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Defining Menopausal Status in Epidemiologic Studies: A Comparison of Multiple Approaches and their Effects on Breast Cancer Rates

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Abstract

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Ethical Approval: Each registry within the Breast Cancer Surveillance Consortium (BCSC) and the BCSC Statistical Coordinating Center have received institutional review board approval for either active or passive consenting processes or a waiver of consent to enroll participants, link data, and perform analytic studies. All procedures are Health Insurance Portability and Accountability Act compliant, and all registries and the Statistical Coordinating Center have received a Federal Certificate of Confidentiality and other protection for the identities of women, physicians, and facilities who are subjects of this research.

Objectives—Menopausal status is a common covariate in epidemiologic studies. Still, there are no standard definitions for menopausal status using observational data. This study assesses distinctions between menopausal status definitions using commonly collected epidemiologic data, and explores their impact on study outcomes using breast cancer rates as an example.

Study Design—Using survey data from 227 700 women aged 40–64 who received screening mammograms from the Breast Cancer Surveillance Consortium, we classified menopausal status under five different definitions: one complex definition combining multiple variables, two definitions using age as a proxy for menopausal status, one based only on menstrual period status, and one based on age and menstrual period status

Main Outcome Measures—We compared the distribution of menopausal status and menopausal status-specific breast cancer incidence and detection rates across definitions for menopausal status.

Results—Overall, 36% and 29% of women were consistently classified as postmenopausal and premenopausal, respectively, across all definitions. Menopausal status-specific breast cancer incidence and detection rates were similar across definitions. Rates were unchanged when information regarding natural menopause, bilateral oophorectomy, hormone therapy, and timing of last menstrual period were sequentially added to definitions of postmenopausal status.

Conclusions—Distinctions in menopausal status definitions contribute to notable differences in how women are classified, but translate to only slight differences in menopausal status-specific breast cancer rates.

Keywords

menopause; breast cancer; incidence; concordance

1. INTRODUCTION

Given that menopausal status is an important risk factor for breast cancer [1–3], and risk factors for breast cancer differ according to menopausal status [4–7], many breast cancer studies include menopausal status as a covariate of interest. However, determining menopausal status can be complicated: the transition from premenopause to postmenopause is often several years in length, varies in symptomology and duration, and may not be measurable by menstrual patterns in women with a history of hysterectomy or menopausal hormone therapy (HT) use [8–11]. Given these complexities, there is no standardized definition for menopausal status in epidemiologic studies.

Biologically, menopause is defined as the permanent cessation of ovulation, marked by the end of menstruation [8,9]. The menopausal transition is marked by changes in estradiol and follicular stimulating hormone (FSH) levels and in the regularity and length of menstrual cycles [9–11]. Consensus guidelines for staging natural menopausal status developed by the Stages of Reproductive Aging Workshop (STRAW) make use of prospectively collected menstrual diaries and blood specimens, and assessment of physical symptoms to characterize stages in the menopausal transition [9]. Highlighting the complexity of this transition, STRAW describes eight reproductive stages spanning early reproductive years through demise, differentiated by menstrual cyclicality, changes in FSH, and vasomotor symptoms. While STRAW guidelines provide an informative framework, their applicability to population-based studies is limited by the fact that this staging was not intended to apply to women who smoke, have a body mass index >30 kilograms/meters², or have had a hysterectomy. Additionally, in epidemiologic studies, it is rarely feasible to prospectively collect menstrual diaries or serum samples, especially if data collection is retrospective or based on a single questionnaire. Most studies instead define menopausal status as a

dichotomous variable based on current age, time since last menstrual period, history of menopausal surgeries (i.e., hysterectomy, oophorectomy), and HT use, with information collected via self-report or medical record review. Availability of these data elements differs between studies, as does the manner in which they are applied to classify menopausal status. Some studies define menopausal status based on a complex combination of multiple criteria; for example, in the Nurses' Health Study, women are considered postmenopausal if they have not had a menstrual period for >12 months due to natural causes, have had a bilateral oophorectomy, or have had a hysterectomy without bilateral oophorectomy and are aged ≥ 56 (non-smokers) or ≥ 54 (smokers) [12]. Conversely, in the absence of detailed information, some epidemiologic studies consider age alone as a crude proxy for menopausal status (e.g., age <50 / ≥ 50 years) [13].

We undertook an analysis to characterize the distinctions and concordance between epidemiologic definitions of menopausal status using data from the Breast Cancer Surveillance Consortium (BCSC). We also evaluated whether using different definitions for menopausal status resulted in appreciable differences in rates of breast cancer incidence and detection.

2. METHODS

The BCSC is a collaborative effort between seven geographically dispersed mammography registries. Details regarding the BCSC are provided elsewhere [14]. This study was restricted to the four BCSC registries with detailed self-reported information regarding menopausal status: Group Health (western Washington State), the New Hampshire Mammography Network, the San Francisco Mammography Registry, and the Vermont Breast Cancer Surveillance System. Although the list of data elements and the structure of risk factor questionnaires differs somewhat across BCSC registries (<http://breastscreening.cancer.gov/data/elements.html>), all four registries collect information regarding attained age, timing of and reason for cessation of menses (as applicable), current use of hormonal birth control, and current use of HT, through self-administered risk factor questionnaires completed at the time of mammography.

2.1. Study Population

We included women aged 40–64 years who had a screening mammogram at a BCSC facility between 2004–2005. Screening mammograms were identified based on a standard BCSC definition (http://breastscreening.cancer.gov/data/bcsc_data_definitions.pdf), and screening mammograms identified as a woman's first were excluded. If a woman received more than one screening mammogram during the study period, one was randomly selected. Based on these criteria, 252 719 women were eligible for inclusion, of whom 227 700 (90%) had sufficient data to classify menopausal status under all definitions considered and were included in the final analysis.

Each BCSC registry and the Statistical Coordinating Center have received institutional review board approval for active or passive consenting processes or a waiver of consent to enroll participants, link data, and perform analytic studies. All procedures are Health Insurance Portability and Accountability Act compliant, and all registries and the Statistical Coordinating Center have received a Federal Certificate of Confidentiality and other protection for the identities of women, physicians, and facilities who are subjects of this research.

2.2. Menopausal Status Definitions

Five definitions for menopausal status were applied to the study population, including the definition currently used by the BCSC and four simplified definitions. Under the 'complex' definition (currently used by the BCSC), women were hierarchically classified into four categories in the following order: postmenopausal, surgical/other reason for amenorrhea, perimenopausal, or premenopausal (Table 1). Women were considered postmenopausal if they met one or more of the following criteria: 1) age ≥ 55 ; 2) self-report of natural menopause; 3) self-report of surgical menopause involving bilateral oophorectomy; or 4) self-reported current use of HT. Women not meeting these criteria who self-reported a surgical menopause that did not involve bilateral oophorectomy (or for which oophorectomy status is unknown) or who reported some other / unknown reason for cessation of menses were classified in a separate 'surgical/other amenorrhea' category. Women not meeting these criteria were considered perimenopausal if they reported being unsure whether their periods had stopped. Finally, remaining women were considered premenopausal if they self-reported continued menstrual periods or current use of hormonal birth control. For a subset of women, information was available on the number of days since last menstrual period; in the absence of other information to inform menopausal status, women who reported their last menstrual period was ≥ 365 days, 180–364 days, or < 180 days prior were classified as postmenopausal, perimenopausal, or premenopausal, respectively.

In contrast to this complex definition, which requires several detailed data elements, we explored four definitions making use of only two data elements: attained age and self-reported menstrual period status (Table 1). In a 'simplistic' definition, we classified all women as postmenopausal if they reported that their menstrual periods had stopped, regardless of age or reason for cessation of menses; all other women were classified as premenopausal. In two 'age-based' definitions we dichotomized women as postmenopausal or premenopausal according to age cut-offs (≥ 50 / < 50 years, and ≥ 55 / < 55 years). In a fourth 'combined simplistic' definition, we combined information on age and current menstrual period status to classify women as postmenopausal (menstrual periods have stopped or age ≥ 55 years), perimenopausal (age 50–54 and unsure whether menstrual periods have stopped), or premenopausal (age < 55 and menstrual periods have not stopped or age < 50 and unsure whether periods have stopped).

2.3. Mammography Results and Breast Cancer Rates

Breast cancers were identified through linkage with cancer registries and/or pathology databases. A woman was considered to have breast cancer if she was diagnosed with an invasive breast cancer or ductal carcinoma *in situ* within one year of her study mammogram and before her next screening mammogram. We calculated breast cancer incidence rates as the number of women diagnosed with breast cancer during this time interval per 1,000 women. Breast cancer detection rates were calculated as the number of women with positive mammograms who were diagnosed with breast cancer within this time interval per 1,000 women. The mammogram result was considered positive if the Breast Imaging-Reporting and Data System (BI-RADS) assessment was 0, 3 (with a recommendation for immediate follow-up), 4, or 5; mammograms with other BI-RADS assessments were considered negative.

2.4. Statistical Analyses

We cross-tabulated criteria involved in determining menopausal status across age groups, and calculated breast cancer incidence and detection rates by menopausal status for each definition. Additionally, we explored the influence of specific criteria for determining postmenopausal status on breast cancer incidence and detection rates by sequentially adding

qualifying criteria for postmenopausal status. All analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

3. RESULTS

The distributions of study population characteristics are illustrated in Table 2. The majority of the study population was non-Hispanic white (78%) and college-educated (51%). Overall, 57% of women reported their menstrual periods had stopped due to natural menopause (56%) or other reasons (including surgical amenorrhea) (44%). Under the complex definition, 53% (N=119 982) of women were classified as postmenopausal, 7% (n=17 022) as having 'surgical / other amenorrhea', 5% (N=10 749) as perimenopausal, and 35% (N=79 947) as premenopausal (Table 3).

Overall, 36% (N=81 591) of women were consistently classified as postmenopausal and 29% (N=66 186) were consistently classified as premenopausal, regardless of the definition used. Some groups of discrepantly classified women were evident from comparisons between definitions. In particular, 18% (N=15 453) of women aged 40–49 reported their menstrual periods had stopped and were therefore classified as premenopausal under age-based definitions and as postmenopausal under simplistic and combined simplistic definitions. Among women aged 55–64, 5% (N=3,892) reported either that their menstrual periods had not stopped or were unsure whether their periods had stopped and were classified as premenopausal under the simplistic definition but not other definitions. Additionally, 1.4% (N=2,061) of women aged 40–54 reported they were current users of HT but also reported that either their periods had not stopped or were unsure whether their periods had stopped; these women were classified as postmenopausal under the complex but premenopausal under the simplistic definition.

Neither of the age-based classifications nor the simplistic definition included groupings corresponding to the surgical / other amenorrhea or perimenopausal groupings under the complex definition. Among women aged 40–54 who reported their menstrual periods had stopped (N=49 429), 34% (N=17 000) could not be classified as postmenopausal under the complex definition because they reported either a hysterectomy without a bilateral oophorectomy (or with unknown oophorectomy status) (N=3,516), some other surgical amenorrhea (N=4,186), or did not report a natural or surgical menopause as the reason their periods had stopped (N=9,298). Approximately 8% (N=10 749) of women aged 40–54 reported being unsure whether their periods had stopped or that their last period was 180–364 days prior and were classified as perimenopausal under the complex definition; all of these women were classified as premenopausal under the simplistic definition. Including a perimenopausal group under the combined simplistic definition distinguished only some of these women: 46% (N=4,948) of women classified as perimenopausal under the complex definition were classified as premenopausal under the combined simplistic definition.

Breast cancer incidence and detection rates among postmenopausal women were largely unchanged when using the simplistic, combined simplistic, or complex definition, although the number of women classified as postmenopausal varied considerably (Table 4). Rates in postmenopausal women were slightly lower under all three of these definitions as compared to rates using age-based proxies for postmenopausal status.

Premenopausal breast cancer incidence and detection rates were also similar across simplistic, combined simplistic, and complex definitions. Under these definitions, incidence rates in premenopausal women were similar to rates in postmenopausal women. There was especially little distinction between breast cancer detection rates for premenopausal versus postmenopausal women under the simplistic definition.

The sequential addition of qualifying criteria to a definition for postmenopausal status had little impact on breast cancer rates (Table 5). Incidence and detection rates were largely unchanged when information regarding natural menopause, bilateral oophorectomy, current HT use, and timing since last menstrual period were added to age-based definitions of postmenopausal status. Adding age to the qualifying criteria for postmenopausal status had a substantial impact on how many women were classified as postmenopausal, but did not strongly influence breast cancer incidence or detection rates.

4. DISCUSSION

Our results indicate that differences in the criteria used to define menopausal status affect how women are classified as premenopausal or postmenopausal and the distribution of certain characteristics, such as age, within menopausal status groups. These differences did not translate into marked differences in menopausal status-specific breast cancer incidence or detection rates. Within the age range of this analysis, there was little difference between premenopausal versus postmenopausal rates for breast cancer incidence and detection when menopausal status was based solely on whether a woman's menstrual periods had stopped, suggesting that additional information may be necessary to properly discriminate between premenopausal and postmenopausal women.

In a previous study, Morabia and Flandre assessed the overlap and effects of discrepancies between definitions of postmenopausal status based solely on attained age (i.e., age >45, >50, or >55 years) or solely on time since cessation of menses (i.e., >3 months, >12 months, >24 months, or >10 years) [15]. In that study it was reported that menopausal status-specific associations between nulliparity, age at first birth, and breast cancer risk were not appreciably altered by the choice of definition for menopausal status. The authors of that analysis found that, in the absence of menstrual history information, using a cutoff age of 50 to distinguish premenopausal from postmenopausal women offered the highest specificity for the lowest false positivity compared to menstrual history-based definitions. However, the fact that most studies report a later age at menopause among breast cancer cases than controls means that misclassification bias due to the use of an age-based proxy for menopausal status will be differential by case status.

Our results suggest that stratification by age as a proxy for menopausal status offers modest overlap with definitions using comprehensive self-reported epidemiologic data. While comparison to age-based definitions is dependent on the age structure of the study population, 25% of women aged 50–54 were classified as premenopausal under the complex definition used by the BCSC, and 10% of women aged 40–49 were classified as postmenopausal. By comparison, the Study of Women's Health Across the Nation (SWAN) reported that the median age at natural menopause was 51.4 years, where menopausal status was classified using more detailed information on the duration and reasons for cessation of menses [16]. Discordance between definitions of menopausal status noted in this analysis (and the impact of such discordance), however, is likely to vary between populations according to the distribution of factors associated with menopausal status and age at menopause (e.g., age, race/ethnicity). Additionally, small to moderate shifts of women between menopausal status groups may have less impact when the outcome of interest is a rare event (e.g., breast cancer), than might be observed with a more common outcome. Thus, studies with different population structures or outcomes may be more impacted by the choice of definition for menopausal status. We also cannot rule out the possibility that similarities in breast cancer rates across menopausal status groups are the result of extensive misclassification across groups. Furthermore, although it was beyond the scope of this analysis, residual confounding due to misclassification of menopausal status is a practical

concern and the use of different definitions for menopausal status could contribute to differences in effect estimates adjusted for menopausal status.

Certain caveats must be considered when interpreting these findings. We had no gold-standard for determining menopausal status. While it would be preferable to collect prospective data to more accurately stage menopausal status and to distinguish women in various stages of the menopausal transition using clinical criteria (e.g., the STRAW guidelines [9]), the limited scope of our data is consistent with the situation faced by most epidemiologic studies, where menopausal status must be classified based on limited cross-sectional or retrospective self-reported data. Thus, the results of these analyses cannot speak to the validity of different definitions for menopausal status, but do address the impact and trade-offs of using differing levels of detail in menopausal status definitions. These trade-offs are important for studies to consider when deciding how to ascertain menopausal status. Depending on the purpose of the study, a simplistic definition may be sufficient, especially if menopausal status is not a main effect or key covariate, and could save time and resources from collecting more detailed data. Collecting cross-sectional or retrospective information on the duration and variability of menstrual cycles (in addition to the time since last period) and history of vasomotor symptoms may be useful for drawing comparisons to STRAW stages and more finely categorizing stages of menopausal transition. However, such data collection assumes adequate recall of potentially complicated menstrual histories and does not capture the experience of women with surgical menopause or the variability between women in symptomology of the menopausal transition.

While including information on the reason for cessation of menses and type of surgical menopause in the definition for postmenopausal status did not impact breast cancer rates for postmenopausal women, such information does allow for the identification of a subgroup of women who have a distinct risk factor profile: women whose menstrual periods have stopped but who may not be truly postmenopausal (i.e., women with surgical / other amenorrhea). The observation that breast cancer incidence and detection rates were lower in this subgroup of women presents some rationale for distinguishing this subgroup from postmenopausal and premenopausal women. Similarly, breast cancer rates in women classified as perimenopausal under the complex definition were distinct from those for women classified as postmenopausal and premenopausal, suggesting some utility in separately classifying perimenopausal women. However, the usefulness of distinguishing perimenopausal and surgical menopause groups must be weighed against the practicality of collecting the information necessary to make such distinctions, and the potential for bias in that information.

Menopausal status is a key main effect, covariate, and/or stratification factor in many epidemiologic studies of breast cancer and other diseases. Still, the complexity of defining menopausal status contributes to the lack of a standardized definition for this factor in the epidemiologic literature. Differences between studies in how menopausal status is defined raise questions about the comparability of findings based on those classifications. Our results indicate that distinctions in how menopausal status is defined contribute to notable differences in terms of how women are classified, but may translate to only slight differences in menopausal status-specific breast cancer incidence and detection rates. However, since there is no standardized approach to classifying menopausal status in epidemiologic studies, differences in such classification must be considered when comparing results across studies.

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Abbreviations

(STRAW)	Stages of Reproductive Aging Workshop
(BCSC)	Breast Cancer Surveillance Consortium
(HT)	hormone therapy

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TABLE 1

Hierarchical definitions for menopausal status

DEFINITION	MENOPAUSAL STATUS CLASSIFICATION CRITERIA ^a		
	Postmenopausal	Surgical / other amenorrhea	Perimenopausal
Simplistic	Menstrual periods have stopped	<i>ELSE</i> →	Menstrual periods have not stopped OR Not sure whether menstrual periods have stopped
Age-Based			
<50 / ≥50	Age ≥50	<i>ELSE</i> →	Age <50
<55 / ≥55	Age ≥55	<i>ELSE</i> →	Age <55
Combined simplistic	Age ≥55 OR Menstrual periods have stopped	<i>ELSE</i> →	Age <55 AND Menstrual periods have not stopped OR Age <50 AND Not sure whether periods have stopped
Complex ^b	Age ≥55 OR Report of natural menopause OR Both ovaries removed OR Current use of HT OR 365+ days since last menstrual period ^c	<i>ELSE</i> →	Menstrual periods have not stopped OR Current use of birth control hormones OR <180 days since last menstrual period ^c
	Hysterectomy without bilateral oophorectomy OR 'Other' or 'not specified' surgical menopause OR 'Other' response to whether periods have stopped	<i>ELSE</i> →	Not sure whether periods have stopped OR 180–364 days since last menstrual period ^c

^aClassification of menopausal status performed hierarchically, with identification first of women meeting criteria for postmenopausal status, then women meeting criteria for surgical / other amenorrhea, perimenopausal, and premenopausal status, in that order.

^bDefinition currently used by the Breast Cancer Surveillance Consortium

^cTiming of last menstrual period used as a qualifying criteria only when menopausal status cannot be otherwise determined based on other criteria

TABLE 2

Characteristics of women included in this study with a screening mammogram in the Breast Cancer Surveillance Consortium, 2004-2005 (N=227 700)

	N	(%)
Age (years)		
40–44	37 857	17
45–49	49 848	22
50–54	54 512	24
55–59	49 886	22
60–64	35 597	16
Race / ethnicity		
White, non-Hispanic	173 236	78
African-American	6,017	3
Hispanic white	10 704	5
Asian / Pacific Islander	25 119	11
Other	6,288	3
Unknown	6,336	
Education		
Less than high school	11 173	5
High school graduate / GED	39 535	18
Some college	59 201	26
College / post-college graduate	113 675	51
Unknown	4,116	
Status of menstrual periods		
Still having periods	84 120	37
Natural menopause	73 253	32
Surgical / other menopause	57 767	25
Not sure whether periods have stopped	12 560	6
Surgical menopause history		
<i>Bilateral oophorectomy</i>		
Yes	8,854	7
No	93 474	69
Unknown – Surgical menopause	33 924	25
Missing ^a	91 448	
<i>Hysterectomy</i>		
Yes	16 382	14
No	65 123	54
Unknown – Surgical menopause	38 203	32
Missing ^a	107 992	
Days since last menstrual period		
<180	23 070	95
180–364	513	2

	N	(%)
≥365	686	3
Unknown ^b	203 431	
Current hormone therapy use		
Yes	26 013	12
No	190 734	88
Unknown	10 953	
Current hormonal birth control use		
Yes	10 815	5
No	193 586	95
Unknown	23 299	

^aUnknown status largely reflects skip pattern among women not self-reporting a surgical menopause.

^bInformation regarding date of last menstrual period is only collected by two BCSC registries. Unknown status in this variable also reflects skip pattern among women reporting that menstrual periods have not ceased.

TABLE 3

Distribution of criteria used in classification of menopausal status by attained age and menstrual period status^a

Classification per complex definition	Qualifying Criteria ^a	ATTAINED AGE				TOTAL
		Age 55–64	Age 50–54	Age 40–49	TOTAL	
POSTMENOPAUSAL:	TOTAL	85 483	25 736	8 763	119 982	
	Age ≥55 years	85 483	0	0	85 483	
	Natural menopause	49 590	19 475	4 188	73 253	
	Both ovaries removed	5 156	2 217	1 481	8 854	
	Current hormone therapy use	14 461	7 222	4 330	25 653	
	≥365 days since last period ^b	254	106	32	392	
SURGICAL / OTHER						
AMENORRHEA:	TOTAL	0	9 214	7 808	17 022	
	Surgical menopause ^c	0	3 774	3 928	7 702	
	Other / NOS reason periods stopped ^d	0	5 440	3 858	9 298	
PERIMENOPAUSAL:	TOTAL	0	5 801	4 948	10 749	
	Not sure periods have stopped	0	5 763	4 898	10 661	
	180–364 days since last period ^b	0	218	152	370	
PREMENOPAUSAL:	TOTAL	0	13 761	66 186	79 947	
	Still having periods	0	13 761	66 186	79 947	
	Current hormonal birth control use	0	1 027	7 946	8 973	
	<180 days since last period ^b	0	3 683	17 015	20 698	

^aQualifying criteria not mutually exclusive within a menopausal status classification.^bInformation regarding time since last period was available for only a subset of the study population and was used only in the absence of other information to classify menopausal status.^cExcludes women known to have had a bilateral oophorectomy.^dNOS = not otherwise specified.

TABLE 4

Breast cancer incidence and detection rates by menopausal status and definition^a

	Breast Cancer Incidence and Detection Rates (95% Confidence Interval) ^a											
	Postmenopausal		Surgical / Other Amenorrhea		Perimenopausal		Premenopausal					
	Incidence	Detection	Incidence	Detection	Incidence	Detection	Incidence	Detection	Incidence	Detection	Incidence	Detection
Simplestic	[646 total cases / 131,020 women]		N/A	N/A	N/A	N/A	N/A	N/A	[478 total cases / 96,680 women]		4.9 (4.5–5.4)	4.0 (3.6–4.4)
Age-based												
<50 / ≥50 years	[761 total cases / 139,995 women]		N/A	N/A	N/A	N/A	N/A	N/A	[363 total cases / 87,705 women]		4.1 (3.7–4.6)	3.2 (2.8–3.6)
<55 / ≥55 years	[478 total cases / 85,483 women]		N/A	N/A	N/A	N/A	N/A	N/A	[646 total cases / 142,217 women]		4.5 (4.2–4.9)	3.7 (3.3–4.0)
Combined simplistic	[678 total cases / 134,912 women]		N/A	N/A	[32 total cases / 6,155 women]				[414 total cases / 86,633 women]		4.8 (4.3–5.2)	3.8 (3.3–4.2)
Complex	[619 total cases / 119,982 women]		[69 total cases / 17,022 women]		[47 total cases / 10,749 women]				[389 total cases / 79,947 women]		4.9 (4.4–5.3)	3.8 (3.4–4.2)

^aRates per 1000 women. Case counts presented represent total incident cases; detected cases are a subset of these cases.

TABLE 5

Breast cancer incidence and detection rates in postmenopausal women with sequential addition of criteria for postmenopausal status^a

	Sequentially added qualifying criteria for postmenopausal status								
	Exceeds age cut-off	OR	Natural menopause	OR	Both ovaries removed	OR	Current hormone therapy use	OR	≥365 days since last menstrual period
No age criteria									
# Total cases / # Women	N/A		401 / 72 983		436 / 81 948		510 / 96 205		511 / 96 581
Incidence rate	N/A		5.5 (4.9–6.0)		5.3 (4.8–5.8)		5.3 (4.8–5.8)		5.3 (4.8–5.7)
Detection rate	N/A		4.8 (4.3–5.3)		4.7 (4.2–5.2)		4.6 (4.2–5.1)		4.6 (4.2–5.1)
AGE ≥50									
# Total cases / # Women	761 / 139 995		776 / 144 183		781 / 145 659		790 / 148 758		790 / 148 962
Incidence rate	5.4 (5.1–5.8)		5.4 (5.0–5.8)		5.4 (5.0–5.7)		5.3 (4.9–5.7)		5.3 (4.9–5.7)
Detection rate	4.7 (4.4–5.1)		4.7 (4.3–5.0)		4.7 (4.3–5.0)		4.6 (4.3–5.0)		4.6 (4.3–5.0)
AGE ≥55									
# Total cases / # Women	478 / 85 483		578 / 109 146		589 / 112 813		619 / 119 982		620 / 120 276
Incidence rate	5.6 (5.1–6.1)		5.3 (4.9–5.7)		5.2 (4.8–5.6)		5.2 (4.8–5.6)		5.2 (4.8–5.6)
Detection rate	4.9 (4.5–5.4)		4.6 (4.2–5.0)		4.6 (4.2–5.0)		4.5 (4.1–4.9)		4.6 (4.1–4.9)

^aRates per 1000 women.