an APC consistent with increases in breast cancer incidence. In 2001, several years after breast cancer incidence rates started to fall, breast cancer mortality rates began to decrease 1.6% per year. Overall, however, breast cancer mortality has not changed between 1950 and 2015 (Table 4).

Discussion

Several of our results were consistent with previous findings. First, as expected, we found that both breast cancer incidence and mortality rates generally increased with age and that HRT use was highest among women aged 50 to 59 years old (Table 4).

Second, we saw the substantial, sustained decline in HRT use that accompanied the release of findings from the US Women's Health Initiative trial (Fig. 1b–d) [30]. De et al. [10] concluded the drop in Canadian breast cancer incidence after 2002 was associated with the decline in HRT use and the rebound in rates shortly thereafter suggested HRT worked more as a promotor of occult hormone-sensitive breast cancer than as an actual cause of breast cancer. They attributed the spike in breast cancer cases in 2002 to increased mammography screening of women on HRT in light of results from the Women's Health Initiative Study. However, we found that for women aged 50 to 59 years, breast cancer incidence rates had already begun a downward trend in 1999 and, had it not been for the temporary spike in 2002, would have appeared to be unaffected by the release of findings from the Women's Health Initiative Study

(Fig. 1c). This can also be seen, to a lesser extent, among women aged 60 to 69 (Fig. 1d). This downturn in breast cancer incidence rates around 1999 is also noted in US data and has been attributed to a plateau in screening mammography with a consequent decrease in the prevalent pool of undiagnosed breast cancer cases [31]. This is consistent with our findings for women aged 50 to 69 years for whom rates of mammography use within the past 2 years began to slightly decrease or plateau in 1998 (Fig. 1c, d; Table 3). Nonetheless, the more substantial decline in estrogen receptor positive breast tumors associated with the decline in HRT use in the US suggests that both a plateau in rates of mammography use and declines in HRT use contributed to the observed declines in breast cancer incidence [11].

Last, we found that, despite relatively low levels of mammography use, women aged 35 to 39 years demonstrated declines in breast cancer mortality comparable to women of screening age (Table 4) and, for both age groups, the substantial declines coincided with advances in breast cancer treatment, such as the introduction of tamoxifen and adjuvant chemotherapy [15]. These findings have been used to suggest that advances in treatment, not breast cancer screening, are responsible for the breast cancer mortality declines [15], particularly since the substantial declines in routinely collected Canadian mortality statistics (starting in 1989) precede expected declines based on implementation of organized breast cancer screening programs. However, we found substantial proportions of screening-age women reported having had a mammogram as early as 1990—44.3% of women aged 50 to 59 years and 36.7% of women aged 60 to 69 years reported having a mammogram within the past 2 years and 57.8% and 50.0%, respectively, reported ever having a mammogram. Thus, breast cancer screening with mammography was occurring prior to the implementation of organized breast cancer screening programs and prior to the substantial declines noted in breast cancer mortality. Further, the assertion that mammography use had no impact on breast cancer mortality assumes that breast cancer mortality rates would have continued to decrease unabated in the absence of screening [32].

We did not find a consistent relationship between mammography use and breast cancer incidence across age groups. Although women aged 50 to 59 years showed the typical pattern of increasing breast cancer incidence rates with increasing rates of mammography use (Fig. 1c; Table 3), women aged 60 to 79 years did not (Fig. 1d, e; Table 3), reinforcing the importance of additional known risk factors that have changed over time (e.g., age at first pregnancy, decreased parity, obesity, alcohol consumption, physical activity levels, sedentary behaviour, and HRT use). There also exists the possibility that screening programs have shifted breast cancer diagnoses to younger age groups affecting the relationship between mammography and cancer incidence in the older age groups, a high proportion of whom had mammograms in their lifetime.

Our study indicates that self-reported mammography use among screening-age women has substantially increased over time. Between 1990 and 2012, the rate of mammography use within the past 2 years had increased 55.7%, 108.2%, and 184.5% for women in their 50s, 60s, and 70s, respectively. Further, as of 2012, the rate of mammography use within the past 2 years among women in their 50s and 60s had increased to 68.9% and 76.4%, respectively (Table 4), approaching or exceeding the national target of at least 70% screened within the longer time frame of 30 months [7, 33].

Considering that national guidelines have never recommended routine screening for women in their 40s (Table 1), their rate of mammography use was higher than we expected (Fig. 1b). This may be the consequence of inconsistent screening guidelines over time across and within countries [34] resulting in mixed messaging as demonstrated by the observed regional variation across Canada.

Strengths and limitations

To our knowledge, this is the first study to examine long-term, Canadian region- and age-specific trends in breast cancer incidence and mortality alongside mammography and HRT use. Our work provides the most up-to-date summary of how these four indicators have varied over time in relation to each other while acknowledging changing breast cancer screening guidelines and the findings of the Women's Health Initiative Study in regards to HRT use. Nonetheless, several limitations should be acknowledged. First, self-reported mammography and HRT use are vulnerable to error due to non-response, social desirability bias, and poor recall. The overall response rate for the NPHS and CCHS declined over time to less than 70%. Thus, estimates may be biased to the extent that responders systematically differed from non-responders. In regards to accuracy, self-reported estrogen use has been found to substantially agree with physician records [35] and the NPHS enquiring about usage over the past month likely enhanced accuracy. In addition, Canadian research found CCHS-based estimates of mammography use for women aged 50 to 69 years were in close agreement with estimates of mammography use obtained by combining data from the Canadian Breast Cancer Screening Database and provincial ministries of health fee for service billing [36]. The consistency between our and US findings with respect to sustained declines in HRT use and mammography utilization [30, 37] suggests our population-based estimates provide insight into the magnitude and trends of mammography and HRT use in Canadian women.

Second, long-term trends in stage-specific and hormone-receptor-specific breast cancer incidence would have augmented our work but these data elements were only recently

included in the CCR. Last, definitive conclusions regarding relationships between mammography, HRT, and breast cancer incidence and mortality captured at an aggregate level are limited by ecological fallacy and confounding.

Conclusion

Among Canadian women of screening age, rates of mammography use and breast cancer incidence have increased over time while rates of HRT use and breast cancer mortality have declined. No consistent relationship between mammography use and breast cancer incidence was observed across age groups. Rates of mammography use indicated opportunistic screening had begun prior to the implementation of organized breast cancer screening programs in Canada and prior to the substantial declines in breast cancer mortality observed in the late 1980s and early 1990s. Substantial declines in breast cancer mortality have also been experienced by younger women (age 35 to 39 years) with low rates of mammography use reinforcing important treatment advances. Despite the absence of national guidelines recommending routine screening of women in their 40s, a substantial proportion report mammography use within the past 2 years and regional variation exists, reflecting the inconsistency in guidelines within and across countries. Our findings demonstrate how disaggregation by region and age group can impact the relationship between breast cancer surveillance indicators and reinforce the importance of acknowledging confounders, particularly for trends examined over long time periods that capture cohort effects.

Author contributions Both authors contributed to study design, interpretation of results, drafting the manuscript, critical revisions, and approval of the final manuscript. D.Z. performed the analyses.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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