The impact of population screening for cardiovascular disease on quality of life

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Aims	To examine the impact of population screening–generated events on quality of life: invitation, positive test result, initiation of preventive medication, enrolment in follow-up at the surgical department, and preventive surgical repair.
Methods and results	A difference-in-difference design based on data collected alongside two randomized controlled trials where general population men were randomized to screening for cardiovascular disease or to no screening. Repeated measurements of health-related quality of life (HRQoL) were conducted up to 3 years after inclusion using all relevant scales of the EuroQol instrument: the anxiety/depression dimension, the EuroQol 5-dimension profile index (using Danish preference weights), and the visual analogue scale for global health. We compare the mean change scores from before to after events for groups experiencing vs. not experiencing the events. Propensity score matching is additionally used to provide both un-matched and matched results. Invitees reported to be marginally better off than non-invitees on all scales of the EuroQol. For events of receiving the test result, initiating preventive medication, being enrolled in surveillance, and undergoing surgical repair, we observed no impact on overall HRQoL but a minor impact of being enrolled in surveillance on emotional distress, which did not persist after matching.
Conclusion	The often-claimed detrimental consequences of screening to HRQoL could not be generally confirmed. Amongst the screening events assessed, only two possible consequences were revealed: a reassurance effect after a negative screening test and a minor negative impact to emotional distress of being enrolled in surveillance that did not spill over to overall HRQoL.
Keywords	Screening • Quality of life • EQ-5D

Introduction

Two large cardiovascular screening trials have recently been published and offer potentially pivotal evidence for improving the prevention of cardiovascular disease (CVD). In the VIVA trial, a 7% relative reduction in all-cause mortality was achieved by screening for abdominal aortic aneurysms, peripheral artery disease, and possible hypertension.[1] In the DANCAVAS trial, an 11% relative reduction in all-cause mortality was reported for the age group of 65–69 years by a broader and computed tomography–based screening.[2,3] For this evidence to benefit populations, decision-makers need to consider a number of additional criteria to survival gains in accordance with the original Wilson–Jungner

principles for screening of the World Health Organization, as well as later consolidated principles.[4,5] An absolute key principle is that the benefits of screening should outweigh any harm. This can obviously be assessed only if such harm is identified, measured, and analysed appropriately.

There are two main sources of harm: physical distress from the screening test and eventual subsequent intervention and psychological distress from risk awareness and eventual enrolment in surveillance programmes. Each of these sources can be measured by the use of generic, health-related quality of life (HRQoL) instruments such as the EuroQol.[6] Although the impact of screening-generated events on

HRQoL might be temporary and relatively small, a large number of individuals are affected due to the population scale of screening such that the total impact adds up. Further, there is an ethical aspect of whether screening-generated harm to healthy individuals, who might have preferred not to have been invited at all, can be accepted. There is essentially no robust evidence from the actual CVD screening context, which is a major uncertainty in relation to health policy decision-making about CVD screening.

There is some evidence from the cancer screening context, which is of questionable generalizability to CVD, but supports hypotheses about an impact of screening on HRQoL, as well as the measurability of such impact. This evidence stems from the contexts of screening for lung cancer,[7–11] cervical cancer,[12–15] breast cancer,[16,17] and prostate cancer,[18,19] and generally suggests that attenders at screening may be better off HRQoL-wise than non-attenders, and that HRQoL may be temporarily affected after a positive screening test. There is, however, uncertainty as to whether such impacts are due to (healthier) individuals' self-selection into screening participation or due to the actual consequences of screening.

One noteworthy difference between CVD and cancer screening in relation to any impact on HRQoL is the consequence of a positive test. Early detection of cancer usually has a curative target, and a high-intensity regimen of diagnostics, staging, and therapy follows within a short time frame. Detection of CVD, on the other hand, usually means that life-long and often low-intensity, pharmacological prophylactic therapy is recommended to moderate cardiovascular risk factors and prevent future events including diabetes. The fact that the prevalence as well as the preventive potential is a lot bigger for CVD than it is for cancer adds to the potential impact of CVD screening on HRQoL.[20] Also, it underlines the need for specific evidence to inform the current considerations about new programmes including screening for abdominal aortic aneurysms, familiar hypercholesterolaemia, hypertension, atrial fibrillation, coronary artery calcification, and Type 2 diabetes.[21]

One exception to the list of new CVD screening programmes without robust evidence is screening for abdominal aortic aneurysms, which has been already implemented in Sweden, England, Scotland, Wales, Northern Ireland, Ireland, and Germany, and is recommended for ever-smokers in the USA.[21] From the HRQoL studies reported alongside these national programmes, it is suggested that a positive test result is associated with a short-term negative impact on HRQoL.[22] There is divergent evidence with respect to any emotional distress of being enrolled in ultrasound surveillance with a small abdominal aortic aneurysm (AAA).[23,24] What is clear from, however, is that a longitudinal and controlled design is warranted for valid estimates of a causal impact of screening on HRQoL. Further, a more complete foundation that includes the possible impact of all screening-generated key events such as invitation, initiation of pharmacological therapy, and preventive surgical repair is needed.

The objective of this study is to examine the impact of population screening–generated events on HRQoL: invitation, positive test result, initiation of prophylactic pharmacological therapy, enrolment in a surveillance scheme at a surgical department, and surgical repair.

Methods

Study design

We use a difference-in-difference (DID) design to estimate the mean difference between groups, experiencing vs. not experiencing the screening-generated events, in their differences over time: from before to after for those experiencing the event and over a similar period for those not experiencing the event.

The design piggy-back on two randomized controlled screening trials including all men aged 60–74 and living in the region of South Denmark from 2014 to 2019.[25] These trials generated the screening events and included baseline HRQoL measurements for all invited to screening and a 20% random sample of those not invited for screening (see Supplementary material online, *Figure S1*). Repeated measurements were conducted in annual rounds during the second quarter each year, from 2015 through 2018. Due to the staggered inclusion into the trials, not everybody was invited for repeated measurements of HRQoL. In the current design, we take advantage of the scale of measurements, and, for each event of interest, we sample individuals with before- and after-event measurements and use the DID design to control for risk selection as well as secular trends.

The DID design is a quasi-experimental design, which is commonly used to study causal relationships in social sciences when randomization is infeasible or unethical.[26] In the current case, it is infeasible to randomize to events except for the invitation (where randomization was actually conducted). The before- and after-event difference control for selection, which is stable over time, whereas the comparison with a control group's before- and after-event differences control for secular trends. The DID design provides unbiased effect estimates when the intervention and control group trends would have been similar without intervention. It should be noted that it is not necessary that the groups have similar before levels of HRQoL or similar individual characteristics, as long as their trends are parallel. For example, estimates of the effect of a positive screening test will be unbiased despite negatives being in better health than positives, if their change scores would have been parallel in the absence of a test result. In cases where the assumption about parallel trends appears unreasonably strong, it can be relaxed by combining the DID design with analytical weighting,[26,27] which was done as a robustness check, as described below.

Comparators

We assess the impact of five major events generated by screening: receiving an invitation with information about risk (yes/no, assessed amongst all), receiving the test result (positive/negative, assessed amongst all attenders), initiation of preventive medication (yes/no, assessed amongst all with a positive test and no use of preventive medication within the most recent 6 months), enrolment in surveillance to monitor the need for surgical repair (enrolled/not enrolled, assessed amongst all with indication for surveillance), and preventive surgical repair (yes/no, assessed amongst all with indication for surveillance).

Sampling and data sources

The comparators are specified from actual event dates in the event group, and for the no-event groups without date (no initiation, no surveillance, and no surgical repair), a synthetic date data were constructed based on the means for the event groups. For each event, we then look up any before and after HRQoL measurements in the trial data and include individuals in the current study if they have a before and an after measurement. Event status, event date, HRQoL, and smoking status are thus informed from the trial data. These data are supplemented with demographics and socioeconomic status from national registry data.

Health-related quality of life measurements

All measurements are undertaken using the three-level EuroQol 5-dimension (EQ-5D) health profile and the EuroQol visual analogue scale (EQVAS).[6] In the EQ-5D, the respondent is asked to choose the statement that 'best describes your health TODAY' across five health dimensions with three response levels each (e.g. I have no problems in walking about, I have some problems in walking about, I am confined to bed). The profile can be analysed for individual dimension scores (based on an assigned score of 1–3) or weighted into a profile index based on preference weights.[28] In the EQVAS, the respondent is asked to directly rate his or her global health on a scale from 0 to 100 where 0 indicates 'the worst health you can imagine' and 100 'the best health you can imagine'.

Due to the focus on emotional distress in relation to screening, we analyse (i) the single dimension focusing on anxiety and depression (hereafter referred to as 'item', range 1–3 with higher values representing more distress), the health profile weighted into an index using Danish preference weights (hereafter referred to as 'index', range −0.59 to 1 with higher values representing higher HRQoL), and the direct observations of the EQVAS (hereafter referred to as VAS, range 0–100 with higher valuers representing better health). It should be noted that the three scales are

Table 1 Characteristics of the study populations used for assessment of impact of screening-generated events on health-related quality of life

	Invitation		Test result		Enrolment surveillance		Initiation medication		Surgical repair	
	Event	No event	Event	No event	Event	No event	Event	No event	Event	No event
Response to first measurement	15 704 (69)	3861 (35)	8457 (>99)	5684 (>99)	872 (100)	7596 (>99)	2354 (94)	505 (>99)	440 (95)	789 (>99)
Response repeated measurements	NA	NA	4154 (49)	2753 (48)	113 (13)	3492 (46)	1049 (45)	248 (49)	72 (16)	605 (77)
Age in years (mean, SE)	**67 (0.03)**	**66 (0.06)**	**67 (0.06)**	**66 (0.07)**	**69 (0.29)**	**66 (0.07)**	**66 (0.12)**	**65 (0.24)**	69 (0.42)	68 (0.14)
Current smoker	2287 (16)	NA	**742 (18)**	**276 (10)**	23 (20)	593 (17)	**220 (21)**	**38 (15)**	16 (23)	127 (21)
Living alone	**2701 (17)**	**750 (19)**	**701 (17)**	**364 (13)**	15 (13)	580 (17)	167 (16)	50 (20)	14 (20)	106 (18)
Education										
Lower secondary	3451 (22)	861 (22)	**901 (22)**	**195 (19)**	26 (23)	753 (22)	195 (19)	46 (19)	17 (24)	134 (22)
0–3 years further	8332 (53)	2020 (52)	**2220 (53)**	**575 (55)**	62 (55)	1863 (54)	579 (55)	114 (46)	38 (53)	331 (55)
>3 years further	3921 (25)	980 (25)	**1033 (25)**	**275 (26)**	25 (22)	876 (25)	275 (26)	88 (35)	(178 24)	140 (23)
Working	**6147 (39)**	**1878 (49)**	**1677 (40)**	**1368 (50)**	**22 (19)**	**1502 (43)**	509 (49)	126 (51)	20 (28)	164 (27)
Household income										
1st quartile	**2750 (18)**	**677 (18)**	**995 (17)**	**313 (11)**	**13 (12)**	**573 (16)**	159 (15)	33 (13)	17 (24)	112 (19)
2nd quartile	**4305 (27)**	**923 (24)**	**1142 (27)**	**640 (23)**	**41 (36)**	**925 (26)**	242 (23)	59 (24)	19 (26)	197 (33)
3rd quartile	**4373 (28)**	**1045 (27)**	**1179 (28)**	**787 (29)**	**38 (34)**	**1000 (29)**	307 (29)	73 (29)	22 (31)	162 (27)
4th quartile	**4256 (27)**	**1216 (31)**	**1138 (27)**	**1013 (37)**	**21 (19)**	**994 (28)**	341 (33)	83 (33)	14 (19)	134 (22)
Self-rated global health										
0–100 (mean, SE)	81 (0.12)	81 (0.27)	**80 (0.23)**	**84 (0.25)**	79 (1.37)	80 (0.26)	**84 (0.37)**	**86 (0.72)**	77 (2.11)	80 (0.60)

Values are *n* (%) unless otherwise stated. Statistically significant differences at $P < 0.05$ are marked in bold.
NA, not available; SE, standard error.

conceptually different and focus on: (i) emotional distress related to anxiety and depression, (ii) utility from HRQoL, and (iii) global health.

Statistical analysis

Population characteristics for each of the five event-based sets of comparators are assessed by frequencies and χ^2 tests for categorical variables and by means and t-tests for continuous variables.

For the main analyses of the impact of events, we report parallel results of unmatched and matched DID estimates. The matched results are based on 1:1 nearest neighbour propensity score matching with a focus on key factors that may affect HRQoL and change unevenly between the groups over time: current smoker (yes/no), living alone (yes/no), working (yes/no), household income (quartile dummies), and self-reported global health (continuous). In addition, age (continuous) was added to the models where the no-event date was synthetic. Propensity scores are estimated from probit regression and separately for each event and for each of the HRQoL scales due to slight differences in the within-event response to the different HRQoL scales. The distributions of the propensity scores are evaluated graphically (see Supplementary material online, Figures S2–S6) and the balancing of covariates after matching is assessed by the percentage bias (see Supplementary material online, S1–S5). For the calculation of standard errors (SEs), we take into account that the propensity scores are estimated.[29]

For each of the event and no-event groups, we report the mean before-, after-, and change score over time with SEs. For the main results of the DID estimators, we report the unmatched and the matched means with 95% confidence intervals (CIs).

Research ethics

This study was conducted in accordance with the relevant guidelines and regulations of the Declaration of Helsinki.[30,31] All analyses were conducted on anonymized data and in conformity with the General Data Protection Act (approvals 14/9140 and 17/5994).

Consent

The study is based on participant-reported data. Participants were invited to participate by an invitation letter with the EuroQol questionnaire attached. Consent was obtained by participants returning the questionnaire.

Public involvement

This study has been preceded by interviews and preference elicitation among screening participants. It has been discussed with patient representatives from the Department of Cardiology at the Odense University Hospital.

Results

This study included 33 769 men from two screening trials, who were invited to report their HRQoL at baseline and during annual survey rounds for repeated measurements (Table 1). For each of the five main analyses, a before and an after measurement is required for each individual in the event and in the no-event groups, respectively. Amongst the 33 769, everybody will be invited to screening or not, whereas not everybody will have a test result (only those attending screening) and so forth for events flowing from a positive test. This means that the sample size decreases for increasing severity of events. Baseline characteristics and their differences between the groups of event and no event are as expected and will be considered by the analytical strategy as detailed below.

For each of the comparators, propensity score models are specified to balance the baseline differences that could change over time at an uneven speed. Despite smaller n as the events become more severe, the propensity score matching reasonably balanced the key covariates (see Supplementary material online, Tables S1–S5). No statistically significant bias remained after matching and there was common support for all observations (see Supplementary material online, Figures S2–S6).

Receiving an invitation for screening appears to be associated with statistically significant reduced emotional distress ($P < 0.001$) and increased HRQoL ($P < 0.001$). This is consistent across the matched and the unmatched estimators and corresponds to a relative reduction in emotional distress of around 2% and a relative increase in HRQoL of around 3% (Table 2).

Receiving a positive screening test result does not impact emotional distress or HRQoL, which is again consistent across the unmatched and matched DID estimators (Table 3). At baseline, those ending with a positive test had higher emotional distress and poorer HRQoL than those ending with a negative test, but their trends over time appear to be parallel. In terms of global health, there is a tendency for those testing negative to improve over time on the unmatched DID estimator, which corresponds to around a 1% change relative to baseline. After matching, this becomes statistically significant ($P < 0.001$) and is estimated to 1.62 point on the global health scale from 0 to 100, which corresponds to around a 2% increase as a probable reassurance effect on self-perceived health.

The most common outcome of CVD screening is a recommendation for initiation of preventive medication such as antihypertensives, statins, and antithrombotic agents. Initiation of preventive medication does not appear to impact emotional distress or HRQoL (Table 4), but global health is impacted negatively with up to 2.72 points, which corresponds to a 3% reduction. The fact that the impact is isolated on the physical health scale and not the emotional or general quality of life suggests that the impact could be related to possible that side effects of medication.

Enrolment in surveillance at a surgical centre reflects a more severe diagnosis than the comparator of having a positive test (with indication

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Table 2 The impact of invitation for screening on health-related quality of life

EuroQol	Invited	Non-invited	Difference	
	n	n	Unmatched	Matched
	Mean (SE)	Mean (SE)	Mean (95% CI)	Mean (95% CI)
Item	15 675	3845	**−0.02 (−0.03 to −0.01)**	**−0.03 (−0.04 to −0.01)**
	1.12 (<0.01)	1.14 (<0.01)		
Index	15 594	3803	**0.03 (0.02 to 0.04)**	**0.03 (0.03 to 0.04)**
	0.90 (<0.01)	0.87 (<0.01)		
VAS	15 537	3724	−0.29 (−0.84; 0.27)	**−0.10 (−0.19 to <0.01)**
	81.18 (0.12)	81.41 (0.27)		

Statistically significant differences at $P < 0.05$ are marked in bold.
CI, confidence interval; SE, standard error; VAS, visual analogue scale.

Table 3 **The impact of the screening test result on health-related quality of life amongst those who attend screening**

EuroQol		Positive	Negative	DID	
		n Mean (SE)	*n* Mean (SE)	Unmatched Mean (95% CI)	Matched Mean (95% CI)
Item	Before	4127 1.13 (<0.01)	2737 1.10 (<0.01)		
	After	4127 1.14 (<0.01)	2737 1.10 (<0.01)		
	Difference	4127 0.01 (0.01)	2737 <0.01 (0.01)	<0.01 (−0.01 to 0.02)	<0.01 (−0.02 to 0.02)
Index	Before	4059 0.89 (<0.01)	2693 0.92 (<0.01)		
	After	4059 0.88 (<0.01)	2693 0.91 (<0.01)		
	Difference	4059 −0.01 (<0.01)	2693 −0.01 (<0.01)	<0.01 (−0.01 to <0.01)	<0.01 (−0.01 to 0.01)
VAS	Before	3996 80.46 (0.23)	2690 83.93 (0.24)		
	After	3996 80.58 (0.25)	2690 84.53 (0.25)		
	Difference	3996 0.13 (0.20)	2690 0.60 (0.21)	−0.47 (−1.06 to 0.12)	**−1.62 (−2.33 to −0.91)**

Statistically significant differences at $P < 0.05$ are marked in bold.
CI, confidence interval; DID, difference-in-difference; SE, standard error; VAS, visual analogue scale.

Table 4 **The impact of initiation of preventive medication on health-related quality of life amongst those with a positive test who did not use preventive medication before screening**

EuroQol		Initiation	No initiation	DID	
		n Mean (SE)	*n* Mean (SE)	Unmatched Mean (95% CI)	Matched Mean (95% CI)
Item	Before	1043 1.09 (0.01)	246 1.07 (0.02)		
	After	1043 1.09 (0.01)	246 1.09 (0.02)		
	Difference	1043 −0.01 (0.01)	246 0.02 (0.02)	−0.03 (−0.07 to 0.01)	<0.01 (−0.04 to 0.04)
Index	Before	1028 0.92 (<0.01)	242 0.94 (0.01)		
	After	1028 0.92 (<0.01)	242 0.93 (0.01)		
	Difference	1028 <0.01 (<0.01)	242 −0.02 (0.01)	0.01 (−0.01 to 0.03)	0.01 (−0.01 to 0.03)
VAS	Before	1020 84.64 (0.37)	241 86.41 (0.73)		
	After	1020 84.05 (0.25)	241 87.36 (0.70)		
	Difference	1020 −0.58 (0.35)	241 0.95 (0.62)	−1.53 (−3.06 to 0.02)	**−2.72 (−4.53 to −0.91)**

Statistically significant differences at $P < 0.05$ are marked in bold.
CI, confidence interval; DID, difference-in-difference; SE, standard error; VAS, visual analogue scale.

Table 5 The impact of surveillance for disease progression at specialized hospital clinic on health-related quality of life for those with a positive screening test

EuroQol		Surveillance n Mean (SE)	No surveillance n Mean (SE)	DID Unmatched Mean (95% CI)	DID Matched Mean (95% CI)
Item	Before	112 1.11 (0.03)	3466 1.12 (0.01)		
	After	112 1.20 (0.04)	3466 1.14 (0.01)		
	Difference	112 0.09 (0.04)	3466 0.01 (0.01)	**0.08 (0.01 to 0.14)**	0.06 (−0.03 to 0.15)
Index	Before	112 0.86 (0.01)	3410 0.90 (<0.01)		
	After	112 0.84 (0.02)	3410 0.88 (<0.01)		
	Difference	112 −0.03 (0.01)	3410 −0.02 (<0.01)	−0.01 (−0.04 to 0.01)	0.02 (−0.01 to 0.06)
VAS	Before	110 78.96 (1.39)	3343 80.70 (0.26)		
	After	110 76.42 (1.81)	3343 80.49 (0.27)		
	Difference	110 −2.55 (1.40)	3343 −0.22 (0.23)	−2.33 (−4.82 to 0.18)	−1.66 (−4.38 to 1.06)

Statistically significant differences at *P* < 0.05 are marked in bold.
CI, confidence interval; DID, difference-in-difference; SE, standard error; VAS, visual analogue scale.

for preventive medication only). Across all the unmatched and matched DID estimators, the only consequence of enrolment appears to be an around 7% increase in emotional distress (DID estimator 0.08, 95% CI 0.01 to 0.14, *P* = 0.018), which reduces to around 5% and becomes statistically insignificant after matching (DID estimator 0.06, 95% CI −0.03 to 0.15, *P* = 0.193) (*Table 5*).

Elective surgical repair is the least common but possibly also the most serious event that flow from screening. Nevertheless, we observe that the event and no-event groups follow remarkably similar trends over time on all scales (*Table 6*). If anything, there is a non-significant tendency for the no-event group deteriorating more over time on the global health than the event group.

Discussion

In this DID design piggy-backing on two large population screening trials, we found that invitees report to be better off than non-invitees whereas the often-claimed emotional distress related to screening participation or the events flowing thereof such as receiving the test result, initiation of preventive medication, enrolment in surveillance programmes, or undergoing preventive surgical repair appears to be limited. In fact, the only consequences observed were a possible reassurance effect after a negative screening test, and a possible impact to emotional distress of being enrolled in surveillance that did however not spill over to overall HRQoL.

To the best of our knowledge, this is the first study to examine the impact of individual screening events on HRQoL in a causal DID design. This design originates from social science but is increasingly recognized also in CVD.[32] Unbiased estimates of the possible harm of screening are of high importance for ethical as well as for health policy reasons as

decision-makers are increasingly considering the evidence for cost-effectiveness based on quality-adjusted life years (QALY). The QALY typically captures the benefit of screening by the mortality risk reduction whereas the harm to HRQoL is much less straightforward because it may fluctuate over time as individual events are faced. With the QALY being an area-under-the-curve measure, assumptions are required for every day HRQoL is not directly measured. The present study captures the average impact for an average of 6 months after the events (due to the annual measurement rounds). For a precise reflection of the fluctuation in HRQoL over time, hundreds of repeated measurements would be required—or indeed a qualitative design identifying when and how often measurements would be needed.

The usual concern about selection bias due to non-response apply. Dedicated trial staff ensured very high response rates to the first measurement round but due to the study design, which was based on annual rounds which ended before the trials did, not everybody was invited to reply to repeated measurements. We consider this cause of non-response for pseudo-random and thus not necessarily an issue to selection bias. We further choose one of the strongest designs for tackling selection with a combination of the DID design where unobserved heterogeneity cancels out as long as it is stable, and propensity score matching where we included both lifestyle (smoking), living conditions (socioeconomic status [SES]), and self-perceived health. Nevertheless, poor response rates to the repeated measurements for the events which fall late after screening is a possible weakness to the study.

One important finding is that preventive surgical repair does not seem to affect future HRQoL, which would otherwise be a serious harm. This is in consensus with the results of an early study conducted alongside the UK small aneurysm trial[33] and could mask a complex network of emotions from relief of the uncertainty related to surveillance to handling the mortality risk associated with surgery. The strength of

Table 6 The impact of surgical repair on health-related quality of life for those with indication for surveillance

EuroQol		Surgical repair n Mean (SE)	No surgical repair n Mean (SE)	DID Unmatched Mean (95% CI)	Matched Mean (95% CI)
Item	Before	72 1.22 (0.06)	604 1.15 (0.01)		
	After	72 1.19 (0.05)	604 1.15 (0.01)		
	Difference	72 −0.03 (0.06)	604 <0.01 (0.01)	−0.03 (−0.12 to 0.06)	<0.01 (−0.13 to 0.13)
Index	Before	70 0.84 (0.02)	594 0.87 (0.01)		
	After	70 0.84 (0.03)	594 0.87 (0.01)		
	Difference	70 <0.01 (0.02)	594 <0.00 (0.01)	<0.01 (−0.03 to 0.04)	<0.01 (−0.06 to 0.04)
VAS	Before	66 78.55 (2.04)	577 79.96 (0.61)		
	After	66 78.24 (2.40)	577 79.07 (0.67)		
	Difference	66 −0.30 (2.15)	577 −0.89 (0.57)	0.59 (−3.03 to 4.22)	2.76 (−2.83 to 8.37)

CI, confidence interval; DID, difference-in-difference; SE, standard error; VAS, visual analogue scale.

this study is not to disentangle such emotions but to provide a valid average estimate in order to strengthen the foundation for policy-making. The use of the EQ-5D is another strength due to the popularity of this instrument and well-established psychometric properties.[34] In line with many screening studies trying to balance ease of response with sensitivity of instruments, we used the three-level version of the EQ-5D. However, this is also the main limitation of this study, in that a five-level version has been developed because of concerns about the sensitivity of the three-level version.

Lead author biography

Rikke Søgaard is a professor of health economics, who has been involved in large screening trials over the past 15 years, and who has published in leading medical, epidemiological, and health services research journals on this topic. She is also a member of the advisory board on current and future national screening programmes at the Danish National Board of Health.

Supplementary material

Supplementary material is available at *European Heart Journal Open* online.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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