Breast cancer screening in Madeira 1999-2018: Comparison between participants and non-participants

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Introduction

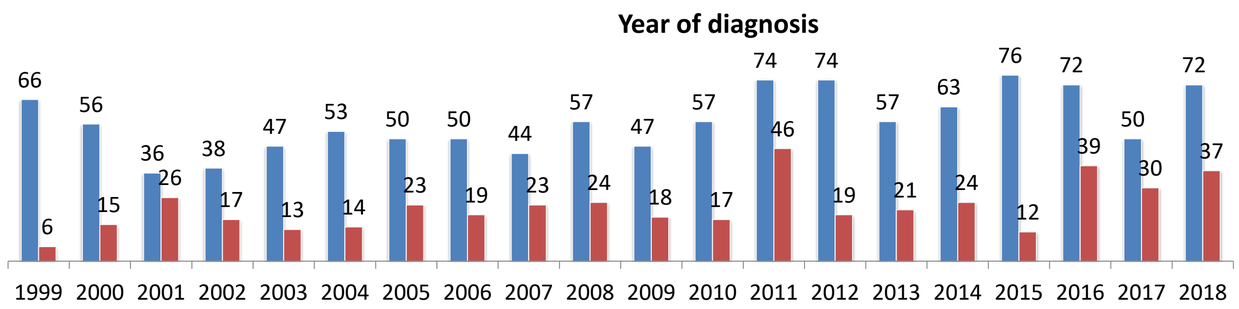
Female breast cancer (BC) is the most frequently diagnosed cancer in most countries and the leading cause of cancer death among women worldwide. Since 1999, a population-based bi-annual BC screening mammography programme for women aged 45-69 has been in place in Madeira, with participation reported at 57% of all eligible females of the archipelago population (255,000). While all women receive an appointment letter to attend screening, many BCs are detected outside the network of the screening programme as ascertained by the Madeira Cancer Registry (Registo Oncológico Regional); here called "non-participants." To date, despite this long period of activity, an assessment of the impact of the BC screening programme on BC mortality in Madeira has not been carried out. Making use of available data, we compared the characteristics and survival of BC tumors between participants and non-participants of this screening programme in an effort to initiate more elaborate analyses of the impact of the screening program.

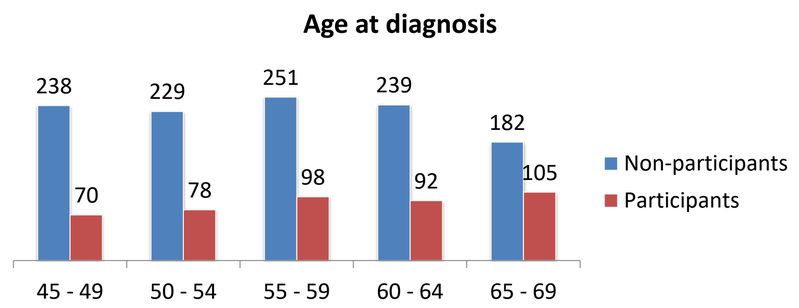
Methods

BC cases from the Madeira Cancer Registry from 1999-2018 were identified to compare stage at diagnosis distributions, hormonal receptors types, and risk of death using cause-specific survival Cox regression between participants and non-participants in the Madeira BC screening program.

Results

A total of 1582 BC cases were registered during 1999-2018, 1139 among non-participants with mean age of 56.6 years and 443 among participants with mean age of 58.03 years. Among non-participants 3.0% were in situ tumors and 97.0% were invasive; among screening participants 3.4% were in situ and 96.6% were invasive BC.





The municipality with the highest proportion of BC diagnosis was Funchal (46.4%) followed by Santa Cruz (13.6%) and Câmara de Lobos (10.0%). Non-participants had 28.4% of tumors diagnosed in late stages (III, IV), significantly higher than screening programme participants at 21.0% (p<0.05). From 2012-2018, years for which full data on hormonal receptors was available, participants had higher proportions of hormone+/HER2- while non-participants had significantly higher prevalence of HER2+ only and triple-negative tumors (p<0.05).

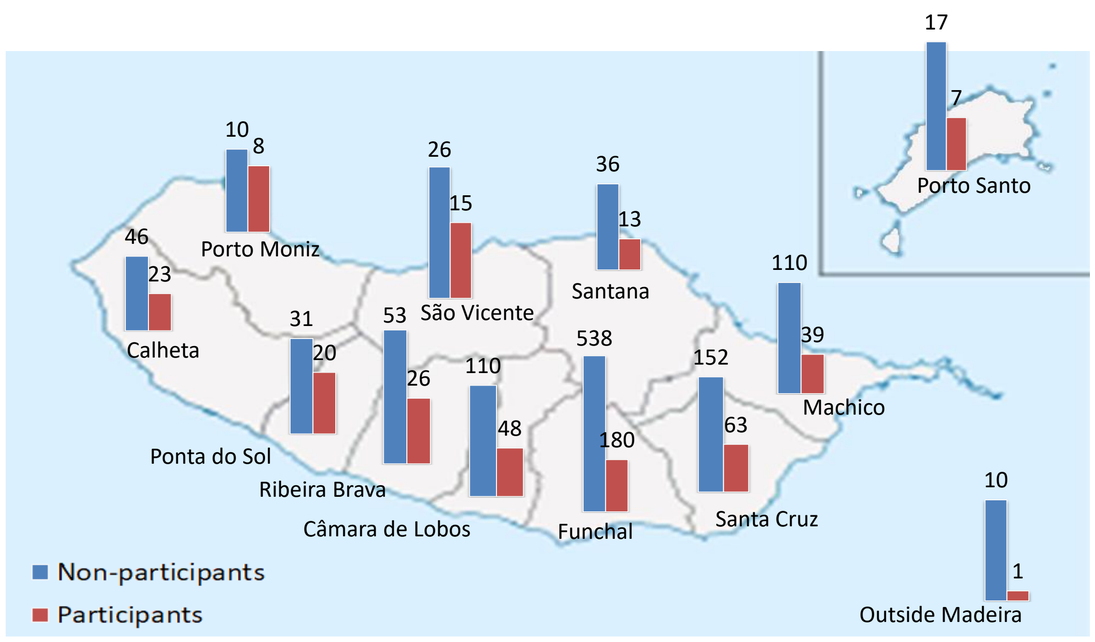
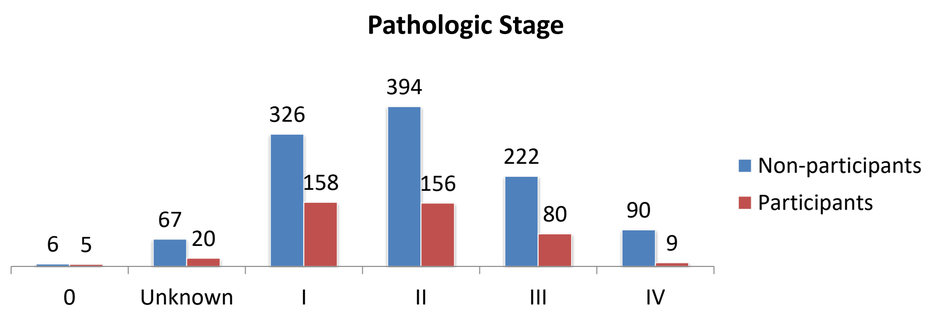


Figure 1. Distribution of diagnosis by municipality



Hormonal Receptor Status	Non-participants		Participants	
	N	%	N	%
Hormone + /HER2+	79	17.60	22	12.80
Hormone + /HER2-	266	59.20	132	76.70
Hormone - /HER2+	20	4.50	2	1.20
Triple Negative	28	6.20	2	1.20
Unknown	56	12.50	14	8.10

Table 1. Hormonal receptor status among non-participants and participants (p<0.001)

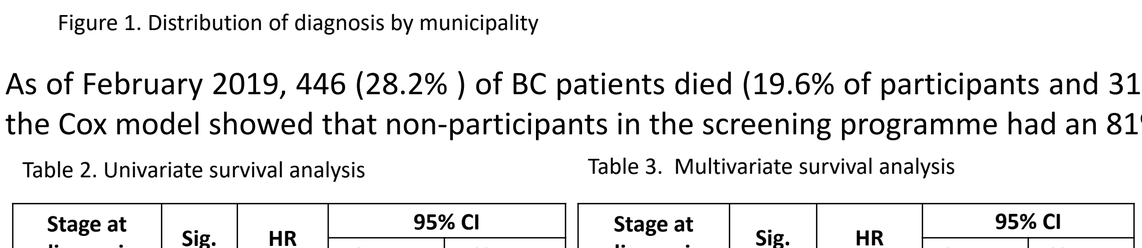
As of February 2019, 446 (28.2%) of BC patients died (19.6% of participants and 31.5% of non-participants). After adjustment for age, stage at diagnosis, and year of diagnosis, the Cox model showed that non-participants in the screening programme had an 81% higher risk of BC death (HR:1.81; 95%CI 1.34-2.42) than participants.

Table 2. Univariate survival analysis

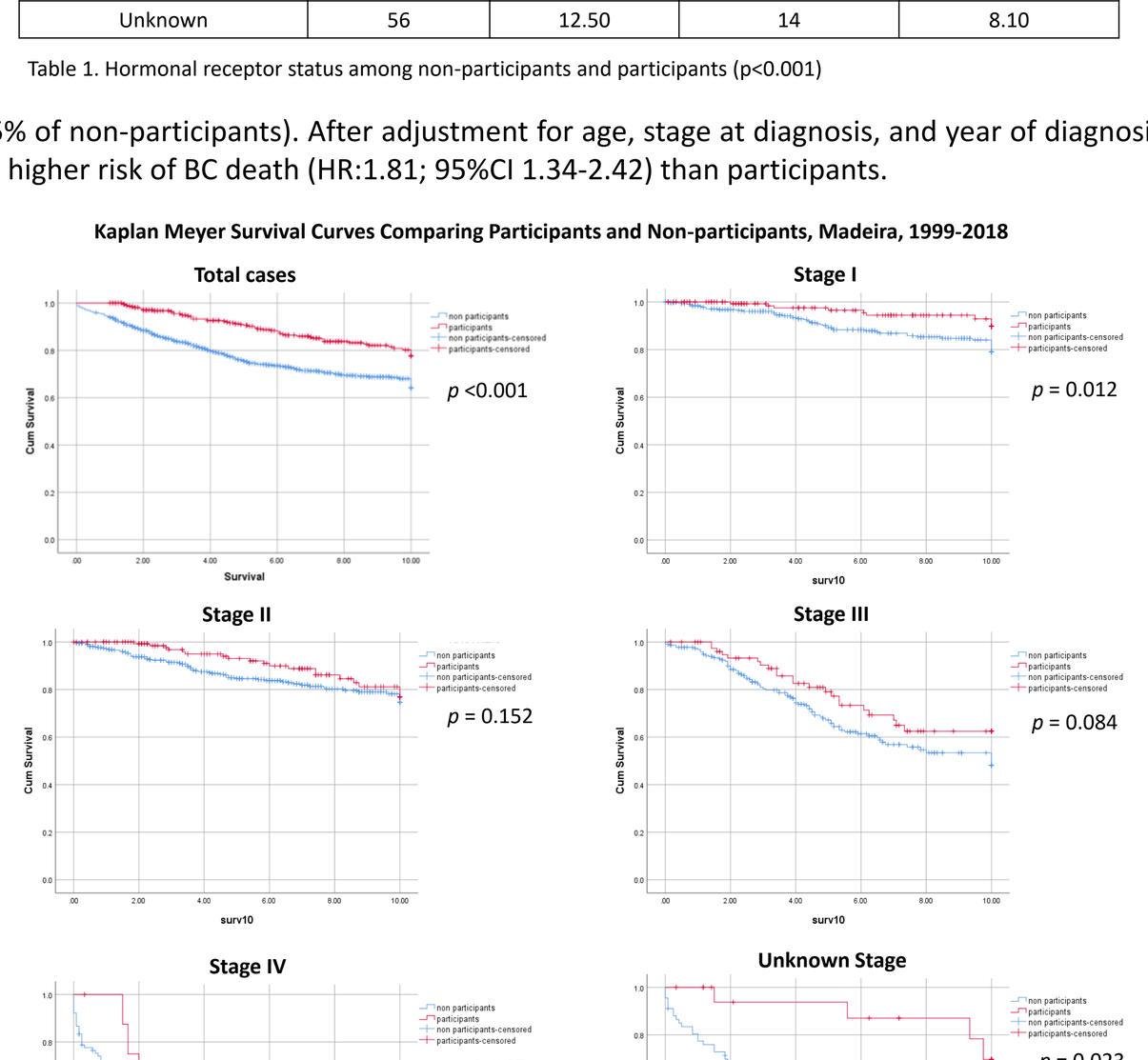
Stage at diagnosis	Sig.	HR	95% CI	
			Lower	Upper
Stage I	<0.001			
Stage II	0.006	1.61	1.15	2.27
Stage III	<0.001	4.13	2.95	5.77
Stage IV	<0.001	20.04	13.85	29.01
Unknown Stage	<0.001	4.12	2.69	6.31
Age at diagnosis	**Sig.**	**HR**	**95% CI**	
			Lower	Upper
45-49	<0.001			
50-54	0.036	1.45	1.03	2.06
55-59	0.002	1.69	1.22	2.35
60-64	0.029	1.46	1.04	2.05
65-69	0.041	0.64	0.42	0.98
Municipality of residence at diagnosis	**Sig.**	**HR**	**95% CI**	
			Lower	Upper
Outside Funchal	0.116	0.85	0.68	1.04
Screening participation	**Sig.**	**HR**	**95% CI**	
			Lower	Upper
No screening	<0.001	2.21	1.66	2.95

Table 3. Multivariate survival analysis

Stage at diagnosis	Sig.	HR	95% CI	
			Lower	Upper
Stage I	<0.001			
Stage II	0.009	1.58	1.12	2.23
Stage III	<0.001	3.93	2.81	5.50
Stage IV	<0.001	18.32	12.59	26.66
Unknown Stage	<0.001	4.11	2.68	6.33
Age at diagnosis	**Sig.**	**HR**	**95% CI**	
			Lower	Upper
45-49	<0.001			
50-54	0.012	1.57	1.11	2.23
55-59	0.001	1.79	1.29	2.49
60-64	0.002	1.73	1.23	2.45
65-69	0.424	0.84	0.54	1.29
Municipality of residence at diagnosis	**Sig.**	**HR**	**95% CI**	
			Lower	Upper
Outside Funchal	0.29	0.89	0.72	1.10
Screening participation	**Sig.**	**HR**	**95% CI**	
			Lower	Upper
No screening	<0.001	1.81	1.34	2.42



Three-year moving average rates are per 100,000 and age-adjusted to the European Standard Million (18 age groups).



Discussion/Conclusions

In the 20 years analyzed, breast cancer mortality rates in Madeira have decreased faster than in the mainland but the impact of the screening program on the mortality indicator has never been assessed. Here, we assess for the first time differences in survival indicators between participants and non-participants in the population-based BC screening programme. As expected, tumor characteristics were more favorable among participants in the screening program than among non-participants. Adjusted survival over time was 81% worse among non-participants. However, the strong limitation of lead time bias in screening programs is unavoidable in this analysis. Furthermore, we were unable to distinguish between prevalent, screening-detected and interval cancers. On the plus side, BC survival was not significantly different by area of residence: living in rural areas or Funchal (the capital city and main urban area). Notably, the total number of BC cases detected among participants was surprisingly lower than the expected number given evidence from other population-based screening indicators, which warrants further investigation. As such, this analysis highlights the urgent need for more comprehensive scrutiny of Madeira's population-based BC screening program to effectively improve BC outcomes among women in Madeira.