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RELIABILITY OF SELF-REPORTED DIAGNOSTIC RADIATION HISTORY IN BRCA1/2 MUTATION CARRIERS

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ABSTRACT

We assessed reliability of self-reported diagnostic radiation history in BRCA1/2 mutation carriers with and without breast cancer. Within the frame-work of the HEBON study, 401 BRCA1/2 mutation carriers completed a baseline (1999-2004) and a follow-up questionnaire (2006-2007). Test-retest reliability of self-reported exposure to chest X-rays, fluoroscopies and mammograms was assessed for the entire study population and by case status. Overall proportion agreement on reporting ever/never exposure was good (>75%), while the corresponding kappa coefficients were between 0.40 and 0.75, indicating at least moderate reliability beyond chance. Reliability of number of exposures was also good (>75%). Proportion agreement on reporting age at first mammogram was low (40%) for exact consistency and moderate (60%) for consistency ±1 year. Reliability of age at first mammogram was higher for cases than for unaffected carriers (P<0.001) but this difference disappeared when excluding diagnostic mammograms (P=0.60). In unaffected carriers proportion agreement on age at last mammogram was 50%. In general, the direction of disagreement on all items was equally distributed. More consistent reporting was mainly determined by a younger age at questionnaire completion. In conclusion, inconsistent self-report of diagnostic radiation by BRCA1/2 mutation carriers was mainly non-differential by disease status.

INTRODUCTION

Exposure to low dose ionizing (or: diagnostic) radiation may increase the risk of breast cancer in the general population, especially when exposure occurred at young age[1,2]. Because BRCA mutations are associated with a reduction in DNA repair efficiency[3], it has been hypothesized that BRCA1/2 mutation carriers might experience greater risk of radiation-induced breast cancer. In two recent studies, exposure to chest X-rays, especially at young ages, was associated with an increased breast cancer risk among carriers[4,5], but in two other studies on exposure to mammograms no association was observed[6,7]. However, these results must be interpreted with caution since the studies relied on self-reported diagnostic radiation history and had a retrospective design (with potential recall and/or survival bias). In the Netherlands, carriers are currently recommended to start breast cancer screening by MRI from age 25 and mammography from age 30 onwards[8], but in the past carriers may have started mammographic screening at younger ages[6,7].

Both retrospective and prospective studies rely on self-reports rather than medical record review because of the time and cost constraints of medical record abstraction as well as the difficulties in assessing diagnostic radiation history from medical records, especially for exposures that occurred during childhood or in the distant past[9]. It is important to investigate the accuracy of self-reported diagnostic radiation histories. In retrospective studies inaccuracy may lead to non-differential and/or differential misclassification which would affect the risk estimates in an epidemiological study.

A number of studies on reliability[10-16] and validity[9,17-19] of self-reported diagnostic radiation exposure in the general population have been conducted. Test-retest reliability varies within the measure of self-reported mammography[10-16] and consistency of reporting lifetime number of mammograms decreases with increasing number of exposures[11,12]. Differences in accuracy of self-reported diagnostic radiation history between affected and unaffected women were so far only investigated in a few validation studies[17,18,20]. Although these studies showed a certain amount of disagreement between self-reports and medical records, there were no differences in disagreement between cases and controls (non-differential misclassification).

This is the first study investigating reliability of self-reported diagnostic radiation exposure at young ages in BRCA1/2 mutation carriers. Based on their positive family history, associated cancer screens, and DNA testing in a clinical setting, these women are probably more health conscious than the general population, regardless of whether they had breast cancer or not. Furthermore, because of their high-risk status, their exposure to diagnostic radiation is relatively high since they are screened more intensively from a relatively young age onwards.

METHODS

STUDY POPULATION

This study on reliability of self-reported diagnostic radiation history among BRCA1/2 mutation carriers was conducted within the framework of the HEBON study, of which the design was described earlier[21]. In brief, the HEBON study is an ongoing nationwide retrospective cohort study with prospective follow-up among members of BRCA1/2 families in the Netherlands. For the present study, woman were eligible if they (a) carried a BRCA1 or BRCA2 mutation; (b) had no personal history of breast and/or ovarian cancer on January 1, 1960, or born after 1960; and (c) were at age 18 or older at study entry. Figure 1 depicts the identification of the study population for the present study. Between 1999 and 2004, 524 BRCA1/2 mutation carriers completed a baseline risk factor questionnaire and were eligible for a follow-up questionnaire in 2006-2007. Hundred carriers could not be invited for the follow-up questionnaire, mainly because they had died during follow-up period (7%) or indicated at baseline that they did not want to be invited again (9%). Of the 476 carriers (45% affected with breast cancer) invited for the follow-up study, 401 responded (84%). Thirteen carriers were diagnosed with a primary invasive breast cancer in the period between baseline and follow-up. Since this event might have influenced reporting in the follow-up questionnaire, and the number of incident cases was too small for a subgroup analysis, we excluded them from the analysis. Thus, information from 388 carriers (167 prevalent breast cancer cases) was used for the reliability analysis.

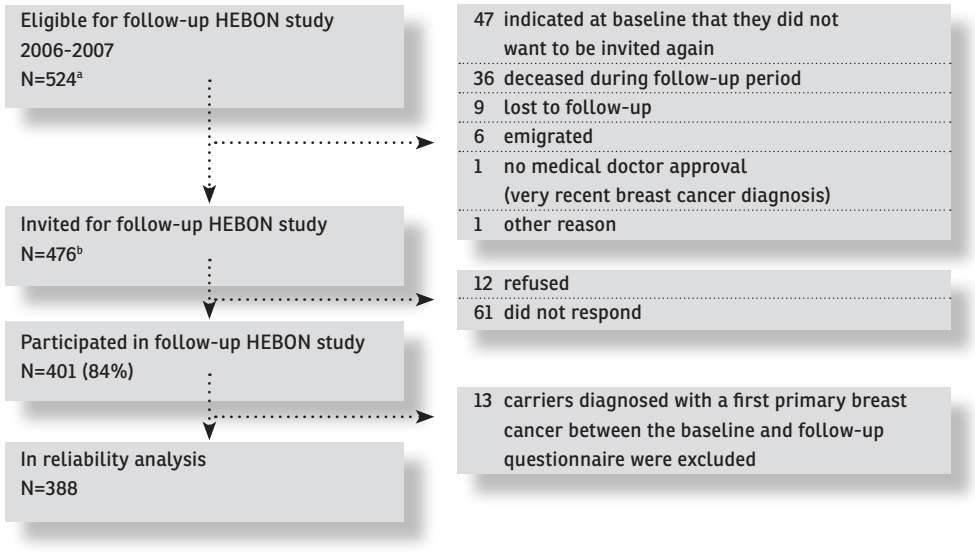

FIGURE 1. Identification of the study population (N=401)

a Carriers registered at 7/8 Clinical Genetic Centres

b Includes 52 carriers from 1 centre invited through other Clinical Genetic Centres

DATA COLLECTION

In the baseline questionnaire, assessment of diagnostic radiation exposure was based on the following questions: ever/never having had a chest X-ray before age 20, fluoroscopy for tuberculosis (TB) (screening), and/or mammogram. For fluoroscopies and mammograms the age at first exposure was asked (and for mammograms also the age at last exposure). Number of exposures was reported in categories (fluoroscopies and chest X-rays before age 20: 1-3, 4-6, 7-9, 10 or more; mammograms before age 30: 1-2, 3-4, more than 4; lifetime number of mammograms: 1-4, 5-10, more than 10).

The follow-up questionnaire contained indication-based questions on lifetime diagnostic and therapeutic radiation exposure (fluoroscopies, chest X-rays, CT-scans, mammograms, radiotherapy, and other radiographic procedures using ionizing radiation like DXA scans). For fluoroscopies, chest X-rays, and mammograms the age at first and last exposure were reported, as well as the exact number of exposures before age 20, between age 20 and 29, and between age 30 and 39. For mammograms, the lifetime number was also asked in categories (1-3, 4-6, 7-9, 10 or more).

Informed consent was obtained from each subject. Information on cancer history and prophylactic surgeries was either collected through the Netherlands Pathology Database (PALGA)[22] and the Netherlands Cancer Registry (NCR) until August 2007 and/or self-reported for the period not covered by the registries (<1989). Ninety-six percent of breast cancers diagnosed after 1988 were confirmed by PALGA/NCR.

STATISTICAL ANALYSIS

Reliability was assessed by proportion agreement and Cohen's kappa coefficient (κ), which accounts for the effect of chance agreement. Reliability was considered poor if $\kappa \leq 0.40$, moderate if $0.40 \geq \kappa \leq 0.75$, and excellent if $\kappa > 0.75$[23]. We also investigated the direction of disagreement, i.e. under- and/or overreporting of exposure in one questionnaire versus the other.

Self-reported exposure to chest X-rays before age 20, fluoroscopies before age 30, mammograms before age 30, and mammograms lifetime was compared between the baseline and the follow-up questionnaire in the entire study population and in prevalent cases and unaffected carriers separately. First, reliability of ever/never exposure was assessed. Then, among women who reported to have been exposed in both questionnaires, reliability of age at first exposure (fluoroscopies before age 30, mammograms before age 30, and mammograms lifetime) and number of exposures (chest X-rays before age 20, fluoroscopies before age 30, and mammograms before age 30) was assessed. In the baseline questionnaire, number of exposures was reported in categories, while in the follow-up questionnaire the exact number was reported. We examined if the exact number fitted the indicated category. For reliability analysis of mammogram exposure, we excluded 13 carriers who had received their first mammogram after the baseline questionnaire.

In affected carriers lifetime exposure to diagnostic radiation was for a large part due to their breast cancer diagnosis. Such exposures are not taken into account in an epidemiological study of diagnostic radiation exposure and breast cancer risk.

Therefore, we also assessed reliability of prediagnostic mammograms by excluding all mammograms that occurred in the year before breast cancer diagnosis and thereafter. For number of mammograms before age 40 and age at last mammogram, the pre- and postdiagnostic period could not be distinguished. Therefore, reliability of these measures was assessed in unaffected carriers only. For the reliability analysis of age at last mammogram, women who had their last mammogram (as reported in follow-up questionnaire) after baseline questionnaire completion were excluded.

Multivariate logistic regression was used to find predictors of inconsistent self-reporting of diagnostic radiation exposures. The dependent variable in this model was disagreement (no/yes) with agreement as the reference category. The following potential determinants were examined: case status, age at questionnaire completion, number of years between baseline and follow-up questionnaire completion, educational level, nulliparity, having had prophylactic surgery (risk reducing mastectomy (RRM) and/or bilateral prophylactic (salpingo-) oophorectomy (BPSO), and menopausal status. For disagreement on the age at first mammogram we also examined the reason for the first mammogram, lifetime number of mammograms, and length of recall (age at questionnaire minus age at first mammogram).

Differences in proportion agreement and other discrete variables between prevalent cases and unaffected carriers were examined by Pearson's $\chi 2$ test. Differences in continuous variables were examined by Student's t-test. Two-sided P-values ≤ 0.05 were considered statistically significant. Missing values were excluded from reliability analysis. All analyses were performed using STATA/SE 10.0 (StataCorp LP).

RESULTS

The general characteristics of the study population are summarized in Table 1. The age (mean ± standard deviation) at baseline questionnaire completion was 43.9 ± 12.2 years. Prevalent cases were older at questionnaire completion than unaffected carriers

TABLE 1. Characteristics of the study population (N=388)

	Total (N=388)		Prevalent cases (N=167)		Unaffected (N=221)	
Characteristic	**N**	**%**	**N**	**%**	**N**	**%**
Nulliparous	100	26%	38	23%	62	28%
Postmenopausal						
At baseline questionnaire	248	64%	140	84%	108	49%
At follow-up questionnaire	301	78%	155	93%	146	66%
Ever RRM	203	52%	89[a]	53%	114	52%
Ever BPSO	260	67%	130[b]	78%	130	59%
Educational level[c]						
Low	157	41%	83	50%	74	34%
Medium	133	34%	44	27%	89	40%
High	97	25%	39	23%	58	26%

RRM, risk reducing mastectomy; BPSO, bilateral prophylactic (salpingo-) oophorectomy

a All after breast cancer diagnosis

b 5/130 Before breast cancer diagnosis

c Low, primary school; medium, secondary school; high, college or university

(48.5 ± 10.4 and 40.5 ± 12.4 years, respectively; P<0.001) and they had a lower educational level (P<0.05). Mean time between questionnaires was 5.4 ± 0.8 years, and there was no difference between cases and unaffected carriers (P=0.731).

The current study population did not differ substantially from the eligible group in general characteristics like age, parity, oral contraceptive use, and menopausal status (data not shown).

Tables 2 and 3 show the results of the reliability analysis on reporting chest X-rays before age 20, and fluoroscopies and mammograms before age 30. Overall proportions agreement on ever/never chest X-rays exposure before age 20 and fluoroscopies and mammograms before age 30 were 79, 77 and 90%, respectively. Disagreement tended to involve a change from 'ever' in the baseline questionnaire to 'never' in the follow-up questionnaire rather than vice versa for chest X-rays and fluoroscopies, but not for mammograms. Prevalent cases had a significantly lower agreement (of ~10%) for ever/never fluoroscopy before age 30 than unaffected carriers (P=0.043), while there were no differences in the direction of disagreement (P=0.512). For all items on ever/never exposure the kappa was moderate, except for ever/never chest X-rays before age 20 in unaffected carriers where it was poor (0.34). Agreement on age at first fluoroscopy exposure was poor (43%) and kappa was just below moderate (0.39), and this was similar for prevalent cases and unaffected carriers (P=0.637). The mean age at first fluoroscopy was 16.4 ± 5.3 years in the baseline and 16.0 ± 5.5 years in the follow-up questionnaire, respectively; there were no differences between prevalent cases and unaffected carriers (P=0.444 and P=0.771 for baseline and follow-up questionnaire comparison, respectively). Reliability of age at first mammogram before age 30 was lower for unaffected carriers than for prevalent cases (P=0.030), but for cases this analysis included diagnostic mammograms. For consistency within 1 year, agreement improved to 81% and the difference in agreement between prevalent cases and unaffected disappeared (P=0.375). For both age at first fluoroscopy and age at first mammogram before age 30, the direction of disagreement was equally distributed and not different between prevalent cases and unaffected carriers (P=0.340 and P=0.650, respectively). Agreement on number of exposures for all three diagnostic procedures was good (>70%) and no differences between prevalent cases and unaffected carriers were found. However, for number of chest X-rays and mammograms kappa was poor (0.26 and 0.35), and for number of fluoroscopies kappa was moderate (0.46). For number of fluoroscopies and mammograms before age 30 kappa was higher in prevalent cases than in unaffected carriers. For all items on number of exposures, the direction of disagreement was equally distributed and not different between prevalent cases and unaffected carriers. The size of disagreement on number of exposures was generally small, e.g. for all women who disagreed on number of mammograms before age 30, the difference in number was between 1 and 4 exposures (Table 4).

TABLE 2. Comparison of self-reported exposure to chest X-rays before age 20 and fluoroscopies before age 30 between baseline and follow-up questionnaire for the entire study population (N=388) and for prevalent cases (N=167) and unaffected carriers (N=221) separately

	Total (N=388)		Prevalent cases (N=167)		Unaffected (N=221)		
	N	%	N	%	N	%	P*
Chest X-rays < 20							
Ever/never							
(baseline/follow-up)							
never / never	250	67%	101	64%	149	70%	
never / ever	27	7%	10	6%	17	8%	
ever / never	50	13%	22	14%	28	13%	
ever / ever	45	12%	25	16%	20	9%	
Agreement (%)	*79.3%*		*79.8%*		*79.0%*		*0.855*
Kappa	*0.41*		*0.48*		*0.34*		
No. of exposures[a]							
(baseline/follow-up)							
1-3 / 1-3	28	65%	15	65%	13	65%	
1-3 / >3	6	14%	3	13%	3	15%	
>3 / 1-3	5	12%	3	13%	2	10%	
>3 / >3	4	9%	2	9%	2	10%	
Agreement (%)	*74.4%*		*73.9%*		*75.0%*		*0.692*
Kappa	*0.26*		*0.23*		*0.29*		
Fluoroscopy for TB < 30							
Ever/never							
(baseline/follow-up)							
never / never	185	48%	58	38%	127	61%	
never / ever	12	4%	8	5%	4	2%	
ever / never	71	20%	35	23%	36	17%	
ever / ever	90	28%	50	33%	40	19%	
Agreement (%)	*76.8%*		*71.5%*		*80.7%*		*0.043*
Kappa	*0.52*		*0.45*		*0.54*		
Age at first[a]							
equal	23	43%	13	46%	10	40%	
baseline<follow-up	13	25%	8	29%	5	20%	
baseline>follow-up	17	32%	7	25%	10	40%	
Agreement (%)	*43.4%*		*46.4%*		*40.0%*		*0.637*
Kappa	*0.39*		*0.42*		*0.35*		
No. of exposures[a,b]							
(baseline/follow-up)							
1-3 / 1-3	32	46%	14	36%	18	60%	
1-3 / >3	9	13%	4	10%	5	17%	
>3 / 1-3	9	13%	6	15%	3	10%	
>3 / >3	19	28%	15	38%	4	13%	
Agreement (%)	*73.9%*		*74.4%*		*73.3%*		*0.907*
Kappa	*0.46*		*0.49*		*0.32*		

TB, tuberculosis (screening)

* P-value of Pearson's $\chi 2$ test difference in proportion agreement between prevalent cases and unaffected carriers

a Reliability analysis in women who reported to ever have been exposed in both baseline and follow-up questionnaire. The numbers in the categories of age at first exposure and number of exposures do not always add up to 100% of ever/ever group due to missing values

b The number of exposures before age 30 reported in baseline questionnaire was based on the reported lifetime number of exposures, assuming that the majority had occurred before the age of 30

TABLE 3. Comparison of self-reported mammograms before age 30 between baseline and follow-up questionnaire for the entire study population (N=388) and for prevalent cases (N=167) and unaffected carriers (N=221) separately

	Total (N=388)		Prevalent cases (N=167)		Unaffected (N=221)		
	N	%	N	%	N	%	P*
All mammograms < 30							
Ever/never							
(baseline/follow-up)							
never / never	251	67%	132	80%	119	59%	
never / ever	13	4%	7	4%	6	3%	
ever / never	24	7%	7	4%	17	8%	
ever / ever	78	21%	18[a]	11%	60	30%	
Agreement (%)	*89.9%*		*91.5%*		*88.6%*		*0.368*
Kappa	*0.74*		*0.67*		*0.75*		
Age at first[b]							
equal	39	53%	13	76%	26	46%	
baseline<follow-up	13	18%	3	18%	10	18%	
baseline>follow-up	21	29%	1	6%	20	36%	
Agreement (%)	*53.4%*		*76.5%*		*46.4%*		*0.030*
Kappa	*0.48*		*0.71*		*0.40*		
Agreement ± 1 year (%)	*80.8%*		*88.2%*		*78.6%*		*0.375*
No. of exposures[b,c]							
(baseline/follow-up)							
1-2 / 1-2	9	20%	6	38%	3	11%	
1-2 / >2	6	14%	2	13%	4	14%	
>2 / 1-2	7	16%	2	13%	5	18%	
>2 / >2	22	50%	6	38%	16	57%	
Agreement (%)	*70.5%*		*75.0%*		*67.9%*		*0.617*
Kappa	*0.35*		*0.50*		*0.18*		

* P-value of Pearson's $\chi 2$ test difference in proportion agreement between prevalent cases and unaffected carriers

a Includes 13 women with breast cancer diagnosis before age 30

b Reliability analysis in women who reported to ever had a mammogram before age 30 in baseline and follow-up questionnaire. The numbers in the categories of age at first mammogram and number of mammograms do not always add up to 100% of ever/ever group due to missing values

c Women who were <30 years at baseline questionnaire completion were excluded (n=35).

TABLE 4. Comparison of self-reported number of mammograms before age 30 between baseline and follow-up questionnaire (N=49)

		Follow-up questionnaire												
		1	2	3	4	5	6	7	8	9	10	>10	missing	*Total*
Baseline	1-2	6	3	3	1	2	0	0	0	0	0	0	3	*18*
questionnaire	3-4	2	3	2	6	2	2	0	1	0	0	0	1	*19*
	>4	0	2	3	0	0	1	0	1	1	0	3	0	*11*
	missing	0	0	1	0	0	0	0	0	0	0	0	0	*1*
	Total	*8*	*8*	*9*	*7*	*4*	*3*	*0*	*2*	*1*	*0*	*3*	*4*	*49*

Reliability of lifetime exposure to mammograms was assessed for all mammograms lifetime (including diagnostic) and for prediagnostic mammograms only, separately (Table 5). Reliability of ever/never mammograms was excellent, however, the categories were hardly discriminant. Among women who reported to have ever had a mammogram in both questionnaires, the mean age at first mammogram was 35.4 ± 9.3 years in the baseline and 36.0 ± 9.6 years in the follow-up questionnaire, respectively (data not shown). Reliability of age at first mammogram lifetime was significantly poorer for unaffected carriers than for prevalent cases (P<0.001). However, when diagnostic mammograms were excluded, reliability of age at first prediagnostic mammogram was poor in prevalent cases as well, and no longer significantly different from unaffected carriers (agreement 39% and kappa 0.36, P=0.599). The difference in age at first prediagnostic mammogram (age reported in follow-up questionnaire minus age reported in baseline questionnaire) for all women ranged from -11 to +24 years (median -1 year; mean down 2.6 ± 2.1 years; mean up 4.2 ± 4.7 years). In 53/147 (36%) carriers who reported an inconsistent age at first prediagnostic mammogram, the difference in age was only 1 year (43% of carriers differed >2 years and 14% >5 years). For consistency within 1 year, reliability of age at first prediagnostic mammogram increased to moderate (59%) for both prevalent cases and unaffected carriers (P=0.767), and for all mammograms reliability increased to moderate for unaffected carriers and good for prevalent cases (P=0.004). The direction of disagreement on age at first mammogram lifetime was equally distributed, although prevalent cases reported more often a younger age at first (prediagnostic) mammogram in the follow-up questionnaire than in the baseline questionnaire; however, this was not significantly different from unaffected carriers (P=0.326).

Among unaffected carriers (data not shown), agreement on number of mammograms before age 40 was good (81%) and kappa was moderate (0.57). Agreement on age at last mammogram before baseline was 50% and kappa was moderate (0.48). For both items, there were no differences in the direction of disagreement.

We examined determinants of inconsistent reporting of age at first prediagnostic mammogram lifetime (consistency within 1 year) and ever/never exposure to fluoroscopies before age 30 (Table 6). In univariate analysis, the chance of disagreement on age at first mammogram was 4% higher per additional year of age at questionnaire completion (Odds Ratio (OR)=1.04, 95%CI=1.01-1.06), higher for postmenopausal women (OR=1.71, 95%CI=1.00-2.98) and lower when the reason for the first mammogram was having complaints (OR=0.58, 95%CI=0.32-1.06). Unexpectedly, increased time between questionnaires was associated with lower chance of disagreement (OR=0.70, 95%CI=0.50-0.90). Disagreement on ever/never having had a fluoroscopy before age 30 was determined by case status and age at questionnaire completion. However, in the multivariate model of both items, there were no significant associations between any of the potential predictors and the chance of disagreement, although age at questionnaire completion remained a marginally significant determinant of disagreement.

TABLE 5. Comparison of self-reported mammograms lifetime between baseline and follow-up questionnaire for the entire study population (N=388) and for prevalent cases (N=167) and unaffected carriers (N=221) separately

	Total (N=388)		Prevalent cases (N=167)		Unaffected (N=221)		
	N	%	N	%	N	%	P*
All mammograms							
Ever/never							
(baseline/follow-up)							
never / never	6	2%	0	0%	6	3%	
never / ever	2	<1%	2	1%	0	0%	
ever / never	2	<1%	1	<1%	1	<1%	
ever / ever	365	97%	164	98%	201	97%	
Agreement (%)	*98.9%*		*98.2%*		*99.5%*		*0.218*
Kappa	*0.74*		-		*0.92*		
Age at first[a] - exact agreement							
equal	148	44%	84	55%	64	35%	
baseline<follow-up	91	27%	32	21%	59	32%	
baseline>follow-up	96	29%	36	24%	60	33%	
Agreement (%)	*44.2%*		*55.3%*		*35.0%*		*<0.001*
Kappa	*0.42*		*0.53*		*0.33*		
Age at first[a] - agreement ± 1 year							
equal	219	65%	112	74%	107	58%	
baseline<follow-up	63	19%	22	14%	41	22%	
baseline>follow-up	53	16%	18	12%	35	19%	
Agreement (%)	*65.4%*		*73.7%*		*58.5%*		*0.004*
Kappa	*0.64*		*0.73*		*0.57*		
Prediagnostic mammograms							
Ever/never							
(baseline/follow-up)							
never / never	95	26%	89	57%	6	3%	
never / ever	6	2%	6	4%	0	0%	
ever / never	15	4%	14	9%	1	<1%	
ever / ever	247	68%	46	30%	201	96%	
Agreement (%)	*94.2%*		*87.1%*		*99.5%*		*<0.001*
Kappa	*0.86*		*0.72*		*0.92*		
Age at first[a] - exact agreement							
equal	82	36%	18	39%	64	35%	
baseline<follow-up	70	31%	11	24%	59	32%	
baseline>follow-up	77	33%	17	37%	60	33%	
Agreement (%)	*35.8%*		*39.1%*		*35.0%*		*0.599*
Kappa	*0.34*		*0.36*		*0.33*		
Age at first[a] - agreement ± 1 year							
equal	135	59%	28	61%	107	58%	
baseline<follow-up	48	21%	7	15%	41	22%	
baseline>follow-up	46	20%	11	24%	35	19%	
Agreement (%)	*59.0%*		*60.9%*		*58.5%*		*0.767*
Kappa	*0.58*		*0.59*		*0.57*		

* P-value of Pearson's $\chi 2$ test difference in proportion agreement between prevalent cases and unaffected carriers

a Reliability analysis in women who reported to ever had a mammogram before age 30 in baseline and follow-up questionnaire. The numbers in the categories of age at first mammograms do not always add up to 100% of ever/ever group due to missing values

TABLE 6. Estimated Odds Ratios (95%CI) for disagreement on age at first mammogram lifetime and ever/never exposure to fluoroscopies before age 30

	Age at 1st mammogram lifetime[a]		Ever/never exposure to fluoroscopies before age 30	
	N=229		N=358	
Potential determinants of disagreement	**Univariate OR (95%CI)**	**Adjusted OR[b] (95%CI)**	**Univariate OR (95%CI)**	**Adjusted OR[b] (95%CI)**
Case status (unaffected vs. prevalent case)	1.10 (0.57 – 2.14)	1.44 (0.67 – 3.11)	0.60 (0.37 – 0.99)	0.52 (0.26 – 1.05)
Age at follow-up questionnaire (per year)	1.04 (1.01 – 1.06)	1.03 (0.98 – 1.08)	1.02 (1.00 – 1.04)	1.01 (0.97 – 1.04)
Time between questionnaires (per year)	0.70 (0.50 – 0.90)	0.76 (0.53 – 1.10)	0.92 (0.67 – 1.26)	0.95 (0.70 – 1.31)
Educational level (high vs. low)	0.88 (0.45 – 1.72)	1.16 (0.55 – 2.44)	0.96 (0.70 – 1.30)	1.04 (0.75 – 1.43)
Nulliparous (yes vs. no)	0.71 (0.37 – 1.37)	1.04 (0.50 – 2.19)	0.70 (0.39 – 1.25)	0.77 (0.40 – 1.48)
RRM (ever vs. never)	0.83 (0.49 – 1.41)	0.72 (0.35 – 1.50)	0.89 (0.52 – 1.53)	1.48 (0.71 – 3.06)
BPSO (ever vs. never)	1.35 (0.76 – 2.40)	1.55 (0.75 – 3.21)	1.08 (0.64 – 1.82)	0.78 (0.42 – 1.46)
Menopausal status (post vs. pre)	1.73 (1.00 – 2.98)	0.82 (0.33 – 2.04)	1.57 (0.93 – 2.66)	1.23 (0.55 – 2.75)
Reason 1st mammogram[c] (complaints vs. screening)	0.58 (0.32 – 1.06)	0.70 (0.35 – 1.42)	NA	NA
Lifetime no. of mammograms[c] (>7 vs. 1-6)	0.96 (0.56 – 1.64)	0.64 (0.30 – 1.38)	NA	NA
Length of recall[d] (per year)	1.01 (0.97 – 1.05)	0.99 (0.94 – 1.05)	NA	NA

RRM, risk reducing mastectomy; BPSO, bilateral prophylactic (salpingo-) oophorectomy; OR, odds ratio; CI, confidence interval; NA, not applicable

a Prediagnostic mammograms; agreement within 1 year

b Obtained from multivariate logistic regression model, adjusted for all applicable variables listed in table

c As reported in the follow-up questionnaire

d Length of recall: age at follow-up questionnaire completion minus age at 1st mammogram reported in follow-up questionnaire

DISCUSSION

To our knowledge, this is the first study on reliability of self-reported diagnostic radiation exposure history in BRCA1/2 mutation carriers. Proportion agreement on reporting ever/never exposure was good (>75%), while the corresponding kappa coefficients were between 0.40 and 0.75, indicating at least moderate reliability beyond chance. Reliability of number of exposures was also good (>75%). Reliability of reporting age at first mammogram was low (40%) for exact consistency and moderate (60%) for consistency within 1 year. Reliability of age at first mammogram was higher for cases than for unaffected carriers (P<0.001) but this difference disappeared when excluding diagnostic mammograms (P=0.599). Reliability of exact reporting of age at last mammogram was 50% in unaffected carriers. In general, the direction of disagreement on all items was equally distributed, i.e. there was as much underreporting as overreporting of exposure in one questionnaire versus the other. However, for chest X-rays before age 20 and fluoroscopies before age 30, disagreement tended to involve a change from 'ever' in the baseline questionnaire to 'never' in the follow-up questionnaire for both cases and unaffected carriers. Being an unaffected carrier and being younger

at questionnaire completion were associated with more consistent reporting of ever/never exposure to fluoroscopy for tuberculosis before age 30. For all other measures, agreement was non-differential by disease status. More consistent reporting of age at first mammogram was mainly determined by younger age at questionnaire completion. Previous reliability studies[10-16] on self-reported diagnostic radiation history were all on mammography in the setting of evaluation of screening programmes. Reliability varied by measure of self-reported mammography: agreement on ever/never having had a mammogram, lifetime number of mammograms, and date of most recent mammogram was approximately 90%[10-16], 60%[11,12,16], and 35%[10,12,13,15,16], respectively. Our results on reliability of mammograms are in line with these studies, although we observed a somewhat higher proportion agreement on number of mammograms. Since the interval between questionnaires was longer than in the other reliability studies (i.e. 5.4 years vs. 1 week to 2.6 years, respectively), reliability could have been expected to be lower in our study but this appeared not to be the case. Another difference between our study and the other reliability studies is that most of these studies used in-person and/or telephone interviews[10,11,13-16] instead of self-administered mailed questionnaires. Personal or telephone interview may enhance memory but may also lead to overreporting compared to questionnaire methods[19].

It is generally assumed that cases recall past exposures more accurately than controls. Self-report may also be influenced by whether the respondents are selected from the general population, or from a clinical setting, where they may have become more familiar with medical procedures and may remember the exposures better due to cues in a health care setting. We had expected that reliability would be good and similar for prevalent cases and unaffected carriers since our study population of BRCA1/2 mutation carriers was tested in a clinical setting. Reliability of exact age at first mammogram, which was not investigated in previous studies, was therefore rather disappointing. When including diagnostic mammograms for cases, as expected, reliability of reporting age at first mammogram before age 30 and lifetime was higher in prevalent cases than in unaffected carriers (P<0.001). However, the difference in agreement on age at first mammogram before age 30 disappeared for consistency within 1 year (P=0.375). There was no difference between cases and unaffected carriers in reliability of reporting age at first prediagnostic mammogram (P=0.599 for exact agreement and P=0.767 for agreement within 1 year). Unaffected carriers, however, reported more often a younger age at first exposure before age 30 in the follow-up questionnaire than cases but this was not statistically significant (P=0.107 and P=0.269 for mammogram and fluoroscopy, respectively). In the multivariate models, age at questionnaire completion was the only predictor of disagreement, although this finding was marginally significant. Menopausal status and reason for first mammogram did not predict consistent reporting. In exploratory analysis we found that for a number of women the large difference in age at first mammogram was due to the fact that on one questionnaire women had reported their first screening mammography as being the first mammogram ever made, while in the other they had remembered a single mammogram which was made in the more distant past because of complaints (e.g. when they had felt a lump). This was

independent of the direction of disagreement. The reported age at start of screening was a separate question in a different part of the follow-up questionnaire and only completed when a woman underwent screening at the time of questionnaire completion.
In contrast with other reliability studies[11,12], we found no evidence of an association between number of mammograms and consistent reporting. Reliability of ever/never exposure to chest X-rays before age 20 and fluoroscopies before age 30 was somewhat lower than for mammograms, while reliability of number of exposures was similar. Interestingly, reliability of ever/never exposure to fluoroscopy for tuberculosis before age 30 was significantly higher for unaffected carriers than for prevalent cases and this was not due to the difference in age at questionnaire completion. Since we examined many differences between cases and unaffected carriers, this may be a chance finding.
In general, our results cannot be directly compared with those from validity studies[9,17-19] that compared self-reported information with medical records. Differences between self-report and medical records may be due to both systematic under- or overreporting and lack of reliability. Consistent underreporting by unaffected carriers in both questionnaires can only be assessed in a validation study. But validation of e.g. chest X-rays, especially when occurred in the distant past, is extremely difficult if not impossible because of the different locations, destroyed records, and the fact that negative self-reports can not be verified. Still, most validation studies suggest that women tend to overreport the number of diagnostic radiation exposures and underreport the time since their last exposure ("telescoping")[9,18,19]. We found no evidence of telescoping on reliability; the direction of disagreement on age at last mammogram was equally distributed (data not shown).
Thirteen incident cases were excluded from the analysis. In this group, we investigated reliability of ever/never chest X-rays before age 20 (data not shown). Proportion agreement and kappa were slightly higher than for the other groups: 83% and 0.56, respectively.
When interpreting these results, the strengths and limitations of this study should be considered. This is the first study investigating reliability of self-reported risk factor exposure information in BRCA1/2 mutation carriers. Furthermore, we were able to assess reliability of more than one diagnostic radiation exposure type, to assess reliability of age at first exposure, and to investigate differences in reliability between affected and unaffected women. However, our study also has limitations. The most important limitation concerns the differences between the baseline and the follow-up questionnaire. For instance, general versus indication-based questions and categorical answer categories versus exact numbers for number of exposures. We had expected that more exposures would be reported in the indication-based follow-up questionnaire compared to the baseline questionnaire. However, the amount of disagreement in both directions was similar for most variables, whereas for chest X-rays and fluoroscopies we observed a tendency of a change from 'ever' in the baseline questionnaire to 'never' in the follow-up questionnaire rather than vice versa. Also, for the analysis on number of fluoroscopies before age 30, we based this number in the baseline questionnaire on lifetime number of fluoroscopies because there was no separate question on number of exposures before age 30. Since in the Netherlands screening for tuberculosis by fluoroscopy was mainly done through mass population screening between 1940 and 1960 in relatively young people[24], we assumed that most of the reported lifetime number of fluoroscopies had taken place before age 30. Equal distribution of the direction of disagreement suggested that this assumption was justified. On the other hand, the differences between both questionnaires allowed us to improve the questionnaire for future studies. For instance, the proportion of missing values in age at first fluoroscopy for tuberculosis before age 30 was 36% in the baseline and 9% in the follow-up questionnaire. Future studies measuring diagnostic radiation by self-report may want to consider using an indication-based questionnaire where for example, for mammogram exposure age at start screening should be asked first, followed by a question on ever having had a mammogram prior to the first screening mammogram. For number of exposures the exact number may be asked instead of categories, but in addition it should be possible to give a range if one is not sure. Another limitation concerns the use of Cohen's kappa coefficient. If a population is homogeneous with respect to the characteristic begin studied, like in our study mammographic screening, κ becomes highly sensitive to small departures from perfect concordance[25], which explains the lower kappa for several of the variables, even in presence of relatively high proportion agreement.
Our findings indicate that consistency of self-reported diagnostic radiation by BRCA1/2 mutation carriers was mainly non-differential by disease status. These results add to knowledge about the reliability of self-reported diagnostic radiation history and its effect on relative risks in studies on the association between diagnostic radiation and breast cancer; risks will likely be underestimated.

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APPENDIX

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REFERENCES

1. Ronckers, C. M., Erdmann, C. A. & Land, C. E. Radiation and breast cancer: a review of current evidence. Breast Cancer Res. 7, 21-32 (2005).
2. Hall, E. J. & Brenner, D. J. Cancer risks from diagnostic radiology. Br. J. Radiol. 81, 362-378 (2008).
3. Boulton, S. J. Cellular functions of the BRCA tumour-suppressor proteins. Biochem. Soc. Trans 34, 633-645 (2006).
4. Andrieu, N. et al. Effect of chest X-rays on the risk of breast cancer among BRCA1/2 mutation carriers in the international BRCA1/2 carrier cohort study: a report from the EMBRACE, GENEPSO, GEO-HEBON, and IBCCS Collaborators' Group. J Clin Oncol 24, 3361-3366 (2006).
5. Gronwald, J. et al. Early radiation exposures and BRCA1-associated breast cancer in young women from Poland. Breast Cancer Res. Treat. 112, 581-584 (2008).
6. Goldfrank, D. et al. Effect of mammography on breast cancer risk in women with mutations in BRCA1 or BRCA2. Cancer Epidemiol. Biomarkers Prev. 15, 2311-2313 (2006).
7. Narod, S. A. et al. Screening mammography and risk of breast cancer in BRCA1 and BRCA2 mutation carriers: a case-control study. Lancet Oncol. 7, 402-406 (2006).
8. National Breast cancer Organisation the Netherlands. Guideline Breastcancer. 2008. Utrecht, The Netherlands.
9. Paskett, E. D. et al. Validation of self-reported breast and cervical cancer screening tests among low-income minority women. Cancer Epidemiol. Biomarkers Prev. 5, 721-726 (1996).
10. Bancej, C. M., Maxwell, C. J. & Snider, J. Inconsistent self-reported mammography history: findings from the National Population Health Survey longitudinal cohort. BMC Health Serv. Res. 4, 32 (2004).
11. Rauscher, G. H., O'Malley, M. S. & Earp, J. A. How consistently do women report lifetime mammograms at successive interviews? Am. J. Prev. Med. 22, 8-14 (2002).
12. Rivera, S. et al. Test-retest reliability of self-reported mammography in women veterans. Prev. Med. 42, 320-326 (2006).
13. Barratt, A., Cockburn, J., Smith, D. & Redman, S. Reliability and validity of women's recall of mammographic screening. Aust. N Z J. Public Health 24, 79-81 (2000).
14. Brownson, R. C., Jackson-Thompson, J., Wilkerson, J. C. & Kiani, F. Reliability of information on chronic disease risk factors collected in the Missouri Behavioral Risk Factor Surveillance System. Epidemiology 5, 545-549 (1994).
15. Stein, A. D., Lederman, R. I. & Shea, S. Reproducibility of the women's module of the Behavioral Risk Factor Surveillance System questionnaire. Ann. Epidemiol. 6, 47-52 (1996).
16. Vacek, P. M., Mickey, R. M. & Worden, J. K. Reliability of self-reported breast screening information in a survey of lower income women. Prev. Med. 26, 287-291 (1997).
17. Pogoda, J. M. & Preston-Martin, S. Radiation exposure from diagnostic imaging: agreement between self-report and medical records. Health Phys. 83, 907-917 (2002).
18. Berrington de Gonzalez, A. et al. Comparison of documented and recalled histories of exposure to diagnostic x-rays in case-control studies of thyroid cancer. Am. J. Epidemiol. 157, 652-663 (2003).
19. Howard, M., Agarwal, G. & Lytwyn, A. Accuracy of self-reports of Pap and mammography screening compared to medical record: a meta-analysis. Cancer Causes Control 20, 1-13 (2009).
20. Norman, S. A. et al. Validation of self-reported screening mammography histories among women with and without breast cancer. Am. J. Epidemiol. 158, 264-271 (2003).
21. Pijpe, A. et al. Physical activity and the risk of breast cancer in BRCA1/2 mutation carriers. Breast Cancer Res Treat 120, 235-244 (2010).
22. Casparie, M. et al. Pathology databanking and biobanking in The Netherlands, a central role for PALGA, the nationwide histopathology and cytopathology data network and archive. Cell Oncol 29, 19-24 (2007).
23. Fleiss, J. L. Statistical methods for rates and proportions. John Wiley & Sons, Inc, New York, NY (1981).
24. Sickenga, F. N. Short history of the tuberculosis suppression in the Netherlands 1900-1960 (Korte geschiedenis van de tuberculosebestrijding in Nederlands 1900-1960). KNCV Tuberculosisfoundation, The Hague (1980).
25. Maclure, M. & Willett, W. C. Misinterpretation and misuse of the kappa statistic. Am. J. Epidemiol. 126, 161-169 (1987).