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Evaluation of a mammography screening program within the population-based Vorarlberg Health Monitoring & Prevention Program (VHM&PP)

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ABSTRACT

Objectives: To describe the mammography screening program from 1989 to 2005 within a population-based prevention program in Austria and to appraise it according to recommended quality indicators.
Material and method: From 01.01.1989 all women aged 40 years or older participating in the Vorarlberg Health Monitoring & Prevention Program (VHM&PP) was offered to undergo additionally a "screening mammography". Passive follow-up has been performed by record linkages with the Vorarlberg cancer registry and mortality statistics for information on outcome variables. Interval cancer rates have been estimated and the survival after breast cancer has been calculated by life table technique by examination period and age groups (40–49 years, 50–69 years).
Results: Between 1989 and 2005 50,100 women aged 40 to 69 years participated in the program, of which 123,652 mammogram results have been collected. In the target population the participation rate was 65.1%. During median follow-up time 13.5 years and 633,342 person-years overall 665 invasive cancer and 87 ductal carcinoma in situ (11.6%) cases have been identified. Between 1996 and 2004 the detection rates were 239.9 per 100.000 among women aged 40–49 years and 543.2 per 100,000 among women aged 50–69 years. The rates for interval cancers were 160.4 and 277.4 per 100 000 negative screens, respectively. During median follow-up of 13.5 years 165 deaths occurred with no difference in survival between patients with interval and screen detected cancers.
Conclusion: A mammography screening program has been performed between 1989 and 2005 in Vorarlberg. Till 2005 most quality indicators improved and met the EU-recommendations suggesting that alternative approaches to organized mammography screening based on routine data should be explored.

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1. Introduction

Breast cancer (BC) is the most common cancer diagnosed in women worldwide and the leading cause of cancer death among women, accounting for 23% of the total cancer cases and 14% of cancer deaths [1]. During the following decades increasing breast cancer incidence in Austria is predicted to increase [2]. Therefore, the prevention and management of breast cancer in order to provide high quality health care is an important public health issue.

Mammography is the predominantly applied diagnostic and screening method for breast cancer [3]. Screening aims to achieve early detection of disease in order to change an incurable to a curable status. In the nineties, randomized clinical trials showed that mammography screening can reduce breast cancer mortality [4]. Overall, randomized clinical trials of mammography screening among women aged 50 to 70 years have shown a 15% reduction of breast cancer mortality after 10 years of follow-up [5]. During the past years, the publications of the Cochrane Collaboration fostered discussion about the benefit and harms of mammographic screening [6,7,5]. Mammography screening is also associated with harm, such as false positive results, overdiagnosis and overtreatment [8].

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Recently the Swiss Medical Academy of Medical Sciences decided against the introduction of mammographic screening [9], which has been matter of debate concerning the applied models [10]. However, a small overall advantage in mortality appears for women participating in mammography screening [11].

In Austria, since 1974 mammography is covered by the health insurance and participation in opportunistic screening was high [12]. In 2014, a nationwide quality controlled mammography screening program has been introduced. Data from Tyrol in Austria have shown that opportunistic mammographic screening resulted in a reduction of 26% of BC mortality [13] in women aged 40–79 years. In a pilot project in Tyrol, data of quality indices after introducing organized mammography screening have been reported [14].

In Vorarlberg, mammography screening has been introduced in 1989 as an additional component in the population-wide prevention program. The evaluation of a mammography screening program in a population setting under routine conditions could provide further insight in the value of mammography screening on population level.

Thus, the aim of this study was to describe the mammography screening program from 1989 to 2005 within a community based health prevention program and to appraise it according to recommended quality indicators in order to compare it with those obtained in other studies.

Material and methods

Setting

In Vorarlberg health prevention programs have a long-lasting tradition. In the 70ies, a general health examination as and a gynecological prevention examination have been implemented and documented [15]. The data are electronically available from the 80ies. Organized clinical breast cancer examination (CBE) from the age of 20 years has been performed in the late 70ies and to a minor extent opportunistic mammography screening has been performed, which has not been systematically documented. In 1989 an organized mammography screening program has been implemented. Between 1989 and 2005, 136,488 women participated at least once in the prevention program, of which 69,209 were eligible for the mammographic screening program.

From 01.01.1989 all women aged 40 years or older participating in Vorarlberg health prevention program were invited to undergo additionally a “screening mammography”. The Vorarlberg mammography screening program was organized at that time according to existing standards and quality assurance guidelines such as checks by a health physicist and regular reports for the radiographers.

In 1989, 20,528 women in Vorarlberg were in the age group 40–49 years and 30.573 in the age group 50–69 years. Biennial mammography screening for women from the age of 40 years started on 1 January 1989. Two-view mammography was performed. There were four stationary mammography screening units located in Bregenz, Feldkirch, Dornbirn, and Bludenz. Women were invited to undergo a mammography and data were collected concerning previous mammography, year of last mammography, family history, breast operation, additional examination, height, weight, result of the mammography screening, pill-use, and breastfeeding. Between 01.01.1989 and 31.12.2005 data of 123.652 screening mammograms has been collected. Double reading of the mammograms has been introduced in 2001. From 01.01.2002 information according to the Breast Cancer Imaging Reporting and Data System (BIRADS) classification were collected negative, benign finding, probably benign finding, suspicious finding, highly suggestive for malignancy and known biopsy proven malignancy [16]. For the entire period the information on the outcome of screening mammography was reclassified as unknown, negative, follow-up in a short period of time, and (highly) suspicious. Ethical approval for the evaluation of the VHM&PP data was obtained by the ethics committee of Vorarlberg.

1.2. Outcome data

Data on participation in the mammography prevention program was linked to the Vorarlberg cancer registry data in order to identify incident and prevalent cases of ductal in-situ and invasive carcinoma as well as to the Vorarlberg death index for mortality follow-up. The Vorarlberg cancer registry is an epidemiological cancer registry collecting cancer cases since 1978 and contributing to the WHO publication Cancer Incidence in Five Continents [17]. Breast tumors were coded according the International Classification of Diseases, tenth revision (ICD-10): C 50) and carcinoma in situ cases (DCIS) as D05 without ICDO-M3 = 8520/2, respectively. The censoring date was 31.12.2011. Time under risk following an examination was defined as time to an incident cancer event or to death or to end of study period, whatever was observed first. Prevalent cases with invasive breast cancer ($N = 109$) and prevalent carcinoma in situ ($N = 4$) have been excluded. Tumor stage was classified according to the TNM classification of malignant tumors [18] and summarized according to the Union for International Cancer Control (UICC) classification in (UICC I-IV) to categorize tumor spread [19]. Any tumor stage with positive regional lymph nodes was classified as UICC stage II+. Coverage was defined as percentage of eligible women attending an examination per two years. Screen detected cancers were defined as registered cancer after suspicious finding or recall.

1.3. Interval carcinoma

Invasive or in-situ carcinoma registered within two year follow-up of mammographic screening round after negative screening round (without pathological finding or recall) were defined as interval invasive or in-situ carcinoma, respectively. Tumors with lag time of 2 months after the mammography were considered. The occurrence of interval tumors was evaluated separately up to 1 year (2–12 months) and between first and second year (12–24 months) after the screening mammography. Rates for interval carcinoma were calculated per women screened negative.

1.4. Statistical analysis

We calculated rates by age strata of 40–49 years and 50–69 years at the first mammographic examination by year of examination (1989–1995 and 1996–2005). Coverage rate has been calculated by counting the screening examinations (N_{Screens}) in women aged 40–49 years and 50–69 years in relation to the female Vorarlberg population in these age groups in 1989–1995 and 1996–2005 (population in person years), assuming biannual attendance.

$$\text{Coverage} = \left(N_{\text{Screens}} \times \frac{2}{\text{Population}} \right) \times 100$$

Participation rate has been calculated by counting each woman once during the observation period in the health prevention program. Life table techniques were applied to calculate survival after invasive breast cancer and interval cancer. The results were illustrated by Kaplan–Meier-plot and compared using log-rank test. In addition, we calculated population-based rates for incident in-situ and invasive carcinoma, for which we used the official data on population, by sex and 5 year age classes as supplied by statistics Austria. All statistical analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC, USA.).

Table 1
Characteristics of the mammography screening cohort.

	Prevalence round	All rounds
Age baseline, mean (SD) years	49.6 (8.3)	52.9 (8.3)
Screening mammograms, *N*	50.100	123.652
1989–1995	28.241	44.016
1996–2005	21.859	79.636
Cancer cases, *N*	258	752
T- classification, *N*		
DCIS	26	87 (11.6 %)
T1	147	419
T2	65	206
T3/4	14	27
TX	6	13
N-classification		
Nodal- negative	129	369
Nodal- positive	86	242
Miss.	16	62

MA = mammography CA = invasive breast cancer, DCIS = ductal carcinoma in situ.

2. Results

From January 1989 until 30th of December 2005 50,100 women participated in the Vorarlberg mammography screening program (Table 1). Mean age at baseline was 49.3 (SD 8.3) years. In the age group 40–49 years 29,752 women (mean age 43.6 (SD 2.9) years) participated and in the age group 50–69 years 20,336 women (mean age 58.2 (SD 5.6) years). In all screening rounds, data from 123,652 mammographic screening examinations were documented. On average data of about 7000 screening mammograms per year were collected. During median follow-up time 13.5 years and 633,342 person-years overall 665 invasive cancer cases and 87 DCIS cases have been diagnosed.

In both the prevalence and the subsequent rounds the percentages of negative screening results increased between 1989–1995 and 1996–2005 in women aged 40–49 years and 50–69 years (Table 2). As expected the numbers for (highly) suspicious findings were higher in the prevalence round and in the age group 50–69 years (1.25% and 1.22% vs. 0.68% and 0.83%, respectively).

Among participants of the health prevention program aged 40–69 years 65.1% underwent at least one screening mammography. Overall the coverage rate of the mammography screening program in the entire population of rate in the Vorarlberg was 25%. The coverage rate in the age group 40–49 years was 25.6% in 1989–1995 and 26.6% in 1996–2005 (Table 3). The numbers for the age group 50–69 years were 22.5 % and 26.2% respectively.

Overall, 11.6% DCIS cases were registered. Among women aged 50–69 years the rate increased from 9.0% in 1989–1995 to 11.1% in 1996–2005. The detection rate increased between 1989–2005 in the prevalence round among women aged 40–49 years (204.3, 236.6 per 100,000 screens) and women 50–69 years (605.4, 637.9 per 100,000 screens). The numbers for the subsequent rounds were 319.8 and 243.1 per 100,000 screens among women in the age group 40–49 years and 417.7 and 529.9 per 100,000 screens for the age group 50–69 years. For screening detected carcinoma (Fig. 1), the percentage of tumors with diameter up to 2 cm (T1) decreased between the time intervals 1989–1995 and 1996–2005 in the prevalence round (68.9%, 59.3%) and increased in the subsequent rounds (61.4%, 64.5%). The numbers for interval cancers were 69% and 53.1% in prevalence round and 48.2 % and 59.5% in the subsequent rounds, respectively.

The rate of interval cancers increased between 1989–1995 and 1996–2006, with higher rates in the subsequent round and among women 50–69 years. Between 1989–1995 and 1999–2005 the rate of first year interval carcinoma in the subsequent rounds decreased from 40.1 to 36.6 per 100,000 negative screens in the age group 40–49 years and from 55.9 to 36.5 per 100,000 negative screens in the age group 50–69 years. The rates for second year carcinoma increased over time from 100.3 to 121.9 and from 130.5 to 184.9 per 100,000 screens, respectively. Tumor stage differed between interval and screening detected breast cancer cases. In the interval detected cancer cases 51.3% were nodal negative and in the screen detected 57.7%. During mean follow-up of 12.8 (SD 4.8) years of follow-up 165 deaths after breast cancer were observed, of which 54 (33%) occurred after diagnose of an interval carcinoma. Between

Table 2
Mammography screening outcome.

	1989–1995		1996–2005	
Age group [years]	40–49	50–69	40–49	50–69
All rounds	*N* (%)			
Negative	15,752 (84.20)	21,570 (85.23)	29,581 (90.99)	43,909 (93.17)
Follow-up[b]	2,751 (14.71)	3,350 (13.24)	2,638 (8.11)	2,716 (5.76)
(Highly) suspicious	111 (0.59)	255 (1.01)	188 (0.58)	415 (0.88)
Unknown[a]	93 (0.50)	134 (0.53)	103 (0.32)	86 (0.18)
Total	18,707	25,309	32,510	47,126
Prevalence round				
Negative	11,177 (81.55)	11,776 (81.01)	14,485 (90.20)	5,225 (90.09)
Follow-up[b]	2,355 (17.18)	2,446 (16.83)	1,428 (8.89)	491 (8.47)
(Highly) suspicious	83 (0.61)	182 (1.25)	95 (0.59)	71 (1.22)
Unknown[a]	90 (0.66)	132 (0.91)	51 (0.32)	13 (0.22)
Total	13,705	14,536	16,059	5,800
Subsequent rounds				
Negative	4,575 (91.46)	9,794 (90.91)	15,096 (91.76)	38,684 (93.61)
Follow-up[b] in a short-time frame	396 (7.92)	904 (8.39)	1,210 (7.36)	2,225 (5.38)
(Highly) suspicious	28	73	93	344
	(0.56)	(0.68)	(0.57)	(0.83)
Unknown[a]	3	2	52	73
	(0.06)	(0.02)	(0.32)	(0.18)
Total	5002	10,773	16,451	41,326

[a] BIRADS 0 were treated as unknown.
[b] In a short time.

Table 3
Performance criteria overall and according to the screening round by age group and time interval.

	1989–1995		1996–2005	
Age group, years	40–49	50–69	40–49	50–69
All rounds				
Coverage (%)	25.6	22.5	26.8	26.3
Recall rate (%)[a]	14.7	13.2	8.1	5.8
	(2751)	(3350)	(2638)	(2716)
Detection rate (per 100k screens)	235.2	525.5	239.9	543.2
	(44)	(133)	(78)	(256)
Interval cancer rate (per 100k negative screens, within 2 years)	134.0	135.0	160.4	277.4
	(25)	(34)	(52)	(130)
(per 100k negative screens, within 2–12 month)	42.9	27.8	37.0	34.1
	(8)	(7)	(12)	(16)
(per 100k negative screens, within 12–24 month)	69.7	99.3	111.0	177.1
	(13)	(25)	(36)	(83)
UICC Stage II+/all screen detected cancers (%)[b]	47.5	32.5	40.6	39.2
	(19/40)	(37/114)	(26/64)	(78/199)
Invasive cancers/all screen detected cancers (%)	88.6	88.7	85.9	86.7
	(39/44)	(118/133)	(67/78)	(222/256)
Node-negative/all invasive screen detected cancers (%)[c]	63.2	70.5	52.5	62.8
	(24/38)	(79/112)	(31/59)	(120/191)
Prevalence round				
Recall rate (%)[a]	17.2	16.8	8.9	8.5
	(2355)	(2446)	(1428)	(491)
Detection rate (per 100k screens)	204.3	605.4	236.6	637.9
	(28)	(88)	(38)	(37)
Interval cancer rate (per 100k negative screens, within 2 years)	124.3	90.0	149.8	225.6
	(17)	(13)	(24)	(13)
(per 100k negative screens, within 2–12 month)	43.9	6.9	37.5	17.4
	(6)	(1)	(6)	(1)
(per 100k negative screens, within 12–24 month)	58.5	76.1	99.9	121.5
	(8)	(11)	(16)	(7)
UICC Stage II+ /all screen detected cancers (%)[b]	40.0	31.5	40.0	50.0
	(10/25)	(23/73)	(12/30)	(16/32)
Invasive cancers/all screen detected cancers (%)	89.3	93.2	81.6	83.8
	(25/28)	(82/88)	(31/38)	(31/37)
Node-negative/all invasive screen detected cancers (%)[c]	68.0	68.4	50.0	50.0
	(17/25)	(54/79)	(13/26)	(13/26)
Subsequent rounds				
Recall rate (%)[a]	7.9	8.4	7.4	5.4
	(396)	(904)	(1210)	(2225)
Detection rate (per 100k screens)	319.8	417.7	243.1	529.9
	(16)	(45)	(40)	(219)
Interval cancer rate (per 100k negative screens, within 2 years)	160.4	195.7	170.6	284.6
	(8)	(21)	(28)	(117)
(per 100k negative screens, within 2–12 month)	40.1	55.9	36.6	36.5
	(2)	(6)	(6)	(15)
(per 100k negative screens, within 12–24 month)	100.3	130.5	121.9	184.9
	(5)	(14)	(20)	(76)
UICC Stage II+ /all screen detected cancers (%)[b]	60.0	34.2	41.2	37.1
	(9/15)	(14/41)	(14/34)	(62/167)
Invasive cancers/all screen detected cancers (%)	87.5	80.0	90.0	87.2
	(14/16)	(36/45)	(36/40)	(191/219)
Node-negative/all invasive screen detected cancers (%)[c]	53.9	75.8	54.6	64.9
	(7/13)	(25/33)	(18/33)	(107/165)

[a] According to suspicious finding in BIRADS and follow-up in a short period of time in the summarized evaluation.
[b] UICC was missing for 94 screening detected cancers, for 31 in the prevalence round and 63 in subsequent rounds.
[c] Nodal status was unknown for 46 screening detected cancers, for 13 in the prevalence round and 33 in subsequent rounds.

both groups there was no statistically significant difference concerning mortality (Fig. 2).

3. Discussion

The analysis of the mammography screening program showed that in the years 1989 to 2005 50.100 women aged 40–69 years participated in the mammographic screening program in Vorarlberg. Increasing age was associated with increasing incidence of breast carcinoma. Some quality indicators met the EU recommendations.

In Vorarlberg organized mammography screening has been introduced in 1989 after clinical breast examination and opportunistic mammography screening over many years, which could have diluted the evaluation of the outcome criteria. This mammography screening program has been implemented without additional funding based on an ongoing baseline annual gynecological screening program. Record linkages with routine cancer and mortality registries were performed to obtain information on outcome criteria. Among the strengths of the present program are the long-lasting mammography screening program implemented in routine health care and record linkage with high quality cancer

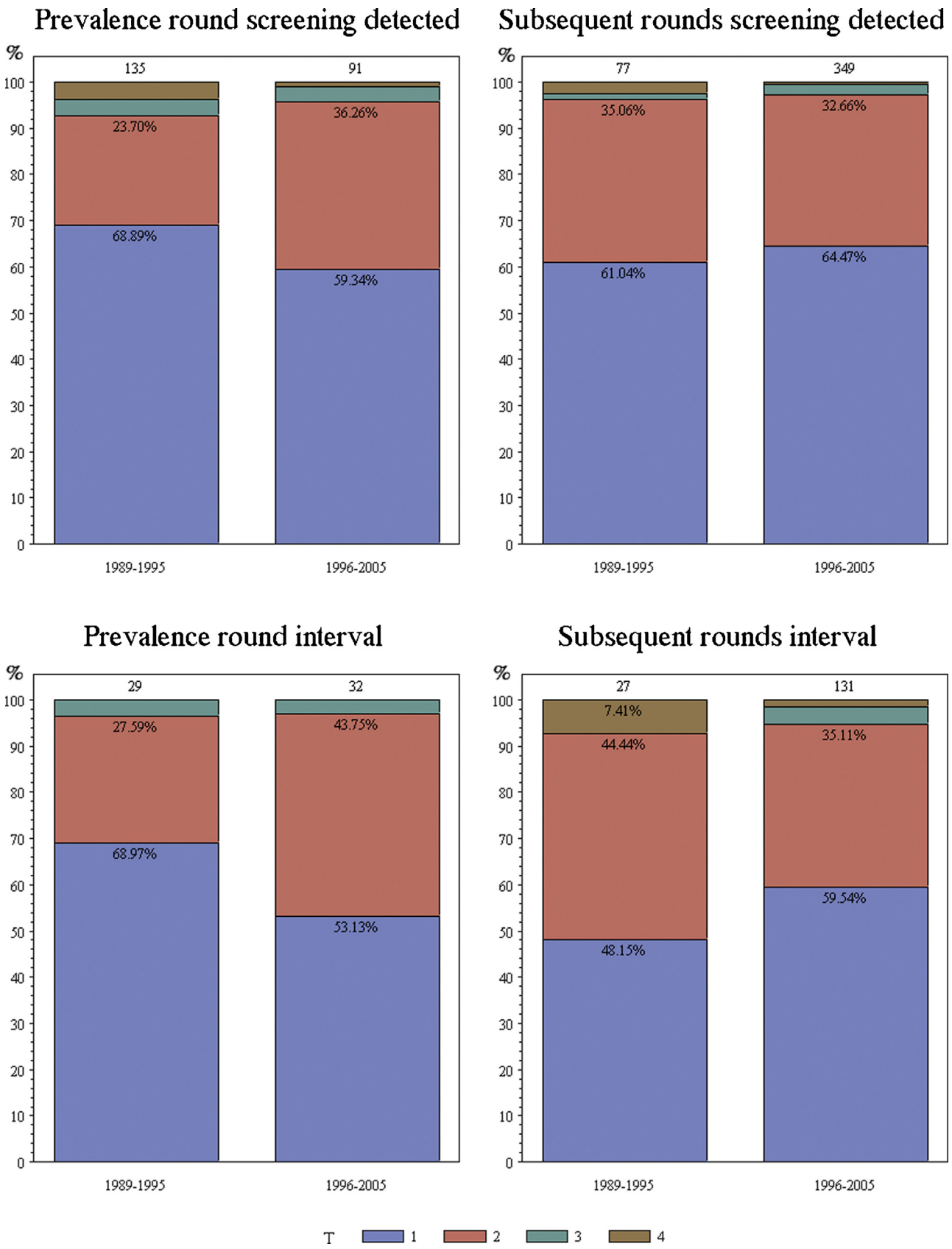
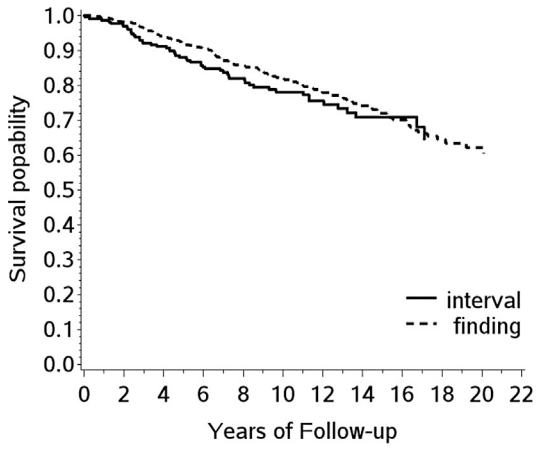


Fig. 1. T-classification for screening detected and interval cancers in the prevalence and subsequent rounds by year (without Tx, T0).



	Screen detected cancer cases	Interval cancer cases
N	446	227
Death, N (%)	111 (24.9)	54 (23.8)
Follow-up [years], mean (SD)	13.6 (4.9)	11.9 (4.6)
Age at diagnosis [years], mean (SD)	56.5 (7.9)	55.7 (7.8)
Nodal state, N (%)[1]		
Negative	254 (57.7)	115 (51.3)
Positive	146 (33.2)	96 (42.9)
Unknown (N='X')	40 (9.1)	13.(5.8)
Five year survival (%) / N Remaining	91.9 / 410	88.1 / 196
Ten year survival (%) / N Remaining	82.0 / 253	78.1 / 109
15 year survival (%) / N Remaining	72.0 / 122	70.9 / 31

[1] no information for 6 detected and 3 interval cases

Fig. 2. Survival interval versus screening detected breast cancer cases among women aged 40–69 years participating in the screening program between 1989 and 2005 in Vorarlberg.

registry and mortality data. The long lasting and well established health programs may have influenced the participation rate and the stage distribution after implementation of mammography screening program with invitation in 1989. The program has been provided to women from the age of 40 years and till the age of 69 years in a two-step population approach. Since 2002 BIRADS categories were used to manage recall. Limitations of the study are that there is no information on the invitation on individual level or reasons for non-participations in the mammographic screening program. Participation in non-organized/opportunistic mammographic screening could have occurred. Unfortunately we had no information on the diagnostic work-up of any recalled mammogram or the diagnostic procedures of any interval carcinoma; therefore we cannot quantify the prevalence of unnecessary biopsies or wrong positives findings

In the present study, the participation rate in the target population was 65.1%, which is below the EU recommendation of 70%, but higher than the rates in many other programs [20]. In relation to the entire Vorarlberg population about 25% of all women in this age groups could be approached which was lower than in most other European populations in the years between 2001 and 2007 [20]. However, the Vorarlberg screening program was not been designed to include all women aged 40–69 year in the entire population. Besides the organized screening in the VHM&PP opportunistic screening was performed. In 2014 national mammography screening has been implemented in Austria, which is likely to increase the participation in the population. In the Tyrol screening program the participation rate in the first year was 31.6 % and 52.5 % for the second year [21]. Compared to the study in Tyrol, in our study, the mammography has been a component of an ongoing health prevention program, which could have influenced the participation rate.

The rate of observed DCIS in our program is in the range of other studies [22],[23] and slightly higher than the percentages (9.8% in women ages 40–49 years and 8.8% in women aged 50-96 years) observed in the Tyrolean pilot study [21]. However, the Vorarlberg data were comparable to 10.8% of carcinoma in situ reported for the years 2009/10 in Austria [24]. Differences could be attributed to the data collection. In Tyrol case verification was performed, while the Statistics Austria and the Vorarlberg cancer registry depend on routine case notification.

In the present study the recall rate was slightly higher among younger women and declined over time. Overall 16 women per 1000 screens were invited for an additional intermediate mammography up to 9 months. In the pilot study of the organized mammography screening program in Tyrol 15 women per 1000 screens were re-invited within 6 months [21]. The recall rate of about 15% in 1989–1995 could be due to lack of BIRADS classification at that time and the limited use of ultrasound. In addition, we used routine cancer register data to appraise the screening effects which may limit the evaluation. However, in Denmark register data we found to be a valuable tool to evaluate screening activities [25]. During the observation time the completeness and quality of the Vorarlberg cancer registry may have improved, which may explain differences between the 1989–1995 and 1996–2005.

For women aged 50–69 years the detection rate of cancers was in the range of other mammographic screening programs [26]. Both the percentage of carcinoma in situ and tumors up to 2 cm diameter (T1) increased over time. Between 1996 and 2005 they met the EU recommendations. The proportion of tumor UICC stage II+ among women aged 50–69 years was slightly above the EU-recommendations. This could be attributed to the stage distribution in the population and the lack of double reading before 2001 in the present program and due to some missing values in the T-classification. However, in 2007 overall stage distribution showed 49.8% cases of localized breast cancer in Austria [27]. Our observation is also in line with a comparison of breast cancer incidence (1983–2000) and mortality (1980–2001/2) of Austrian opportunistic screening with Finland and Sweden [28].

With approximately 80% the percentage of invasive cancers was in the range of the EU-recommendations and other screening programs [29]. In our study, the interval carcinoma rate between 1996 and 2005 was 225.6 per 100.000 among screened women aged 50–69 years in the prevalence and 284.6 in the subsequent rounds. These data are consistent with the numbers observed in the German Mammography Screening program [30]. Our overall data on early interval cancers were somewhat higher among women aged 40–49 years then in the pilot study in Tyrol, while in the age group 50–69 years similar rates were observed [21]. The numbers for second year interval carcinoma for women aged 50–69 years in the years 1996–2005 were higher than German data where rates between 59.1 and 138.3 per 100.000 have been observed [30]. Our observation that more interval cancers were found in the later time interval and among older women is consistent with other data [31,32]. Our observation that stage and survival did not substantially differ between interval and screen-detected cancer cases could also suggest that among the screening attenders, women who already had symptoms were more prevalent. However, other authors found

interval cancers differ in term of biological features such as hormone receptor status and the expression of the proliferation marker Ki-67 and the tumor antigen p53 [33,34].

Since 1997 breast cancer mortality in Austria has been decreasing [27], suggesting an influence of both the widespread use of systemic treatment and earlier diagnosis due to saturation of mammography [35,36]. In addition the change in use of hormone replacement therapy may have influenced breast cancer risk during the past decade [37]. Further follow-up of the Vorarlberg screening program is necessary to appraise the long-term effects of this pragmatic approach.

In conclusion, a mammography screening program has been performed between 1989 and 2005 in Vorarlberg. Till 2005 most quality indicators improved and met the EU-recommendations. Further research is needed to implement well-tailored mammography screening programs such as targeting women with high risk of breast cancer.

Conflict of interest

The authors declared that they have no conflict of interest.

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