Screening the CITY: optimizing population-based cancer screening in the Netherlands from a primary care perspective

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In dierbare herinnering aan Fons

Contents

CHAPTER 1

General introduction

Cancer is a heterogenic group of diseases characterized by uncontrolled growth of abnormal cells with the potential to invade surrounding tissue or spread throughout the body.[1] Each type has its own causes, symptoms, and specific treatment.[2] Worldwide, cancer is a major and growing health problem, and one of the leading causes of death.[3] The increase of cancer cases can be largely attributed to the aging and growing population, as well as to current and persisting lifestyle habits.[4] Recent numbers show that worldwide one in five men (20%), and one in six women (17%) will get cancer at some point in their lives. Approximately one in eight men (13%), and one in 11 women (9%) who develop cancer, will also die as a result of the disease.[5] Many people around the world will thus encounter cancer (directly or indirectly). According to the World Health Organization (WHO) between 30% and 50% of the cancer cases can be avoided through the effective implementation of prevention strategies.[6]

Currently in the Netherlands, more than 120,000 people are diagnosed with cancer each year (incidence) and about 600,000 people live with a cancer diagnosis (prevalence).[7, 8] Since both the incidence and prevalence are expected to further increase in the upcoming years, it is not surprising that cancer also plays an important role in primary care, and in general practice (GP)- practices.[9, 10] Not only are GPs involved in recognising early symptoms and diagnosing the disease, they are also involved in the guidance of cancer patients during and after treatment. The Dutch College of General Practitioners (NHG; Nederlands Huisartsen Genootschap) stated that GPs have an increasingly important role to ensure continuous and person-centred care with respect to the care for cancer patients.[11] Per standard practice (around 2500 patients) a GP is encountered by an average of 25 new adult patients with (different types of) cancer per year, which equals one new patient per two weeks.[12] During the course of their disease, these patients require substantial high levels of care and support. The future increase of patients will therefore also lead to a further increase of the cancer related activities for GPs and GP-practices.

Cancer screening

Since cancer requires time to develop, cancer screening can be used as an important tool for reducing the cancer related burden and mortality worldwide. Cancer screening aims to detect a specific cancer in an early or precursor stage, when symptoms are minimal, chances of recovery are highest, and less intense treatment options with fewer side effects are often available. Therefore, most developed countries have established some form of cancer screening. In Europe and other Western-countries, screening is most often offered in the context of a population-based cancer screening programme (CSP).[13] As cancer is a heterogenic disease, not all types of cancer are suitable for screening. Already

in 1968, Wilson and Jungner established specific criteria to help determine whether a certain disease is eligible for screening.[14] These criteria include that the disease must be an important health problem, there must be an effective treatment available, the natural history of the disease must be well understood, the test must be suitable for mass application, and the outcome of the screening programme (SP) should be monitored and evaluated. The WHO added a couple of extra criteria in 2008, regarding: the availability of diagnostic and treatment services, a suitable infrastructure, acceptability to the population, and several ethical and social issues.[15] One of these ethical criteria states that the benefits of screening should outweigh the potential disadvantages of the screening. As this appears to be rather complicated to determine, there is a strong and ongoing debate on the effectiveness of the CSPs.[16-19] While proponents indicate that cancer-specific mortality is decreasing, critics indicate that it has changed little or nothing in absolute mortality within screened populations.[20, 21] In general, most people do have a rather positive attitude towards the CSPs, and in the current literature there seems to be consensus that current (European) CSPs lead to a better prognosis, as well as to fewer and less severe side effects of the treatment(s).[22-24] Consequently, most European countries have implemented population wide CSPs aiming at early diagnosis of cervical, breast, and colorectal cancer.[25] In order for a screening programme (SP) to be successful the amount of attenders – i.e. the attendance rates – must be adequately high and should be evaluated.[26-28] Modelling studies aimed to predict the effect on cancer mortality of CSPs were found to be highly dependent on the attendance rates.[26, 29] According to the WHO at least 70% of a target population, without further pre-selection, should be screened in order for a CSP to be effective on population level.[4, 30, 31]

Cancer screening in the Netherlands

The Netherlands currently hosts three centrally organized population-based cancer screening programmes (CSPs) aiming at cervical, breast, and colorectal cancer. These CSPs are offered free of charge by the Dutch government to all citizens of a specific age and gender. The National Institute for Public Health and the Environment (RIVM; Rijksinstituut voor Volksgezondheid en Milieu), and the national screening organisation (Bevolkingsonderzoek Nederland) are in charge of organizing and coordination these programmes.[32, 33] The Netherlands has a strict law on population screening (Wbo; Wet op het Bevolkingsonderzoek), which has been in place since 1996.[34] Attendance is voluntary and monitored yearly by RIVM.[35-37] Although all three CSPs show many similarities, each CSP has its unique procedures and organization, mainly due to differences in screening methods and recruitment system (Table 1).

Table 1. Key characteristics of the current CSPs in the Netherlands

	Cervical CSP	Breast CSP	Colorectal CSP
Available since (year)	1979 (pilots from 1976)	1990 (pilots from 1984)	2014 (fully operational since 2019)
Population Age boundaries	30-60	50-75	55-75
Sex	F	F	F + M
Interval (years)	5	2	2
Screening test	HPV-test, if HPV positive then cytology (Pap-smear)	Mammography (bilateral)	FIT
GP involvement	Performing Pap-smear, discuss outcome, hospital referral[a]	Discuss outcome, hospital referral[b]	None[c]; discuss outcome
Screening outcome	HPV absent, present or unclear (re-testing). When applicable Pap-classification and HPV-typology	Abnormality absent (BI-RADS 1-3), abnormality present (BI-RADS 4-5), not enough information (BI-RADS 0)	Negative (no examination needed), positive (examination needed), unclear (re-testing)
Financing Invitation, screening test(s) and analyse	Dutch government		
Secondary test(s) and treatment	Standard healthcare, hence depending on one's individual insurance policy		

CSP= Cancer Screening Programme, F= Female, M= Male, HPV= Human Papillomavirus, GP= General Practitioner, FIT= Faecal Immunochemical Test

[a] From 2017 onward, women can opt to receive a self-sampling test (after being invited). The outcome of the self-sampling test is not automatically shared with the GP due to privacy legislation. Outcomes will only be shared with the GP, if it is explicitly stated that the GP is allowed to receive this information. Hence, the GP no longer plays an essential role in this CSP. If HPV is detected, women are recommended to contact their GP to have a smear test taken at the GP-practice.

[b] In cases no abnormalities are detected, the GP will not be involved.

[c] Since 2017 the GP no longer automatically receives the outcome of a FIT. Outcomes will only be shared with the GP if it is explicitly stated that the GP is allowed to receive this information. After a positive FIT patients are encouraged to seek contact with their GP. When a patient visits the GP, he/she can provide an overview of a patient's medical record, which the colonoscopy centre could ask for.

General practitioner involvement in cancer screening

As already briefly described, general practitioners (GPs) are involved in the current cancer screening programmes (CSPs) in the Netherlands and have certain 'formal' tasks. This involvement is however limited, varies between the programmes and has changed over time. GPs are relatively closely involved with the screening programme (SP) aiming at cervical cancer. Mostly they perform the Pap-smear, discuss the outcome, and refer the patient to the gynaecologist if necessary. Since 2017 procedures changed, and women have the option of using a self-sampling test. When women opt for this, the outcome of the self-sampling test is not automatically shared with the GP, due to privacy legislations. Outcomes will only be shared with the GP, if it is explicitly stated that the GP is allowed to receive this information. Regarding the CSP on breast cancer, the GP is involved in discussing the outcomes with participating women if abnormalities are detected (BI-RADS 4-5), or if insufficient clarity could be obtained (BI-RADS 0), and also arranges the referrals to the hospital when indicated. As for the colorectal CSP, the GP is the least involved. The GP will only discuss the outcomes with the patient upon request, and subsequently provides an overview of the patient's medical record for intake at the colonoscopy centre when indicated (Table 1).

In addition to these 'formal' tasks, GPs also have certain other, less strict defined tasks, such as explaining the pros and cons of participating in the CSPs when patients ask for that, and/or following requests for the guidance of patients who received outcomes of the screening test(s).[38-41]

Regardless of the specific role GPs have regarding the CSPs, GPs will always have a vested interest in well-organized and effective operating CSPs, as they will be the first health professionals to notice the effects when they are not functioning properly.

Challenges in current cancer screening

Current Dutch cancer screening programmes (CSPs) face numerous challenges, of which several concern the uptake of screening participation. Both nationally and regionally, the average attendance rates of the CSP targeting cervical cancer have become insufficient already for a decade. In addition, at a national level, the attendance rates for all three CSPs have declined over the past years (Figure 1). Whereas the latest percentages for the three CSPs (2022) were 54.8%, 72.5%, and 70.6%, for the programmes aiming at cervical, breast and colorectal (CRC) respectively, the attendance rates in 2010, for the cervical and breast CSPs, were still 65.5% and 80.7% respectively.[35-37] Since the CRC-SP has only been fully operational since 2019 (in all age groups), it is too early to

draw any conclusions on longer trends regarding this screening programme (SP). In this context, it should be noted that in literature, the CRC-SP is considered a success story; despite its recent introduction, it already achieved decent screening participation rates. Furthermore, at the regional level, there is a wide variation in screening participation rates, with lowest screening uptake among the four largest cities of the Netherlands, all way below the minimal intended effective rate of 70%, as stated by the WHO, for all three CSPs.[32] Moreover, there is a growing belief among GPs working in the large cities – the highly urbanised areas – of the Netherlands, that the people who could potentially benefit most from participating in screening are the least likely to participate. These screening participation challenges are not unique to the Netherlands, as they also occur in other similar countries, such as the Scandinavian countries, the United Kingdom and Australia.[42-45]

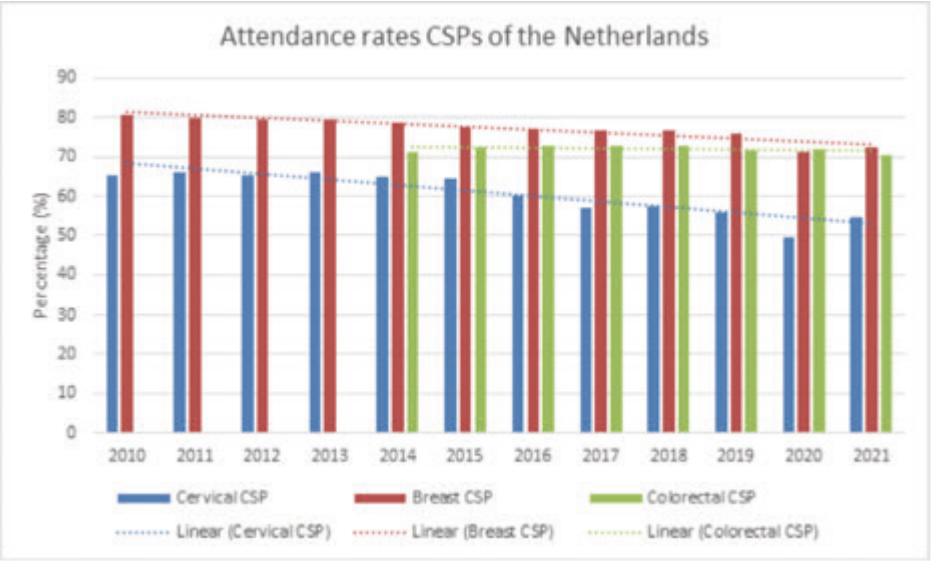

Figure 1. Attendance rates between 2010 and 2021. Based on the yearly monitoring rapports of RIVM. The horizontal grey line at 70% indicates the minimal effective rate as stated by the WHO. CSP= Cancer Screening Programme

Besides the challenges related to screening participation, there are other challenges related to both screening-eligible people and GPs. Issues which will be discussed in this thesis, are illustrated by the case of the Janssen family.

The story of the Janssens family – The Questions

The Janssen family lives in a big city in the Western part of the Netherlands. The family consists of three members: Maria, the mother, 54 years old; John, the father, 59 years old; and their daughter Sarah, 30 years old. They all see their general practitioner (GP) because they have questions concerning the cancer screening programmes (CSPs). Sarah just recently received an invitation to participate in the CSP aiming at cervical cancer. Maria and John recently had a discussion on participating in the colorectal cancer (CRC) screening programme (SP).

When Sarah consults the GP, she indicates that she does not know whether she wants to participate in the SP. She has read several stories on the internet, including that it has to do with changing sexual partners. Sarah just had one and the same boyfriend for many years now. Sarah tells the GP, that her mother Maria said to not act so weird and that she should 'just participate'. Maria's argumentation is: "The CSPs are very important and for a serious cause, so why not just participate?". Sarah does agree that the programmes are for a serious case, but also wonders about the disadvantages of participating. Thereby she read something about the self-sampling test, but she doubts that she is able to perform it herself.

When Maria gets invited for one of the CSPs, she always faithfully participates. She does think the CSPs are a bit of a hassle, but afterwards she is always relieved when nothing abnormal is found.

When Maria and John visit the GP, John mentions that he recently received an invitation (he might have overlooked an earlier invitation) to participate in the CSP on CRC. He indicates that he does not understand what he has to do with the stool test, and in addition, he says he was very surprised that he was suddenly invited. He thinks it is really strange that he actually never heard about the CSPs before.

The GP answers the family's questions as best as possible, but after the consultations he starts thinking on the advises and about the CSPs in general. Does Sarah have a point that it does not actually make sense for her to participate in the SP? What are actually the benefits and harms of participating in CSPs? Is it still best practice for everyone to always participate, thinking about Maria? Or is there any evidence why people are sometimes better off not participating? And what about John. Would there be many people who do not understand the invitation and have no idea about the CSPs at all? Finally, what is actually his role as a GP regarding the CSPs? Are the programmes organised efficient and effective, and as a GP, should he actually have a role in the CSPs?

Objective and outline of this thesis

The overall aim of this thesis was to identify cues that might contribute to optimizing the current attendance rates of the cancer screening programmes (CSPs) in the Netherlands, with a focus on the potential role of primary care. We explicitly use the term 'optimize', as it was not our intention to conduct studies with the main aim of increasing screening attendance. The presented studies in this thesis have the overarching goal to identify ways to screen screening-eligible people at highest risk, i.e., people who are a priori most likely to develop (one of) the screening-specific tumours. We stated our hypothesis as follows: where current CSPs handle a 'one-size-fits-all' approach, with a limited role for primary care and GPs, it may be more beneficial, also with respect to the sustainability of the CSPs, to shift to a more targeted approach for subpopulations at relatively higher risk, and with targeted and/or more sophisticated involvement of primary care health professionals and healthcare centres to support such a new approach. In order to test this hypothesis, we conducted several studies using different research designs and focussing on most relevant stakeholders (screening-eligible people and GPs) and the determinants of participating. The challenges mentioned in this introduction concerning CSP participation, and as illustrated by the case of the Janssen family will be addressed in this thesis. Presented studies are part of the *Screening the CITY* project, whereby CITY is also an acronym for: 'Cancer screening In The Hague. The influence of social and cultural determinants and health literacY on decision making'.

Chapter 2 provides a systematic overview of the literature regarding determinants of attendance and non-attendance at the CSPs in the Netherlands. This study served as an ideal starting point for this thesis by identifying current knowledge, and knowledge gaps. In **Chapter 3** we compared the CSPs aiming at breast and colorectal cancer in the city of The Hague, in order to understand the background of differing attendance rates and incidence data over a longer period of time. Hereto we gained a data-driven understanding of where possible future optimalisation strategies would be needed most. **Chapter 4** presents in-depth perspectives and beliefs of screening-eligible people in The Hague, concerning cancer screening attendance. Through these perspectives and beliefs, we learned what is (most) important to screening-eligible people when it comes to participating in CSPs. In **Chapter 5** we described how important and effective a targeted proactive primary care approach can be for a specific subpopulation. We were able to conduct a cross-sectional intervention study among marginalized women in the city of Rotterdam. **Chapter 6** describes the perceptions and beliefs of GPs concerning their role and involvement in the CSPs of the Netherlands. Finally, **Chapter 7** summarizes the findings of this thesis and discusses methodologic considerations, implications, and recommendations for future research.

List of abbreviations

CRC	Colorectal Cancer
CSP	Cancer Screening Programme
EU	European Union
GP	General Practitioner
NHG	Dutch College of General Practitioners
RIVM	National Institute for Public Health and the Environment
SP	Screening Programme
WBO	Population Screening Act
WHO	World Health Organization

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CHAPTER 2

Determinants of (non-)attendance at the Dutch cancer screening programmes: a systematic review

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Abstract

Objective

The Netherlands hosts three population-based cancer screening programmes (CSPs): for cervical, breast, and colorectal cancer. For a CSP to be effective high participation rates are essential. Current participation rates in the Netherlands are starting to fall below the minimal effective rate. This study aims to give a systematic overview of the current known determinants of (non-)attendance at the Dutch oncological screening programmes.

Methods

A comprehensive literature search was conducted in the electronic databases Academic Search Premier, Cochrane Libary, Embase, EMCare, PubMed, PsycINFO, Web of Science as well as in grey literature, including all articles published before February 2018. This study followed the PRIMSA guidelines. The I-Change model was used to categorise the identified determinants of screening attendance.

Results

In total 19/1232 identified studies were included, along with 6 grey literature reports. Fifteen studies reported on predisposing factors. Characteristics as social economic status, country of birth and residency are most often reported and correlate with screening attendance. Thirteen studies addressed information factors. Factors on awareness, motivation, ability, and barriers were less often studied.

Conclusion

Current studies tend to describe the general characteristics of (non-)attendance and (non-)attenders, but rarely provide in depth information on other factors of (non-) participation. The I-Change model proofed to be a useful tool in mapping current knowledge on cancer screening attendance and revealed knowledge gaps regarding determinants of (non-)participation at the CSPs. More research is needed to fully understand determinants of participation. This in order to influence and optimize attendance rates over the long term.

Introduction

The Netherlands invests considerable time and effort hosting three population-based cancer screening programmes (CSPs) aimed at cervical, breast, and colorectal cancer (CRC). CSPs aim to detect cancer in an early or precursor stage, thus improving survival via early intervention. On average, this approach is thought to lead to a better prognosis, as well as fewer and less severe side effects of the treatment.[1-4] CSPs in the Netherlands are offered free of charge by the Dutch government to all citizens of a specific age and gender. The National Institute for Public Health and the Environment (RIVM) and five regional screening organisations are charged with organizing and coordinating the programmes.[5] Attendance is voluntary and monitored yearly by the RIVM.[6-8] Although the three CSPs show many similarities, each CSP has its unique procedures and organization, mainly due to the differences in screening methods (Table 1). In Appendix A we describe the individual designs of the three CSPs.

High participation rates are essential for a national CSP to be effective. According to the World Health Organization (WHO) at least 70% of the target population should be screened.[9] Most recent national available attendance rates from the Netherlands (2016) were 60%, 77% and 73% for respectively the CSPs for cervical, breast and CRC. Despite these national numbers might be reassuring, an alarming sign is the downward trend in uptake which can be observed for both the long-lasting CSPs at cervical and breast cancer.[7,8,10] Furthermore, there is a wide regional variation in attendance rates; with the lowest attendance rates among the four largest cities of the Netherlands, which all fall below the 70%, the minimal effective rate, for all three CSPs.[11-13]

In order to influence and optimize attendance rates, it is essential to identify and understand determinants of (non-)attendance and follow-up adherence. This study aims to give a systematic overview of the current known determinants of (non-)attendance at the Dutch oncological screening programmes.

Table 1. Key characteristics of the three national cancer screening programmes in the Netherlands

		Cervical CSP	Breast CSP	Colorectal CSP
Since (year)		1979 (pilots from 1976)	1990 (pilots from 1984)	2014 (will be fully operational in 2019)
Population	Age category	30-60	50-75	55-75
	Sex	F	F	F&M
Interval (in years)		5	2	2
Primary test		hrHPV-test, cytology if necessary (then a Pap-smear as needed)	Mammography (bilateral)	FIT
Involvement GP		Performing cytological smear, discuss outcome, hospital referral[a]	Discuss outcome, hospital referral[b]	None[c]
Primary outcome		KOPAC-code[d]	BI-RADS-code	Negative, positive, unclear.
Financing	Invitation, primary test and analyses, referral when abnormalities are detected	Dutch government		
	Secondary tests & potential treatment	Standard healthcare, thereafter, depending on individual insurance policy		

F= Female, M= Male, hrHPV= high-risk Human papillomavirus, FIT= Faecal Immunochemical Test, GP= General Practitioner

[a]From 2017 onward, women can choose a self-sampling test. The outcome (negative, positive, or unclear) of the self-sampling test is not automatically shared with the GP, so the GP no longer plays an essential role in this CSP. If hrHVP is detected, women are advised to seek contact with their GP to perform a Pap smear at the GP's office.

[b]In cases where no abnormalities are detected the GP will not be involved.

[c]Since 2017 the GP no longer automatically receives the outcome of a FIT. However, after a positive FIT patients are encouraged to seek contact with their GP.

[d]KOPAC-code is a Dutch classification system comparable with the Pap-classification.

Methods

Search strategy

A comprehensive literature search was carried out which included all articles published before February 2018. We searched the following electronic databases: Academic Search Premier, Cochrane Library, Embase, EMCare, PubMed, PsycINFO, and Web of Science. The initial search was constructed in PubMed and included the following MESH terms: 'screening', 'cancer', 'participation' and 'Netherlands'. The full search is listed in Appendix B. The search was then extended to cover the other databases. No limitation was set on year of publication or study design. Grey literature was obtained from databases on the websites of the organizations RIVM,[5] Gezondheidsraad[14] and Volksgezondheidenzorg,[15] which are involved in cancer screening in the Netherlands. Reference lists of the included articles were reviewed for additional references. This review and its procedures were planned, conducted, and reported according to the PRISMA guidelines.[16] In advance our review was registered and accepted in the Prospero register of the National institute for Health Research (CRD42018089444).[17]

Study selection

Studies were included when they evaluated the outcome measurement "attendance/participation", and/or described the determinant measures "reasons for low and non-attendance" and were related to at least one of the current Dutch national CSPs. Studies were excluded when they were not in English or Dutch, or when they were non-original articles. Table 2 summarizes the inclusion and exclusion criteria. After removing duplicates, titles and abstracts were checked for inclusion and exclusion criteria. The abstracts of the remaining articles were independently assessed for applicability by the first and second author. The agreement rate was 92%, calculated over the first 120 articles (110/120). An additional 10% was randomly checked by the second author. In case of discrepancy the full text of an article was checked. The final full text evaluation of all the remaining articles was carried out by both the first and second author. Disagreement on inclusion was resolved by discussion with the full research team.

Table 2. Inclusion and exclusion criteria

	Inclusion criteria
1a.	Study outcome: the uptake/participation of national cancer screening programmes **OR**
1b.	Determinant measurements: reasons for low- and non-attendance (health literacy, decision making, social or cultural differences and organisational factors) AND cancer screening programmes
2.	Results are related to: cervical cancer and/or breast cancer and/or colorectal cancer
3.	The authors are related to Dutch organisations (universities) or the article describes Dutch cancer screening programmes
	Exclusion criteria
1.	Language other than English or Dutch
2.	Non-original articles, e.g. dissertations, reviews, case reports, editorials, oral presentations, poster presentations, book chapters

Quality assessment and data collection

All included scientific studies were subjected to qualitative analyses. For the quantitative studies the Crowe Critical Appraisal Tool (CCAT) was used.[18] For the qualitative studies we used the Consolidated criteria for reporting qualitative research (COREQ), as developed by the Dutch Cochrane Centre.[19] To analyse the determinants in a broad perspective, we used the Integrated Model for Behavioural Change (I-Change model, see Figure 1).

The I-Change model

Since screening attendance can be seen as health behaviour, determinants of this particular health behaviour can be studied by using health behaviour models. We used the Integrated Change model (I-Change model, Figure 1)[20-22] to map all the identified determinants. We chose this model since it incorporates elements from several earlier and highly used and appreciated health behaviour theories such as the Health Belief Model, Protection Motivation Theory, Theory of Planned Behaviour, and Precaution Adoption Process Model.[23-26] The I-Change model includes factors on predisposing, information, awareness, motivational, ability and barriers.

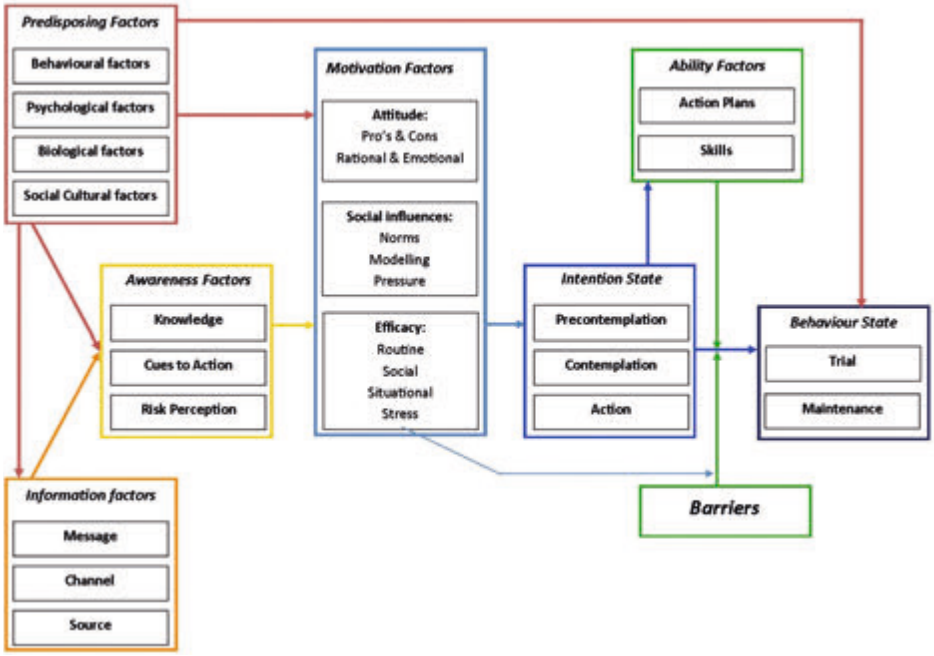

Figure 1. The Integrated Model for Behavioural Change (I-Change Model). The arrows represent the influence between the different factors

Results

Study retrieval

The initial search yielded a total of 2433 articles (Academic Search Premier 73, Cochrane Library 98, Embase 853, EMCare 185, PubMed 604, PsycINFO 23, Web of Science 597; see Figure 2 for the PRISMA flow chart). A total of 1201 articles were identified as duplicates and another 715 articles did not meet the inclusion criteria. Therefore, 517 studies remained after the first exclusion round. After the second round, 81 studies remained and were selected for full text review. In total 19 articles were included in the final selection, including 13 quantitative and 6 qualitative studies. The quality appraisal score of the 13 studies was average to high and ranged from 32 to 38 points (maximum 40), with a rounded average of 36 points. With respect to the qualitative studies, we scored a range from 5 to 6 (maximum 7) with a rounded average of 6 points. Since we did not assign extremely low-quality scores, we did not exclude any studies from further analysis based on the CCAT or the COREQ. Characteristics of the included studies are summarized in Supplementary Tables 1 and 2. Six reports were included as grey literature.[6,7,11,12,13,27] The identified determinants of low or (non-)attendance are presented in Table 3.

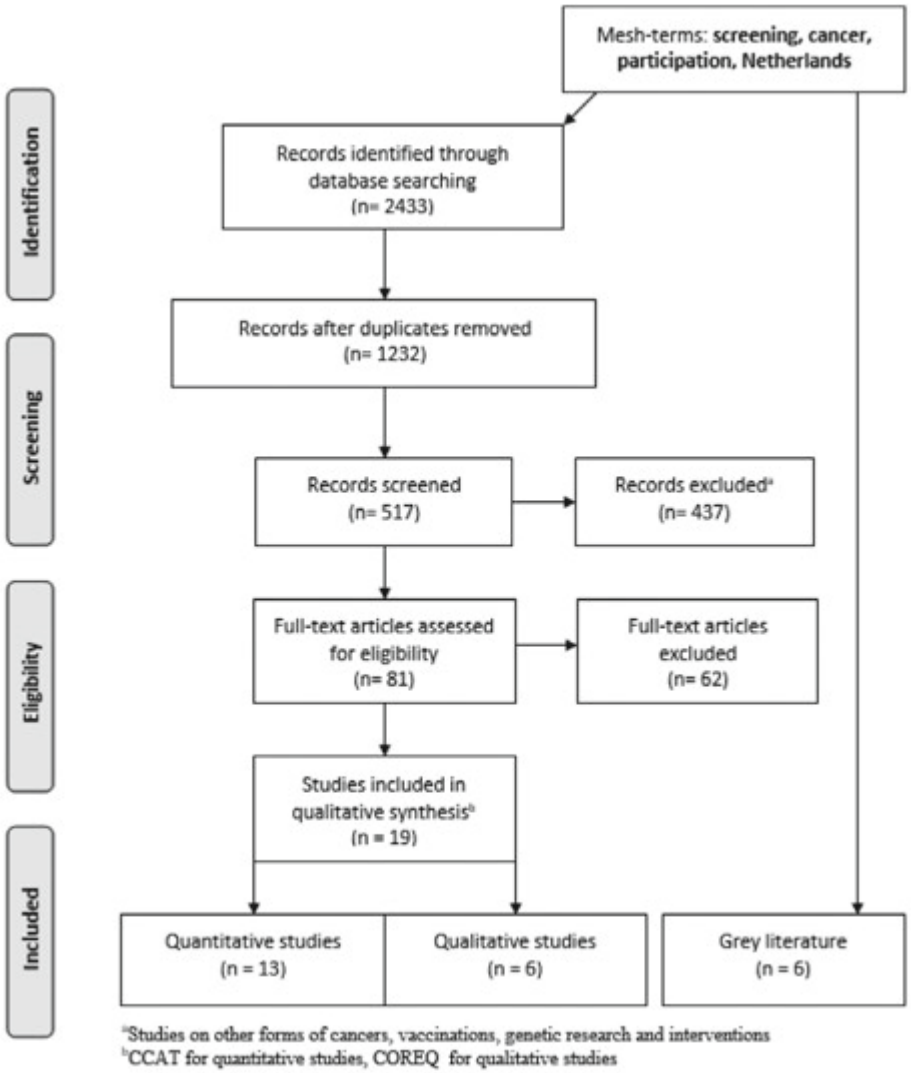

Figure 2. PRISMA flowchart of the search strategy. Search until 1st of February 2018

Predisposing factors

Most studies (n=15) reported on predisposing factors, mainly the general characteristics of (non)attenders.[6,7,11-13,28-37] For all three CSPs country of birth seems to influence attendance, with those not born in the Netherlands showing low(er) uptake.[12,28-33,36,37]

For the cervical and breast CSPs, residency and socio-economic status (SES) were frequently reported determinants of participation.[13,28,30,31,34-36] Women living in more

urbanized regions – the four main cities of the Netherlands: Amsterdam, Rotterdam, Utrecht and The Hague – and women belonging to a low-SES group showed lower attendance.[12,13,35] This is particularly detrimental as most abnormalities of the breast and cervix were found in women born outside the Netherlands and in women in lower SES-groups. Additionally, most unfavourable tumour-node-metastases were also found in the low-SES groups.[33,34,36-38]

Younger age was found to be a determinant of lower attendance in the cervical and the CRC CSPs,[6,7,11,31] whereas being single or divorced or having had only one sexual partner increases the likelihood of screening uptake in the cervical CSP.[28,31]

With respect to screening adherence and the implementation of the self-sampling test among non-responders, native Dutch non-attendees returned more of the self-sampling kits then non-native Dutch non-attenders. Furthermore, women who were screened in the previous rounds seemed to return more self-sampling kits than under-screened or never-screened women.[37]

Information factors

Thirteen studies described information factors to some extent.[29-32,35,38-45] At all three the CSPs several studies addressed the lack of tailored communication tools and strategies to inform subpopulations. The need to develop new tools and strategies has been recognized and would particularly benefit ethnic (minority) groups.[29,32,35,40,41,42,43]

Four studies related to the cervical CSP reported higher attendance rates when the invitation procedure (invitation and reminder) was general practitioner (GP)-based (the channel).[30,31,38,39] This approach was found to be particularly effective among women who were not born in the Netherlands.[30] The in 2017 introduced self-sampling test within the cervical CSP has been described as a promising, feasible and effective procedure for increasing coverage in a screening programme.[38,40,41] Self-sampling responders who did not participate in previous rounds were more often hrHPV positive and had a higher relative risk of ≥cervical intraepithelial neoplasia (CIN) II and ≥CIN III compared with self-sampling women who were screened in the previous rounds.[38,40]

Knops-Dullens et al. stated that in order to motivate Dutch women to participate in the screening programme they need to be convinced that the advantages outweigh the disadvantages.[44]

With respect to the CRC CPS a study adding extra instructions and information and addressing specific concerns should be considered in order to improve informed decision making about participation.[45]

Since January 2018 a GP no longer receives an automatically generated message in case of a pathological result, although patients are encouraged to seek contact with their GP.[27]

Awareness factors

Several studies identified the lack of knowledge as a determinant of non- or low-attendance.[31,37,42,46] Cervical CSP non-attenders felt that they had a lower risk of developing cervical cancer and were more convinced that cervical cancer cannot be cured.[31,40,44] A study among non-native Dutch found that all respondents recognized their susceptibility to CRC, but their knowledge of CRC and the CSP were limited.[42] Attending the CSP was a low priority, and limited concerns about health in general and serious concerns regarding safety were additional reasons for non- or low-attendance.[29,45,46] With respect to the cervical CSP, self-sampling might be a solution for non-attenders because of convenience and self-control.[29] Most often non-attenders reported they forgot to schedule an appointment.[29]

At the CRC CSP non-attenders thought that mainly individuals in poor health and with (cancer) symptoms would benefit from the programme. Knowledge of potential harm associated with CRC CSP was also low.[42]

Motivational factors

Non-attenders of the cervical CSP were less motivated, less often inclined to undergo future screening and experienced greater negative social influences. They reported negative role models and talked less with other people about the CSP.[44] Self-efficacy was identified as an important determinant for CRC CSP attendance.[42]

A positive remark could be found in the quick uptake and adherence of the CRC CSP. A study by Toes-Zoutendijk underlined the importance of real-time monitoring. Only a few months after implementation of the CRC CSP, participation and positive test results were higher than predicted, whereas the positive predictive value was lower than predicted. To reduce the burden of unnecessary colonoscopies and improve colonoscopy capacity, the cut-off level for a positive FIT result was adjusted and a cut-off level of 47µg Hb/g faeces is currently being used in the Netherlands.[43]

Ability factors

In the cervical CSP forgetting to make an appointment was the main reason for non-attendance.[29] The language barrier and low health literacy were other important determinants of non-attendance of the CRC CSP among non-native Dutch.[42]

Barriers

Non-attenders at both the cervical and the CRC CSP experienced more affective disadvantages: they were more insecure, more afraid, had more serious concerns regarding the test and outcome, and anticipated more feelings of shame. Other identified barriers were time-related or were related to being unable to attend the CSP, for example due to other illnesses.[29,44,45,46]

Concerning breast cancers, a study in 2011 stated that despite the absence of financial barriers for participation, SES inequalities in attendance rates existed.[34]

Table 3. Determinants of low-/non-attendance at a Dutch CSP, subdivided by the I-Change model

		Cervical CSP	Breast CSP	Colorectal CSP
Predisposing factors				
Behavioural	Residency: more urban	X[12]	X[13, 35]	
	Marital status: Married/in a relationship	X[28]		
	Several different sexual partners	X[31]		
Psychological				
Biological	Age: younger age	X[7,31]		X[6,11]
	Sex: male	NA	NA	X[8, 24]
	Higher risk (ethnicity)	X[36-38]	X[33,34]	
Social & Cultural	Country of birth: non-native Dutch/non-Western	X[12,28-31,36,37]	X[33]	X[32]
	SES: low(er) SES	X[28,30,31 36]	X[34, 35]	
Information factors				
Message		X[44]		X[45]
Channel	Lack of tailored strategies	X[29,40,41]	X[35,42]	X[32,43]
Source	Non-GP practice-based invitation	X[30,31,38,39]		
Awareness factors				
Knowledge	Misconceptions, lack of knowledge e.g. screening harm	X[31,37]		X[42,46]
Cues to action	Low priority	X[29]		X[45,46]
Risk Perception	Perceived lesser risk of cancer	X[31,40,44]		X[42]

Table 3. Determinants of low-/non-attendance at a Dutch CSP, subdivided by the I-Change model **(continued)**

		Cervical CSP	Breast CSP	Colorectal CSP
Motivational factors				
Attitude	No future testing needed, less moral obligation	X[44]		X[43]
Social influence	Negative social influence, negative role models, talked less with others	X[44]		
Self-efficacy	Low self-efficacy			X[42]
Ability factors				
Action plans	Forgot to make an appointment	X[29]		
Skills	Language barrier/low health literacy			X[42]
Barriers				
	Test: insecure, anxious	X[44]		X[45]
	Outcome of the test: insecure, anxious	X[44]		
	Inconvenience: feelings of shame	X[29, 44]		X[45]
	Time related: forgot, too busy	X[29]		X[46]
	Health related illness: other illnesses			X[46]
	Financial		X[34]	

CSP= Cancer Screening Programme, NA= Not Applicable, GP= General Practitioner

Discussion

This systematic review describes all known determinants of (non-)participation for the three Dutch cancer screening programmes (CSP). Studies tend to describe the more general characteristics of (non-)attenders, but rarely provide in depth information on other factors of (non-)participation. The I-Change model proofed to be a useful tool in mapping current knowledge on cancer screening attendance and revealed knowledge gaps regarding determinants of (non-)participation at the CSPs. Many studies reported on predisposing and information factors giving a general well understanding of these determinants. Factors on awareness, motivation, ability, and barriers were less often studied.

By using a theoretical framework designed to explain health behaviour, the I-Change model[47], we could systematically summarize and merge all information from the identified studies. Similar to other reviews, we were only able to take published literature into account, which could result into a publication bias. We choose for a health behaviour model since screening attendance can be seen as health behaviour. The I-Change model is a widely used and accepted theoretical framework to evaluate health behaviour.[20-22,48] The I-Change model states that behaviours are determined by a person's motivation or intention to carry out a behaviour, which is in turn the result of a person's intentions, abilities, and barriers. Attitudes, social influences, and self-efficacy expectations influence a person's motivation and are determined by various distal factors, such as predisposing (e.g., current lifestyle), information (e.g., source of delivery), and awareness (e.g. knowledge) factors. To the best of our knowledge this is the first review to use this approach to summarize available information on determinants of participation in CSPs. The I-Change model allowed us to identify knowledge gaps and so highlight opportunities for improvement.

For a CSP to be effective high participation rates are essential. The attendance rates for the two long-term CSP programmes in the Netherlands, cervical and breast cancer, are declining. The attendance rates of the cervical CSP are especially low and are below the 70% target which is seen by the WHO as the minimum effective rate. Furthermore, attendance rates show wide variation between regions and subpopulations. Lower attendance rates were found among those belonging to a low-SES group, living in more urban regions and among people who were not born in the Netherlands (in some studies referred to as 'non-native Dutch' and in others as 'non-Western immigrants'). These figures are in line with earlier published reviews.[49-51] Furthermore, younger women show lower attendance rates at the cervical CSP, and men in general show lower attendance

at the CRC CSP. The latter issue was also addressed in an earlier review on CRC CSPs worldwide by Navarro et al.[52]

While several studies have described attendance rates and the characteristics of (non-)attenders, in depth analyses of why people do or do not participate in a CSP are scarce. During our analysis it became clear that while many studies have focused on low attendance groups, little is still known on why these groups fail to attend CSPs and even less is known on why individuals from high attendance groups actually attend CSPs. When we considered various elements of the I-Change model, we were unable to find any studies on the sub-elements' psychological factors (predisposing factors) and message factors (information factors). With respect to the other (sub)elements of the I-Change model, most were only addressed in one study and/or in relation to only one CSP. One study by Hartman *et al*. attempted to interpret knowledge derived from research on the cervical CSP to explain factors concerning the breast CSP.[49] The sub-elements under the predisposing factors are most often reported as characteristics of the non-attenders.

As our focus was on Dutch CSPs, determinants of (non-)participation described in international studies of CSPs were excluded. Although several countries have comparable CSP to the Netherlands, every country has own and unique screening programs adapted to their health system and population. As these inter-nation-differences would cause a problem comparing results we choose to focus only the Netherlands. Some international reviews, however, have focussed on determinants not yet studied in the Netherlands, for example the sex of the screener, the presence of symptoms and the existence of family conflicts.[53-55] Additionally, lessons learned throughout this review might also be applicable to other European/Western countries.

In the Netherlands, the involvement of the general practitioner (GP) in the CSPs has decreased over the past five years. However, it is clear, at least for the cervical CSP, that direct involvement of the GP results in higher attendance rates, especially among the high-risk groups (high cancer risk in known low-attendance groups).[30,31,39] Whether this involvement should be (re)introduced is a matter of debate, but at the very least a more prominent GP role in informing and activating people to participate in CSPs could be further explored. The importance of such a role for GPs is highlighted in several international studies, with highest beneficial effects for the lower socioeconomic and minority groups.[56, 57]

It is often said that financial barriers are irrelevant in the Netherlands,[34] but this is only partly true. While participation in a CSP is free, whenever follow-up research is needed, a patient will have to cover a part of the cost of follow-up research themselves, depending

on their specific insurance plan. Since screening programmes may exacerbate socio-economic and ethnic health differences,[58] future studies are also needed that address this topic.

In this review we not only looked at the three Dutch CSPs individually, but also compared the outcomes of these CSPs. This allowed us to compare characteristics of non-attenders and determinants of participation. Of the three Dutch CSPs, cervical cancer screening shows the lowest attendance rates. In the literature some explanations were offered for why women often fail to attend the cervical CSP. However, a possible explanation for the low uptake might be that a cervical examination remains a greater taboo compared to examination of the breast. An additional explanation might be the concrete appointment arranged by the breast CSP, whereas in the cervical CSP women have to make an appointment with their GP themselves. An advantage of the CRC CSP compared to the cervical CSP is that the CRC faeces test can be completed at home. In 2017 a self-sampling test for HPV infection was introduced within the cervical CSP. The self-sampling test has shown to have high concordance with physician-taken sampling for hrHPV detection and was found to be highly acceptable to women.[59] It would be interesting to see the effect of this self-test on participation rates among the different cervical CSP attendance groups. While the self-sampling test appears promising, we think there is still room for improvement. Women are only informed about the possibility of a self-sampling test in the initial invitation letter from the screening organisation. An application form to actually order the self-sampling test is only attached when a re-invitation has to be sent. Therefore, women themselves still have to take the initiative in order to receive a self-sampling test at home. It would be more logical to include an application form with the initial invitation letter and to include the self-sampling test together with the re-invitation for women who have not yet responded to the first letter. A similar proposal has already (partly) been made by the Health Council of the Netherlands.[60] Besides the different tests used in the three Dutch CSPs, there are also clear differences in the occurrence of the different cancers. Per year 700-800 women are newly diagnosed with cervical cancer, whereas the incidence of breast and CRC is far higher at 16.000 and 13.000 cases per year, respectively. A higher incidence means that people are more likely to be aware of breast and CRC, or to know someone who has had breast or CRC compared to cervical cancer.

In conclusion, although the three CSPs in the Netherlands generally have high attendance rates, large differences are present between different regions and subpopulations. The I-Change model highlighted many knowledge gaps in determinants of (non-)participation and identified opportunities for improvement. Current studies tend to focus on attendances rates and the general characteristics of (non-)attenders, but rarely provide in depth information on determinants of (non-)participation. We therefore feel that more

detailed studies are needed, as only by understanding the determinants of participation can we influence and alter them, and thus optimize current CSPs over the long term.

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Appendix

A. Description of the three Dutch national cancer screening programmes

Cervical cancer screening programme

The cervical CSP was nationally implemented in 1979 and currently invites women aged between 30-60 years to participate at 5-year intervals.[1, 2] Over the past few years several adjustments have been made to the design of this CSP.[3] In 2016 the invitation strategy was altered; whereas potential participants used to be invited by their own GP or by the local screening organization, nowadays this is the exclusive responsibility of the local screening organization. In 2017 adjustments were made regarding the testing procedure and the time interval of the cervical CSP. First, instead of performing a classical Papanicolaou (Pap) smear for cytological abnormalities at the GP's office, a new test for high-risk human papilloma virus (hrHPV) was added prior to investigation of aberrant cells. Several studies have shown that adding an HPV test is both more sensitive and specific in the detection of cervical cancer than cytology alone.[4-6] A second modification was the introduction of the self-sampling test for hrHPV. Before 2017 all women who wanted to participate had to see their GP for a smear, whereas they can now choose to use the self-sampling test instead. However, if this test gives a positive result, they still need to see their GP in order to have a smear that can be checked for cytological abnormalities. The outcome of the hrHPV test is sent by letter by the local screening organization. In case of a positive cytological result, hospital referral will be handled via the GP. A final change, also implemented in 2017, is an adjustment to the length of the interval between individual tests. Women aged between 45 and 55 only receive an invitation if they tested positive in previous rounds or did not attend. The maximum screening interval can therefore be extended by 10 years for women from the age of 40.

Breast cancer screening programme

The breast CSP became nationally available in 1990.[7] All women aged between 50 and 75 years (till 1998 age boundaries were 50-70 years) are biennially invited by letter, via a local screening organization, for a mammography. Women are able to refuse participation by unsubscribing from the invitation letters, either temporarily or for all future invitations. Most mammography's take place at mobile research units, where two independent radiologists assess the mammogram (double reading). The results are shared with the participants via the screening organizations. In case of an unclear outcome of a mammogram or when a disorder is detected, further investigation will be needed, and the GP will be informed. The GP will contact the participant and arrange a hospital referral. Women are informed about the outcome by letter via the screening organization, which also provides information on the subsequent follow-up.[8]

Colorectal cancer screening programme

The CSP for colorectal cancer (CRC) is relatively new (2014) and the entire programme should be fully implemented by 2019.[9] Invitation depends on year of birth, and both men and women aged between 55-75 years are invited. Invitees can choose to unsubscribe from participation. In case of no response a reminder is sent after two months. If a re-invitation remains without response, the potential participant will only be re-invited after an interval of two years.[10] The faecal immunochemical test (FIT) was chosen as screening test, since previous studies found this test to be the most acceptable to the Dutch population.[11] This test can easily be performed at home. FIT screening requires successive screening rounds for optimal programme sensitivity.[11] The cut off level for a positive FIT was increased in mid-2014 from 15 to 47µg Hb/g faeces. This was done in order to reduce the burden of unnecessary colonoscopies and improve colonoscopy capacity. Referral is arranged by the local screening organization.[12] The GP has no active role within this CSP, but patients are advised to seek contact with their GP after a positive FIT.[13]

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B. Mesh terms and free text search. As used for the initial search in PubMed

('Mass Screening'[Mesh] OR 'Mass Screening'[All fields] OR 'Mass Screenings'[All fields] OR 'cancer screening'[All fields] OR 'cancer screening programme'[All fields] OR 'Screening programme'[All fields] OR 'population screening'[All fields] OR 'screening programmes'[All fields] OR 'national population screening'[All fields] OR 'cancer screening programs'[All fields] OR 'screening programs'[All fields] OR 'Early Detection of Cancer'[Mesh] OR 'Early Detection of Cancer'[All fields] OR 'screening'[all fields]) AND ('Breast Neoplasms'[Mesh] OR 'Breast Neoplasms'[All fields] OR 'Breast neoplasm'[All fields] OR 'Breast cancer'[All fields] OR 'Breast cancers'[All fields] OR 'Mammary cancer'[All fields] OR 'Mammary cancers'[All fields] OR 'Breast carcinoma'[All fields] OR 'Breast carcinomas'[All fields] OR Colorectal*[all fields] OR 'colon'[all fields] OR 'Colorectal Neoplasms'[Mesh] OR 'Colorectal Neoplasms'[All fields] OR 'colorectal neoplasm'[All fields] OR 'colorectal carcinoma'[All fields] OR 'Colorectal Carcinomas'[All fields] OR 'Colorectal tumor'[All fields] OR 'Colorectal tumors'[All fields] OR 'colorectal cancer'[All fields] OR 'colorectal cancers'[All fields] OR 'colorectal adenomas'[all fields] OR 'colorectal cancer screening'[all fields] OR 'uterine'[all fields] OR 'uterus'[all fields] OR 'cervix'[all fields] OR 'cervical'[all fields] OR 'Uterine Cervical Neoplasms'[Mesh] OR 'Uterine Cervical Neoplasms'[All fields] OR 'Cervix cancer'[All fields] OR 'cervix cancers'[All fields] OR 'cervix neoplasm'[All fields] OR 'cervix neoplasms'[All fields] OR 'cervical neoplasms'[All fields] OR 'cervical neoplasm'[All fields] OR 'cervix carcinoma'[All fields] OR 'cervical cancer'[All fields] OR 'cervical carcinoma'[All fields] OR 'Neoplasms'[Mesh] OR 'Neoplasms'[All fields] OR 'neoplasm'[All fields] OR 'cancer'[All fields] OR 'cancers'[All fields] OR 'carcinoma'[All fields] OR 'carcinomas'[All fields] OR 'tumor'[All fields] OR 'tumors'[All fields] OR 'cancer screening'[all fields]) AND ('Netherlands'[Mesh] OR 'Netherlands'[all fields] OR 'Netherlands'[ad] OR 'Holland'[tw] OR 'Dutch'[All fields] OR 'hague'[tw]) AND ('No-Show Patients'[Mesh] OR Non attend*[all fields] OR nonattend*[all fields] OR 'Non attending patients'[All fields] OR 'No Show patient'[All fields] OR 'No Show patients'[All fields] OR No-Show*[all fields] OR noshow*[all fields] OR 'uptake'[All fields] OR 'participate'[All fields] OR 'participation'[All fields] OR 'patient participation'[Mesh] OR 'Patient participation'[All fields] OR 'screening uptake'[All fields] OR 'attending'[All fields] OR 'attendance'[All fields] OR 'Mass Screening/utilization'[Mesh] OR 'Patient Dropouts'[Mesh] OR Dropout*[all fields] OR drop out*[all fields] OR dropped out*[all fields] OR 'Patient Compliance'[Mesh] OR 'compliance'[all fields] OR compliant*[all fields] OR comply*[all fields] OR 'utilization' [Subheading] OR 'Utilization Review'[Mesh] OR utilisation*[all fields] OR utilization*[all fields] OR 'Patient Acceptance of Health Care'[Mesh]

Supplementary Table 1. Characteristics of the included quantitative studies, per type of cancer screening programme

Cervical cancer screening programme

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Gok, Heideman et al. 2012) **Ref: 38**	Retrospective observational cohort study	54,482 non-responders Group 1: 27,792 (self-sampling group 1) & 281 (recall/control group). Group 2: 26,145 (self-sampling group 2) & 264 (recall/control group).	Women, age 30-60. Between December 2006 to March 2008. North Holland and Flevoland. Non-responder= Women who had not responded to two invitations from the regular screening programme in 2005 & 2006. Self-sampling tool per group: 1: Delphi-Screener 2: VibaBrush	Age (group) Screening history Method invitation Country of birth Self-sampling: 29% Recall: 12% Group 1: 27% Group 2: 31%	Native Dutch non-attendees responded better than immigrants (32% vs. 22%, p<0.001) and those screened in previous round revealed higher response than underscreened or never screened. ≥ CINII rates were higher amongst responding native Dutch women than immigrants (p<0.001), and higher in under-/never- screened women than in women screened in the previous round (p<0.001). Self-sampling increases efficacy screening programme by targeting a substantial portion of non-attendees of all ethnic groups who have not regularly been screened and are at highest risk of ≥CIN II.	Predisposing factors Awareness factors

Cervical cancer screening programme (continued)

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Gok, Heideman et al. 2010) **Ref: 37**	Prospective observational cohort study	28,073 non-responders 27,792 were assigned to self-sampling group & 281 to the recall group/ control group.	Women, age 30-60. Between December 2006 to December 2007. North Holland and Flevoland. Non-responder = Women who had not responded to two invitations from the regular screening programme.	Age Screening history Self-sampling group 26.6% vs. 16.4% of the control group.	Self-sampling responders who did not participate in the previous rounds of screening had an increased relative risk of ≥CIN II and ≥CIN III compared to self-sampling women who had been screened in the previous rounds. Self-sampling is a feasible and effective method for increasing coverage in a screening programme. Especially because of the higher risk in non-attenders.	Predisposing factors Information factors

Cervical cancer screening programme (continued)

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Bais, Van Kemenade et al. 2007) **Ref: 40**	Interventional trial in addition to the regular population-based cervical cancer screening programme	2,830 non-responders 2,546 were assigned to the self-sampling group & 284 to the recall group/control group.	Women, age 30-50. Between January 2003 and April 2004. North Holland. Non-responder = Women who had not responded to two invitations from the regular screening programme. Control group received second re-invitation.	Age Screening history Self-sampling 34.2% vs. 17.6% of the control group.	hrHPV positive self-sampling responders were less likely to have a prior screening history than screening participants. Self-sampling is attractive adjunct to increase uptake, without markedly increased costs.	Information factors

Cervical cancer screening programme (continued)

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Bulkmans, Bulk et al. 2006) **Ref: 41**	Retrospective observational cohort study hrHPV testing was added to cervical screening in the POBASCAM-trial.	44,102	Women, age 30-60. Between 1999-2002. Amsterdam (North Holland).	Before: 58.7% and after: 61.4% implementation hrHPV testing.	hrHPV testing can be added to cervical screening by cytology without a decrease in participation rate.	Information factors
(Van Leeuwen, De Nooijer et al. 2005) **Ref: 36**	Retrospective observational cohort study	251,446	Women, age 30-60. Between 1998 and 2001. South Holland & Zeeland.	Age SES Country of birth Overall: 55.7% Born in the Netherlands: 56.8% Other Western countries: 45.3% Moroccan: 35.9% Turkey: 48.0% Suriname: 51.3% Dutch Antilles: 46%	Although cervical screening is free of charge, participation rates differ greatly between ethnic groups and between women from different socio-economic strata. Abnormalities were found more often in women who were not born in The Netherlands and in women with lower socio-economic status. These groups show lower attendance at the screening programme.	Predisposing factors

Cervical cancer screening programme (continued)

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(De Nooijer, De Waart et al. 2005) **Ref: 30**	Retrospective observational cohort study	237,719 37.1% by invitation of the GP and 62.9% by Municipal Health Service (GGD).	Women, age 30-60. Between 2000-2003. South Holland & Zeeland.	Age SES Country of birth Invitation Zip code After GP invitation 7.9% higher attendance than by GGD.	After invitation by a GP attendance rates were 7.9% higher for the entire population. This difference was even higher for women born in Morocco, Turkey, Suriname and the Dutch Antilles and for women with low-SES and living in a rural area.	Information factors

Cervical cancer screening programme (continued)

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Hermens, Tacken et al. 2000) **Ref: 39**	Cross-sectional observational study	5,548 Selection of 122 family practices, representative of all family practices in The Netherlands. Approximately 40 practices per approach. Evaluation of three organizational approaches. Comparison between family practice-based, community-based, and a combination of the two.	Women, age 35-60. Between September and November 1996. The Netherlands.	Age Invitation strategy Younger women (≤45): Family practice-based approach: 68% Combination approach: 62% Community-based approach 53% Older women (>45): Family practice-based approach: 58% Combination approach: 60% Community-based approach 47%	A reminder from the family physician increased the attendance rate from 7 to 11%. A family practice-based cervical screening approach appeared to be the most effective at a national level, achieving the highest attendance rate (also highest coverage and control rate).	Information factors

Cervical cancer screening programme (continued)

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Kreuger, van Oers et al. 1999) **Ref: 28**	Retrospective observational cohort study	70,621	Women, aged 35-54, between 1992 and 1994. In 53 neighbourhoods of Rotterdam (South Holland).	SES Marital status Nationality Range: 36-58%, depending on neighbourhood.	Risk groups are clustered in neighbourhoods and can be identified by SES, marital status and nationality. High-SES level of a neighbourhood, low-percentage migrants, single or divorced women correspond with high attendances.	Predisposing factors

Breast cancer screening programme

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Aarts, Voogd et al. 2011) **Ref: 34**	Retrospective observational cohort study	1,067,952	Women, age 50-75, from 1998 to 2006. Southern Netherlands Data combined with the Eindhoven Cancer Registry (ECR). As of 1998 women aged 70-75 were also invited within this screening programme. Before 1998 age boundaries were 50-70.	Age SES Year of invitation Low-SES: 79% Medium-SES: 85% High-SES: 87%	Women with low-SES had an unfavourable tumour-node-metastasis. Despite the absence of financial barriers for participation, SES inequalities in attendance rates exist.	Predisposing factors Barriers

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Vermeer and Van Den Muijsenbergh 2010) **Ref: 35**	Retrospective observational cohort study	977,961 (1997-1998) vs. 1,279,982 (2007-2008)	Women, 50-75 year. Comparison between attendance rates of 1997-1998 and 2007-2008. The Netherlands.	Country of birth Invitation period Screening region Attendance rates 1997-1998: Dutch: 81% Africa, Asia or Latin America: 56% Turkish: 50% Moroccan: 43% Attendance rates 2007-2008: Dutch: 83% Africa, Asia or Latin America: 63% Turkish: 62% Moroccan: 54%	The Western region, where most migrants live, had the lowest attendance rates in 1997-1998 and in 2007-2008. Attendance rates of migrant women increased over the past 10 years. However, specific efforts to increase the attendance rates are needed because current attendance rates are still far below the overall rates.	Predisposing factors Information factors

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Visser, van Peppen et al. 2005) **Ref: 33**	Retrospective observational cohort study	824,916	Women, age 50-75 between 1995 and December 2002. North Holland & Flevoland. Data on invited and/ or screened women in a second or subsequent round. As of 1998 women aged 70-75 were also invited within this screening programme. Before 1998 age boundaries were 50-70.	Age Area of residence Country of birth Overall attendance: 76% Residents of Amsterdam: 68% Attendance rate per country of birth: Netherlands 79% Suriname 59% Turkey 44% Morocco 37%	Women born in non-Western countries attend breast cancer screening less frequently, but also have a low detection rate. This justifies a passive attitude towards the low attendance.	Predisposing factors

Colorectal cancer screening programme

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Toes-Zoutendijk, van Leerdam et al. 2017) **Ref: 43**	Retrospective observational cohort study Monitoring of the newly nationally enrolled cancer screening programme.	741,941	Target population 2014. Males and females reaching age of 63, 65, 57 or 75 years. The Netherlands.	Sex Age 71.3%	A few months into the program it appeared that participation and positive test results were higher than predicted. The positive predictive value was lower than predicted. To reduce the burden of unnecessary colonoscopies and improve colonoscopy capacity, the cut off level for a positive FIT was increased. Close monitoring of the implementation of the program allowed for rapid adjustment.	Information factors Motivational factors

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Deutekom, Rijn et al. 2009) **Ref: 32**	Prospective observational cohort study	10,054	Males and females, age 50-75. Between May 2006 and January 2007. Amsterdam (North Holland). Study was performed before the implementation of the national screening programme. Invitations by Comprehensive Cancer Centre Amsterdam (CCCA).	Age Sex Country of birth Overall: 49%. Dutch: 52% Other Western: 46% Suriname and Antilles: 36% Asian: 38% Middle East and Central East: 21% African: 34%	Participation among ethnic minority groups was significantly lower than among ethnic Dutch. Studies are needed to explore whether groups are not reached or that lower uptake is determined by other causes.	Predisposing factors Information factors

Supplementary Table 2. Characteristics of the included qualitative studies, per type of cancer screening programme

Cervical cancer screening programme

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Bosgraaf, Ketelaars et al. 2014) **Ref: 29**	Questionnaire study	30,130 (non-responders). Analysis of 9,484 with self-sampling device and 682 without.	Women, age 30-60. Between October 2011 to December 2012. North Holland, Flevoland, Utrecht & Gelderland.	Non-attendance: forgot to schedule an appointment. The main reason to use the self-sampling device: own time-setting. Convenience and self-control. 30.9% who did not use self-sampling device preferred after all to have a cervical smear taken instead.	Organisational barriers are the main reason for non-attendance of regular cervical screening. Self-sampling might be a solution for non-attenders because of convenience and self-control.	Information factors Barriers
(Knops-Dullens, de Vries et al. 2007) **Ref: 44**	A computer-assisted telephone survey	165 100 attendees and 65 non-attendees. Random sample of 300 attendees and 600 non-attendees. Drawn from a total of 20,000 women.	Women, age 30-60. Between January and July 2001. Limburg.	Attendees perceived more positive social influence, more positive role models, talked more often with others and perceived a more positive norm. Non-attendees experienced more affective disadvantages, were more insecure and afraid of smear taking, experienced more feelings of shame and were more insecure and anxious about the result.	In order to motivate Dutch women to participate in the screening programme they need to be convinced that the advantages outweigh the disadvantages.	Information factors Awareness factors Barriers

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Tacken, Braspenning et al. 2007) **Ref: 31**	Questionnaire study	Analyses on 1392 women (968 screened and 424 unscreened). 2,224 (1204 screened, 1020 unscreened).	Women, age 30-60. Between December 2000 and February 2001. The Netherlands.	Women aged 40-50 years who felt a high personal moral obligation, who had only ever had one sexual partner, and who were invited and reminded by their own general practice had the greatest likelihood of screening uptake. Women's beliefs are the best predictors of uptake. Non-responders (mainly unscreened) thought they had less risk of cervical cancer, were less motivated, less often intended to take part in future screening, and were more convinced that cervical cancer cannot be cured.	To improve uptake: focus on moral obligation of eligible women, beliefs about the risk of cervical cancer, and available cures. Invitations and reminders within general practices enhance the uptake rate.	Predisposing factors Information factors Motivational factors

Colorectal cancer screening programme

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Woudstra, Dekker et al. 2016) **Ref: 42**	Qualitative interviews (purposive sampling)	30	First-generation immigrants age 48-74. (born in Turkey, Morocco and Suriname). Between February-July 2014. Amsterdam (North Holland)	All respondents felt susceptible to CRC. Knowledge about screening harm and self-efficacy to participate was low. Adult children acted as important mediators. The language and low literacy formed serious barriers to informed participation.	To ensure equal opportunities for informed participation in screening, target strategies should be developed, such as oral and visual, and face-to-face communication in the mother tongue. This will help minority groups in informed decision making in CRC screening.	Information factors Awareness factors Ability factors
(Hummel, Steuten et al. 2013) **Ref: 46**	Web-based questionnaire	167	Target population screening programme, age 55-75. April 2011. Choice between: iFOBT, colonoscopy, sigmoidoscopy, and CT colonography. The Netherlands.	Most preferred was CT colonography. Screening test with highest intention to attend was the iFOBT.	While respondents may recognize the importance of diagnostic effectiveness in the long term, their short-term decision to attend the screening tests may be less driven by this consideration. Inconvenience, safety and frequency of tests are the strongest technique-related determinants of the respondents' intention to participate in colorectal screening programs.	Awareness factors Barriers

Reference	Study design	Number of participants (n)	Participants, collection period, region	Characteristics	Outcomes	I-Change model
(Van Rijn, Van Rossum et al. 2008) **Ref: 45**	Standardized telephone interviews	312 non-participants analysed. Random selection of 500 people out of the non-responders of a cohort of 20,623 people who received an invitation for faecal occult blood test.	Non-participants of the faecal occult blood test, age 50-75. Between November 2006 to May 2007. The Netherlands.	Most reported reasons for non-participation were: time- or priority- related. Other reasons were health-related issues.	Main reasons not to participate reflect low priority. This was associated with a lack of knowledge. Adding extra instructions and information and addressing specific concerns should be considered in order to improve informed decision making about participation.	Information factors Awareness factors Barriers

PRISMA 2009 Checklist			
Section/topic	**#**	**Checklist item**	**Reported on page #**
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4

(continued)

PRISMA 2009 Checklist			
Section/topic	**#**	**Checklist item**	**Reported on page #**
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	17
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4/5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Table 3
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	-
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4

(continued)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	-
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5, Figure 2
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Sup. Table 1/2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	5
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	-
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	-
DISCUSSION			

(continued)

PRISMA 2009 Checklist			
Section/topic	**#**	**Checklist item**	**Reported on page #**
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	7
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	8-10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097
For more information, visit**: www.prisma-statement.org**.

Dubbelpublicatie Huisarts en Wetenschap

Waarom mensen niet deelnemen aan oncologische bevolkingsonderzoeken

Thom Bongaerts, Frederike Büchner, Barend Middelkoop, Onno Guicherit, Mattijs Numans

Oncologische bevolkingsonderzoeken zijn op populatieniveau alleen effectief als een groot deel van de doelgroep eraan meedoet. Nederland kent 3 van dergelijke bevolkingsonderzoeken: naar baarmoederhals-, borst- en darmkanker. Zorgelijk is dat de huidige opkomstcijfers van die onderzoeken een dalende trend laten zien en soms al onder de effectieve grens liggen. Wij hebben de achtergronden van (niet-) deelname in kaart gebracht. Huisartsen kunnen mogelijk een belangrijke rol spelen bij het keren van de dalende trend.

Dit is een bewerkte vertaling van Bongaerts THG, Büchner FL, Middelkoop BJC, Guicherit OR, Numans ME. Determinants of (non-)attendance at the Dutch cancer screening programmes: a systematic review. J Med Screen 2019:969141319887996.

Momenteel zijn er in Nederland 3 oncologische bevolkingsonderzoeken (bvo's): de screeningprogramma's naar baarmoederhals- (BMHK), borst- (BK) en darmkanker (DK). Het idee achter deze bvo's is dat wanneer de specifieke kanker in een vroeg stadium wordt opgespoord, zowel de behandeling als de prognose verbetert. Deel- name is vrijwillig en het primaire screeningsonderzoek is gratis. Potentiële deelnemers worden uitgenodigd op basis van de combinatie van leeftijd en geslacht. Het Rijksinstituut voor Volksgezondheid en Milieu (RIVM) en 5 lokale screeningsorganisaties zijn verantwoordelijk voor de organisatie en coördinatie van deze programma's. De rol van de huisarts is in elk bvo anders en aan verandering onderhevig.

De Wereldgezondheidsorganisatie berekende dat ten minste 70% van de doelpopulatie gescreend moet worden, wil een nationaal screeningsprogramma op populatieniveau effectief zijn.[1] In 2018 lag de deelnamegraad op 57,6%, 76,6% en 73% voor respectievelijk de bvo's naar BMHK, BK en DK. De opkomst bij het bvo-BMHK is dus te laag en de opkomstcijfers van zowel het bvo-BMHK als het bvo-BK laten de afgelopen jaren een dalende trend zien.[2] In de 4 grote steden zijn de opkomstcijfers van alle 3 bvo's lager dan de effectieve grens van 70%.[3,4] Deze cijfers geven daarmee reden tot zorg. Hoewel de oproepen zijn gericht aan (delen van) de algemene populatie, lijkt het er ook op dat

de opkomst ongelijk verdeeld is naar medische risico's en naar sociaal-economische achtergrond. De bvo's kunnen daarom wellicht baat hebben bij een klinische, proactieve en wijkgerichte benadering vanuit de 1e lijn.

Om de huidige opkomstcijfers te begrijpen is het noodzakelijk om een duidelijk beeld te krijgen van de achtergrond van (niet-)deelname en de daarmee gepaard gaande, wellicht beïnvloedbare factoren. Ons onderzoek had als doel om systematisch in kaart te brengen welke determinanten van (niet-)deelname aan de Nederlandse bvo's reeds onderzocht zijn.

Methode

We deden een systematisch literatuuronderzoek waarin we alle artikelen meenamen die voor februari 2018 zijn gepubliceerd. Daarvoor doorzochten we databases Academic Search Premier, Cochrane Library, Embase, EMCare, PubMed, PsycINFO en Web of Science. De initiële zoekstrategie voerden we in PubMed uit met de MESH-termen 'screening', 'cancer', 'participation' en 'Netherlands'. Ook grijze literatuur namen we mee; deze betrof vooral artikelen van het RIVM en de lokale screeningsorganisaties.

Voorafgaand aan de zoekopdracht hebben we de procedure beschreven en geregistreerd.[5] Na het verwijderen van alle duplicaten includeerden we artikelen wanneer deze voldeden aan de volgende inclusiecriteria:

1a. Onderzoeksuitkomst: deelname aan een oncologisch bevolkingsonderzoek; OF
1b. Determinanten: redenen voor lage/niet-deelname EN oncologisch bevolkingsonderzoek;
2. Resultaten gelinkt aan baarmoederhals-, borst- of darm- kanker;
3. Auteurs gelieerd aan Nederlandse organisaties OF het artikel beschrijft een Nederlands oncologisch bevolkings- onderzoek;
4. Beschikbaar in het Engels OF Nederlands;
5. Alleen origineel onderzoek.

WAT IS BEKEND?

- Nederland telt 3 oncologische bevolkingsonderzoeken (bvo's).
- Wil een bevolkingsonderzoek effectief zijn, dan moet de opkomst per bvo ≥ 70% zijn.
- De huidige opkomstcijfers laten een dalende trend zien en geven daarmee reden tot zorg.

WAT IS NIEUW?

- Onbeïnvloedbare determinanten als geboorteland, woonplaats en sociaal-economische status worden het vaakst beschreven in relatie tot deelname aan een bvo.
- De huidige onderzoeken beschrijven slechts zelden meer gedetailleerde informatie over alle, eventueel wél beïnvloedbare factoren van (niet-) deelname.
- De huisarts kan de screeningsdeelname mogelijk positief beïnvloeden. Waarschijnlijk hebben de van oudsher moeilijk bereikbare groepen hier het meeste baat bij.

De 1e en 2e auteur screenden de artikelen op titel en abstract. Wanneer er verschil van mening was over de inclusie van een bepaald artikel bespraken we dit met het hele onderzoeks- team. Voorafgaand aan de definitieve inclusie onderwierpen we de onderzoeken aan een kwaliteitsanalyse. Voor het analyseren van de determinanten gebruikten we het Integrated Model for Behavioural Change (I-Change-model; [**figuur]**). Dit is een gezondheidsgedragsmodel dat is opgebouwd uit eerdere en veelgebruikte modellen uit de gezond- heidspsychologie.[6] We gebruikten dit model omdat screeningsdeelname gezien kan worden als gezondheidsgedrag. Het model beschrijft gedrag dat wordt bepaald door onderliggende motivaties en intenties. De mate van de motivatie is afhankelijk van 3 factoren: attitude, sociale invloed en zelfeffectiviteit. Deze motivatiefactoren worden weer beïnvloed door andere factoren, zoals predispositie-, informatie- en awareness-facto- ren (zie verderop).

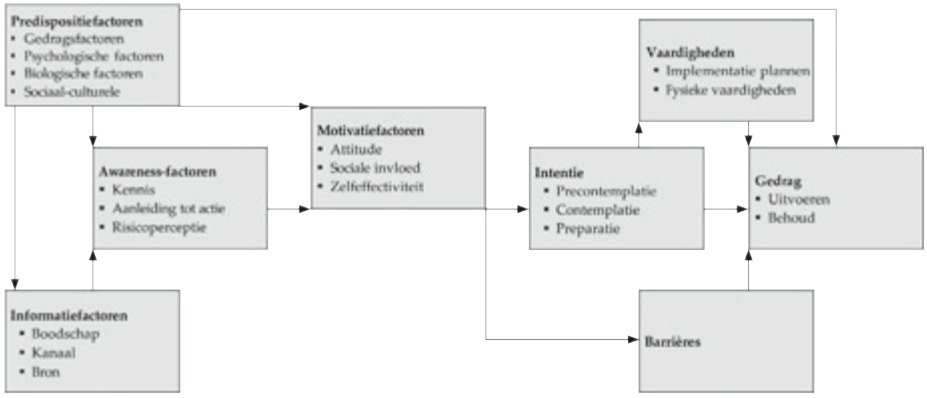
Resultaten

De initiële zoekopdracht leverde 2433 artikelen op. Bijna de helft (n = 1201) betrof duplicaten en 715 artikelen voldeden niet aan de inclusiecriteria. In totaal onderwierpen we 81 artikelen aan een tekstuele beoordeling, waarna we uiteinde- lijk 13 kwantitatieve en 6 kwalitatieve publicaties overhielden. De kwaliteitsanalyse leidde niet tot exclusie van artikelen. De **[tabel]** geeft een samenvatting van alle gevonden determinanten voor lage/niet-deelname.

Predispositiefactoren

Vijftien artikelen beschreven predispositiefactoren. Bij alle bvo's blijkt het geboorteland gerelateerd aan deelname: een geboorteland buiten Nederland correleert met een lagere deelname. Voor het bvo-BMHK en -BK worden woonplaats en sociaal- economische status (SES) als determinanten beschreven. Vrouwen woonachtig in stedelijke gebieden

(Amsterdam, Rotterdam, Den Haag en Utrecht) en/of behorend tot lagere SES-groepen participeren daarbij minder frequent. Een jongere leeftijd hangt bij het bvo-BMHK en -DK samen met een lagere deelname. Vrouwen die getrouwd zijn of een vaste partner hebben nemen eveneens minder vaak deel. Uit de literatuur over de nieuwe zelfafnametest voor het bvo-BMHK blijkt dat vrouwen geboren in Nederland vaker een set terugstuurde dan vrouwen geboren buiten Nederland. Vrouwen die eerder hadden deelgenomen blijken ook meer mee te doen aan vervolgonderzoeken. Onze zoekstrategie leverde geen artikelen op die psychologische factoren beschrijven in relatie tot de screeningsdeelname.



Figuur. Het Integrated Model for Behavioural Change (I-Change model).[6] De pijlen staan voor de onderlinge invloed tussen de verschillende factoren.

Tabel. Determinanten van lage/niet-deelname, onderverdeeld op basis van het I-Change-model.

			Bvo	
		BMHK*	**BK***	**DK***
Predispositiefactoren				
Gedragsfactoren	Burgerlijke staat: getrouwd/vaste partner	1		
	Verschillende seksuele partners	1		
Psychologische factoren				
Biologische factoren	Leeftijd: jongere leeftijd	1		2
	Geslacht: mannelijk	n.v.t.	n.v.t.	2
	Hoger risico (etniciteit): niet-Nederlands/niet-Westers	3	2	

Tabel. Determinanten van lage/niet-deelname, onderverdeeld op basis van het I-Change-model. **(continued)**

		Bvo		
		BMHK*	**BK***	**DK***
Sociaal-culturele factoren	Geboorteplaats: niet-Nederlands/niet-Westers	7	1	1
	Woonplaats: meer stedelijk	1	1	
	SES: lagere SES	4	2	
Informatiefactoren				
Boodschap	Niet overtuigend, niet mogelijk voor- en nadelen tegen elkaar af te wegen	1		1
Kanaal	Gebrek aan op maat gemaakte strategieën	3	2	2
Bron	Uitnodiging niet door de huisarts	4		
Awareness-factoren				
Kennis	Misvattingen: gebrek aan kennis	2		2
Aanleiding tot actie	Lage prioriteit toekennen	1		2
Risicoperceptie	Gevoel minder risico te lopen	3		1
Motivatiefactoren				
Attitude	Geen vervolgonderzoek noodzakelijk, minder een morele verplichting	1		1
Sociale invloed	Negatieve sociale invloeden, negatieve rolmodellen, nauwelijks gespreksonderwerp	1		
Zelfeffectiviteit	Lage zelfeffectiviteit			1
Vaardigheden				
Implementatie plannen	Vergeten een afspraak te maken	1		
Fysieke vaardigheden	Taalbarrière/lage gezondheidsvaardigheden			1
Barrières				
	Onderzoeksmethode: onzeker, angstig	1		1
	Onderzoeksuitkomst: onzeker, angstig	1		
	Ongemak: gevoelens van schaamte	2		1
	Tijdgerelateerd: vergeten, te druk	1		1
	Gezondheidsgerelateerd: andere ziekten			1
	Financiën: geen geld voor deelname aan vervolgonderzoek		1	

Bvo = oncologisch bevolkingsonderzoek, BMHK = baarmoederhalskanker, BK = borstkanker, DK = darmkanker, SES = sociaaleconomische status. * = aantal gevonden artikelen per determinant per bvo.

Voor het bvo-BMHK en -BK worden woonplaats en sociaal- economische status (SES) als determinanten beschreven. Vrouwen woonachtig in stedelijke gebieden (Amsterdam, Rotterdam, Den Haag en Utrecht) en/of behorend tot lagere SES-groepen participeren daarbij minder frequent. Een jongere leeftijd hangt bij het bvo-BMHK en -DK samen met een lagere deelname. Vrouwen die getrouwd zijn of een vaste partner hebben nemen eveneens minder vaak deel. Uit de literatuur over de nieuwe zelfafnametest voor het bvo-BMHK blijkt dat vrouwen geboren in Nederland vaker een set terugstuurde dan vrouwen geboren buiten Nederland. Vrouwen die eerder hadden deelgenomen blijken ook meer mee te doen aan vervolgonderzoeken. Onze zoekstrategie leverde geen artikelen op die psychologische factoren beschrijven in relatie tot de screeningsdeelname.

Informatiefactoren

Dertien artikelen beschreven informatiefactoren. De bestaan- de informatie blijkt niet altijd overtuigend genoeg. Velen vinden het lastig om een goede afweging over deelname te maken. Momenteel is er een gebrek aan op maat gemaakte communicatiemiddelen en -strategieën. Dit lijkt vooral problematisch voor de van oudsher moeilijk bereikbare groepen, die tevens het kwetsbaarst zijn (ze hebben vaker afwijkingen in ongunstigere stadia).

In het verleden vonden selectie en uitnodiging voor het bvo-BMHK plaats vanuit de huisartsenpraktijk. Nadat deze procedure was veranderd, viel de deelname terug. De hoge- re deelname voor de verandering betrof vooral de moeilijk bereikbare vrouwen: niet geboren in Nederland, behorend tot een lagere SES-groep en woonachtig in de stad.

Awareness-factoren

Het gebrek aan kennis over de specifieke soorten kanker en de bijbehorende bvo's is beschreven als determinant voor niet-deelname. Over het algemeen lijken niet-deelnemers sneller te denken dat ze geen/minder risico lopen, waarbij ze ervan uitgaan dat de betreffende vorm van kanker niet te genezen is.

Ook blijkt deelname aan een bvo vaak als laag urgent te worden ingeschat. Enkele artikelen beschrijven de zorgen over (test)veiligheid (en daarmee de weerstand) die potentiële deelnemers hebben.

Motivatiefactoren

Niet-deelnemers rapporteerden vaker negatieve rolmodellen (onder anderen de huisarts), bij wie deelname nauwelijks een gespreksonderwerp vormde.

Vaardigheden
Aan het bvo-BMHK werd vooral niet deelgenomen omdat potentiële deelnemers vergaten om een afspraak te maken. Lage gezondheidsvaardigheden werden het meest gerapporteerd bij het bvo-DK.

Barrières
In de literatuur werden ook problemen beschreven met het begrijpen van de Nederlandse taal en tijdgerelateerde barrières. Voor het bvo-DK gold dat deelnemers weinig vertrouwen hadden in de testprocedure zelf.

Beschouwing

We hebben gekeken welke determinanten voor deelname aan de 3 Nederlandse bvo's er in de literatuur te vinden zijn. Factoren als geboorteland, woonplaats en SES worden het vaakst genoemd. Dit soort determinanten is moeilijk te beïnvloeden. We vonden nauwelijks literatuur met gedetailleerdere informatie en over eventueel wél beïnvloedbare factoren van (niet-) deelname. Toch lijken er voor huisartsen mogelijkheden te bestaan om de screeningsdeelname te beïnvloeden en daarmee de oncologische screening op een zinvolle manier onderdeel te maken van een klinische, proactieve en wijk- of populatiegerichte aanpak.

Uniek aan dit onderzoek is het gebruik van het I-Change-mo- del. Dit theoretische kader stelde ons in staat om alle beschikbare informatie systematisch te achterhalen en te categoriseren. Daarnaast konden we de bvo's onderling met elkaar vergelijken. Zo bleek bijvoorbeeld dat het bvo-BMHK het meest onderzocht is en dat dit bvo de laagste deelnamegraad kent. Hiervoor is (nog) geen eenduidige verklaring gevonden. Misschien is deelname aan het bvo-BMHK voor veel mensen nog steeds taboe. Een mogelijke andere verklaring is dat er voor het bvo-BK een concrete afspraak volgt, terwijl vrouwen voor het bvo-BMHK zelf een afspraak moeten maken. Onder andere daarom is in 2017 de zelfafnametest geïntroduceerd. We hebben ons onderzoek nadrukkelijk niet gericht op buitenlandse bvo's en de daar reeds onderzochte factoren die invloed hebben op de screeningsdeelname. Dat deden we omdat de opzet van de bvo per land verschilt. Dat neemt niet weg dat onderzoek naar buitenlandse bvo's ook nuttige kennis kan opleveren.

De afgelopen jaren is de rol van huisartsen bij de preventie van ziekten veelvuldig besproken.[7] Als gevolg hiervan is hun aandeel bij de bvo's steeds kleiner geworden. Zo worden ze bijvoorbeeld sinds januari 2018 niet meer automatisch op de hoogte gebracht van de uitslag van het bvo-DK.8 Als huis- artsen weer een prominentere rol zouden krijgen, kan dat de informatie-, awareness- en motivatiefactoren, en daarmee

de screeningsdeelname, positief beïnvloeden. Dat is van belang omdat vroege opsporing en signalering van dit soort ziekten ook in de huisartsenpraktijk klinische consequenties hebben. Te denken valt aan een meer effectieve, proactieve, gestructureerde, populatie- en risicogroep gerichte inzet van de huisarts. In het verleden is gebleken dat juist de van oudsher moeilijk bereikbare groepen, die vaak ook de kwetsbaarste mensen betreffen, baat hebben bij een centrale en actieve rol van de huisarts. De persoonlijke en continue wijkgerichte en gezinsgeneeskundige zorg die de huisarts biedt lijkt hierbij van essentieel belang. Zo'n prominente en proactieve benadering past de huisarts en is klinisch relevant.

Toekomstig onderzoek zou het inzicht in de determinanten van screeningsdeelname nog verder moeten vergroten, zodat een veel gerichter stimulerend beleid kan worden vormgegeven. Daarnaast zouden we zowel het onderzoek naar optimalisering van de rol van de huisarts binnen de bvo's, als de discussie hierover willen stimuleren.

Referenties

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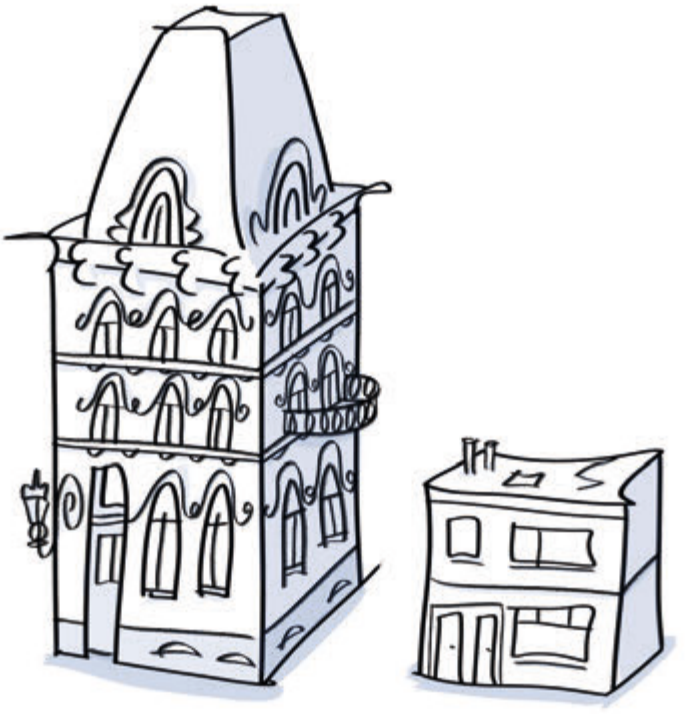

CHAPTER 3

Attendance characteristics of the breast and colorectal cancer screening programmes in a highly urbanised region of the Netherlands: a retrospective observational study

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Abstract

Objectives

Throughout Europe many countries offer population-based cancer screening programmes (CSPs). In the Netherlands two implemented CSPs are targeting people of 50 years and older, aiming at breast cancer (BC) and colorectal cancer (CRC). In order for a CSP to be (cost-)effective, high participation rates and outreach to the populations at risk are essential. People living in highly urbanised areas and big cities are known to participate less in CSPs. The aim of this study was to gain further insight in the participation rates of a screening-eligible population of 50 years and over, living in a highly urbanised region, over a longer time period.

Design

A retrospective observational study.

Setting

Participation data of the regional screening organization, linked to the cancer incidence data derived from the Netherlands Cancer Registry, concerning the city of The Hague, between 2005 to 2019. Attendance groups were defined as attenders (attending >50% of the invitations) and non-attenders (attending ≤50% of the invitations) and were mutually compared.

Results

The databases contained 106.377 unique individuals on the BC screening programme (SP), and 73.669 on the CRC-SP. Non-attendance at both CSPs was associated with living in a lower socioeconomic status (SES) neighbourhood and as a counter effect, also associated with a more unfavourable, relatively late-stage, tumour diagnosis. When combining the results of the two CSPs, our results imply high screening adherence over time. Women who did not participate in both CSPs were older, and more often lived in neighbourhoods with a lower SES-score.

Conclusions

Since low screening uptake is one of the factors that contribute to increasing inequalities in cancer survival, future outreach strategies should be focussed on engaging specific non-attending subgroups.

Strengths and limitations of this study

- For this study, regional screening invitation and attendance data were combined with cancer incidence data from the Netherlands Cancer Registry.
- By comparing the breast and colorectal cancer screening programmes, it allowed comparing a long-term programme with a relatively new programme.
- The city of The Hague can be seen as true 'living lab' to test for differences in screening attendance between different subgroups, due to strong differences between the different neighbourhoods, all well represented by socioeconomic status scores.
- Since the screening programme aiming at colorectal cancer is a relative new screening programme, data were only available on the implementation phase of the programme.

Introduction

Many European countries offer population based cancer screening programmes (CSPs) to its inhabitants.[1] The most common screening programmes (SPs) in Europe focus at the early detection of cervical, breast and colorectal cancer.[1] CSPs aim to detect cancers in an early or precursor stage, and thereby improving chances of survival due to early intervention. Early intervention is thought to lead to a better prognosis, and to less extensive treatment options.[2-4] Also in the Netherlands there are currently three CSPs implemented. The SPs concerning breast cancer (BC) and colorectal cancer (CRC) are most comparable, both target the same age-groups (starting at 50 and 55 years of age, respectively), and biennially invite potential participants.[5] While the BC-SP was phased in as early as 1990 and reached national coverage in 1996,[6] the CRC-SP was only phased in from 2014, and has only been fully operational since 2019.[7]

For a screening programme to be (cost-)effective, it is important that as many of the potential participants that are targeted, indeed participate.[8, 9] The World Health Organization (WHO) suggests that at least 70% of a target population should actually be screened, for the SP in order to be beneficial to population health.[10-12] Throughout Europe attendance at CSPs varies substantially, yet the Netherlands is known for its high attendance rates.[1] Latest Dutch attendance rates – from before the Covid-19 pandemic – were 76% and 72%, for the BC-SP and CRC-SP, respectively.[13, 14] Although these numbers might seem reassuring on a national level, the attendance rates were already declining gradually over the past years, and regional differences in screening attendance increased.[15] Current screening uptake is lowest in the highly urbanised areas and big cities of the Netherlands, and in neighbourhoods with low socioeconomic status (SES).[16]

The city of The Hague is the third largest city of the country and represents a densely populated area, with a rich mixture of different cultures and ethnicities, and with major differences in health outcomes between various neighbourhoods. In 2019 The Hague's average attendance rates were 64% and 57%, for the BC-SP and CR-CSP, respectively.[17] Hence, both are below the minimal intended rate of 70%.

To be able to promote participation in CSPs, it is important that the programmes are designed and operate as well as possible and are in accordance with the targeted populations. Further insight into the characteristics of attenders and non-attenders, especially in highly urbanised regions, is thus needed. The aim of this study was to gain insight in the background of differing attendance rates of a screening-eligible population aged 50 years and over, living in a highly urbanised region, over a longer period of time.

Methods

A retrospective observational study was performed among all screening-eligible people concerning the BC-SP and the CRC-SP living in The Hague, the Netherlands, between 2005 to 2019.

Screening programmes in the Netherlands

The Netherlands hosts CSPs aimed at cervical, breast and CRC. Screening participation is on a voluntary basis, and the screening tests are offered free of charge by the Dutch government.[5]

The BC-SP invites women between 50-75 years of age and uses a bilateral mammography as screening tool. After a an abnormal screening result the participant will be referred to the hospital by the general practitioner (GP).[6]

The CRC-SP invites both women and men aged between 55-75 years and uses a faecal immunochemical test (FIT) as screening tool. After a positive FIT, participants will be scheduled for a coloscopy in a contracted colonoscopy centre by the screening organization.[7]

Data management

In the Netherlands, The National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu, RIVM) and the national screening organisation are in charge of organizing and coordinating the CSPs. Detailed data on national participation rates are publicly available through the RIVM website.[5] Regional screening invitation and attendance data were retrieved via the national screening organisation, region South-West (Bevolkingsonderzoek Zuid-West, BVO-ZW). Cancer incidence data were retrieved from the Netherlands Cancer Registry (NCR) via the Netherlands Comprehensive Cancer Organisation (Integraal Kankercentrum Nederland, IKNL).[18] Both datasets were linked on an individual level by IKNL after approval from the privacy officers of both organisations. On forehand the Ethics Committee of the Leiden University Medical Centre issued a waiver of consent (G18.096). At time of the data extraction (2020), most recent complete datasets were extracted relating to the screening data of BVO-ZW. For the BC-SP extracted data was from 2005 to 2019. For the CRC-SP extracted data was from 2014 to 2019. Since the CRC-SP was only fully integrated and functioning from 2019, included data was of the implementation phase of the CRC-SP.

The BVO-ZW-database contained the variables: gender; year of birth; 4-digit zip code, tests results: mammography and colonoscopy. The NCR-database contained the

variables: gender; year of birth; date of diagnosis of the tumour, tumour type (BC/CRC), and tumour stage. Within the combined dataset several new variables were determined: 'number of times invited', 'number of times participated', and 'percentage participated after being invited'.

For every 4-digit zip code a neighbourhood SES-score was set by the Netherlands Institute for Social Research (Sociaal en Cultureel Planbureau, SCP) on a continues scale in 2017.[19] This score incorporates data on house value and income. We categorised this score into quartiles (1-4: the higher the number, the higher the SES), including all neighbourhoods in the Netherlands. Thereafter the 4-digit zip code for neighbourhoods of The Hague were assigned with a neighbourhood SES-score.

Data analysis

The subdivision of attendance groups for both CSPs was determined over the set time period: how many people were invited, how many people did participate, and how many people were registered with a cancer diagnosis. We distinguished invitees who always (100%), sometimes (>0% and <100%), and never (0%) participated after receiving an invitation.

For further analysis we divided our data in 'attenders' and 'non-attenders'. Attenders were defined as: invitees who participated in the CSPs in more than 50%, after being invited. Non-attenders were defined as: invitees who participated in 50% or less, after being invited. The proportion of attenders and non-attenders was presented descriptively, using counts and percentages. To test independent continuous variables, Mann-Whitney U and Kruskal-Wallis tests were conducted. For categorical independent variables, univariate regression analyses were performed with an α 0.05 and β 0.8. This resulted in odds ratios (ORs) per attendance group, with corresponding 95% confidence intervals (95% CIs). Likelihood Ratio tests were performed to test for the influence of each independent variable in the regression models. Our data was stored and analysed by making use of IBM SPSS (version 25).

Patient and public involvement

The development of the research question, study design and outcome measures were developed by a team of experienced primary care doctors and researchers, who also concerned patients' and public's interests. Patients were not directly involved in these processes. The results of this research work are going to be published open access and disseminated to whom is interested, among others primary care doctors and the Municipal Health Services.

Results

The databases contained 106.377 unique individuals on the BC-SP, and 73.669 on the CRC-SP. Analysis showed an overlap of 38,071 individuals, thus around a third, receiving invitations for both CSPs.

Breast cancer screening programme

Most women received seven invitations (27.0%), with a maximum of nine invitations (0.1%). Within the time period of 14 years, n=48,126 women (45.2%) received their first BC-SP invitation. In total n=79,594 women (74.8%) participated at least once. Among the invitees, n=3,820 (3.6%) women were diagnosed with BC, regardless of whether this tumour was screen-detected.

The largest group of BC-SP invitees always participated in the CSP after receiving an invitation (n=47,087; 44.3%). About a quarter of the invited women never participated (n=26,783; 25.2%). Among the 'always-attenders', 1.6% (n=755) of the women were diagnosed with BC, compared with 6.8% (n=2,198) and 3.2% (n=867) of the 'sometimes' and 'never-attenders', respectively (Figure 1).

A total of 61.9% (n=65,853) of the invitees were identified as 'attenders', hence 38.1% (n=40,524) as 'non-attenders'. Non-attenders were found to be two years younger (Mann-Whitney U: p<.01). The number of BCs were evenly divided between the two attendance-groups (50.6% versus 49.4%). Women in the non-attenders group with BC, were two years younger (Mann-Whitney U: p<.01) and diagnosed with BC five years earlier in live (Mann-Whitney U: p<.01), compared to women with BC in the attenders' group (Table 1).

Table 1. Characteristics invitees and cancer cases, concerning the breast cancer screening programme.

	Total invitees (n=106,377)				Invitees with BC (n=3,820)			
Attendance group*	**Attenders**		**Non-attenders**		**Attenders**		**Non-attenders**	
Proportion % (n)	61.9 (65,853)		38.1 (40,524)		50.6 (1,932)		49.4 (1,888)	
Year of birth Median (25-75%)	1953 (1945–1960)		1955 (1945–1962)		1948 (1942-1954)		1950 (1944–1957)	
Age at diagnosis Median (25-75%)	-		-		65 (59-71)		60 (54-67)	
Neighbourhood SES-score	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
1	17,656	30.5	12,813	38.4	520	27.9	560	31.0
2	12,127	21.0	6,829	20.5	391	20.9	398	22.0
3	4,488	7.8	2,301	6.9	145	7.8	132	7.3
4	23,539	40.7	11,384	34.2	811	43.4	718	39.7
Unknown	8,043		7,197		65		80	

BC= breast cancer, SES= social economic status (SES 1: low; SES 4: high)
*Attenders: people who participated in >50%, after being invited. Non-attenders: people who participated in ≤50%, after being invited.

The neighbourhood SES-score differed statistically significant between attenders and non-attenders (Likelihood Ratio test: p<.01). Women living in a neighbourhood with the highest SES-scores, were more likely to participate (ascending ORs from 1.29 to 1.50; for SES-2 to SES-4, compared to SES-1). The neighbourhood SES-scores were not statistical different between the different attendance-groups with BC (Likelihood Ratio test: p=.08). Despite, people living in a SES-4 neighbourhood were more likely to participate (OR 1.22), compared to people living a SES-1 neighbourhood. Attendance was associated with a lower BC-stage (declining ORs from 0.95 to 0.15). In addition, when the interaction effect for both independent variables was determined, non-attenders were more likely to live in neighbourhoods with lower SES-score and had the more unfavourable cancer stages as an outcome (Likelihood Ratio test: p<.01) (Table 2).3

Table 2. Results univariate regression analyses on attendance, concerning invitees and breast cancer cases.

	OR (95% CI)	p-value	n
SES (invitees)			
SES 1	reference	<.01*	30,469
SES 2	1.29 (1.24-1.34)	<.01*	18,956
SES 3	1.42 (1.34-1.50)	<.01*	6,789
SES 4	1.50 (1.45-1.55)	<.01*	34,923
SES (invitees with BC)			
SES 1	reference	0.08	1,080
SES 2	1.06 (0.89-1.27)	0.55	789
SES 3	1.18 (0.91-1.54)	0.21	277
SES 4	1.22 (1.04-1.42)	0.01*	1,529
Stage			
CIS	reference	<.01*	517
Stage 1	0.95 (0.78-1.16)	0.61	1,469
Stage 2	0.49 (0.40-0.61)	<.01*	1,116
Stage 3	0.32 (0.24-0.42)	<.01*	316
Stage 4	0.15 (0.10-0.24)	<.01*	156
SES x Stage			
SES 4 x CIS	reference	<.01*	217
SES 4 x Stage 1	0.78 (0.57-1.09)	0.15	620
SES 4 x Stage 2	0.46 (0.33-0.64)	<.01*	465
SES 4 x Stage 3	0.35 (0.22-0.56)	<.01*	125
SES 4 x Stage 4	0.17 (0.09-0.32)	<.01*	62
SES 3 x CIS	0.59 (0.30-1.18)	0.13	38
SES 3 x Stage 1	0.68 (0.43-1.08)	0.10	119
SES 3 x Stage 2	0.54 (0.33-0.88)	0.01*	93
SES 3 x Stage 3	0.20 (0.07-0.59)	0.01*	18
SES 3 x Stage 4	0.00 (0.00-0.00)	1.00	1
SES 2 x CIS	0.82 (0.51-1.32)	0.41	107
SES 2 x Stage 1	0.84 (0.59-1.21)	0.35	319
SES 2 x Stage 2	0.32 (0.22-0.47)	<.01*	229
SES 2 x Stage 3	0.26 (0.15-0.44)	<.01*	82
SES 2 x Stage 4	0.13 (0.05-0.34)	<.01*	30

Table 2. Results univariate regression analyses on attendance, concerning invitees and breast cancer cases. **(continued)**

	OR (95% CI)	p-value	n
SES 1 x CIS	0.71 (0.47-1.09)	0.12	155
SES 1 x Stage 1	0.78 (0.56-1.10)	0.15	411
SES 1 x Stage 2	0.38 (0.26-0.54)	<.01*	329
SES 1 x Stage 3	0.18 (0.10-0.31)	<.01*	91
SES 1 x Stage 4	0.09 (0.04-0.19)	<.01*	63

SES= social economic status (SES 1: low; SES 4: high), BC= breast cancer, CIS= carcinoma in situ
*Statistically significant associated with attendance at the cancer screening programmes

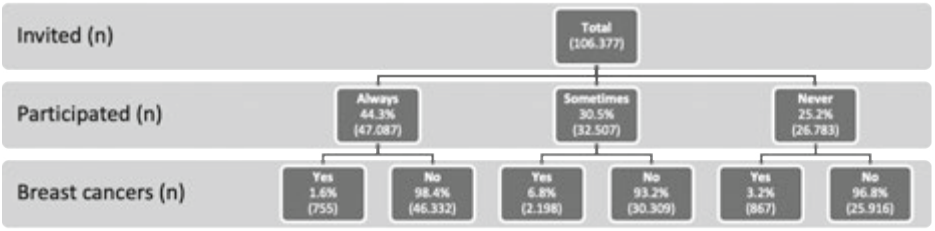

Figure 1. Subdivision of the attendance groups at the breast cancer screening programme.

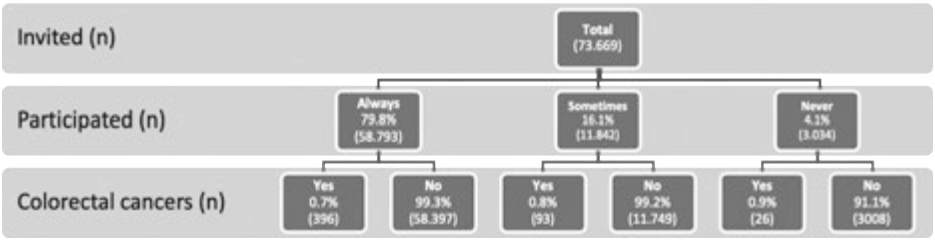

Figure 2. Subdivision of the attendance groups at the colorectal cancer screening programme.

Colorectal cancer screening programme

Most invitees received one invitation (48.2%), with a maximum of three invitations (12.8%). Since all acquired data were from the implementation period of the SP, all invitees received their first invitation during the set time period. In total n=70,638 (95.9%) people participated at least once. Among the invitees, n=515 (0.7%) were diagnosed with CRC, regardless of whether this tumour was screen-detected. The number of male participants with CRC was 1.2 times higher, compared with female participants (55% (n=284) versus 45% (n=231)).

The largest group of CRC-SP invitees always participated in the CSP after receiving an invitation (n=58,3793; 79.8%). Only a very small part of the invitees never participated (n=3,034; 4.1%). Among the 'always-attenders', 0.7% (n=396) of the participants were diagnosed with CRC, compared with 0.8% (n=93) and 0.9% (n=26) of the 'sometimes' and 'never-attenders', respectively (Figure 2).

A total of 83% (n=61,132) of the invitees were identified as 'attenders', hence 17% (n=12,537) as 'non-attenders'. In the attenders-group 46.5% of the people were male, compared with 47.4% in the non-attenders-group (Likelihood Ratio: p=.08). Median age of the non-attenders was found to be two years older (Mann-Whitney U: p<.01). Most CRCs were found in the attenders-group (79.2% versus 20.8%). Median age of the invitees in the non-attenders group with CRC was one year lower (Mann-Whitney U, p=.27), but they were diagnosed with CRC around the same median age (Mann-Whitney U, p=.67), compared to invitees with CRC in the attenders' group (Table 3).

Table 3. Characteristics invitees and colorectal cancer cases, concerning the colorectal cancer screening programme.

	Total invitees (n=73,669)				**Invitees with CRC (n=515)**			
Attendance group*	**Attenders**		**Non-attenders**		**Attenders**		**Non-attenders**	
Proportion % (n)	83.0 (61,132)		17.0 (12,537)		79.2 (408)		20.8 (107)	
Sex % (n)	M: 46.5 (28,450) F: 53.5 (32,681)		M: 47.7 (5,974) F: 52.3 (6,563)		M: 53.9 (220) F: 46.1 (188)		M: 59.8 (64) F: 40.2 (43)	
Year of birth Median (25-75%)	1953 (1947-1958)		1951 (1947-1954)		1948 (1945-1953)		1949 (1946-1952)	
Age at diagnosis Median (25-75%)	-		-		67 (55-77)		67 (64-69)	
Neighbourhood SES-score	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
1	16,908	27.8	4,693	37.6	110	27.0	41	38.3
2	12,664	20.8	2,453	19.7	103	25.2	11	10.3
3	4,697	7.7	869	7.0	38	9.3	7	6.5
4	26,546	43.7	4,451	35.7	157	38.5	48	44.9
Unknown	317		71		0		0	

CRC= colorectal cancer, M= male, F= female, SES= social economic status (SES 1: low; SES 4: high)
*Attenders: people who participated in >50%, after being invited. Non-attenders: people who participated in ≤50%, after being invited.

The neighbourhood SES-score differed statistically significant between attenders and non-attenders (Likelihood Ratio test: p<.01). Women living in a neighbourhood with the highest SES-scores, were the more likely to participate (ascending ORs from 1.43 to 1.66; for SES-2 to SES-4, compared to SES 1). The neighbourhood SES-scores also differed statistically between the different attendance-groups with CRC (Likelihood Ratio test: p=.05). People living in a SES-2 neighbourhood were more likely to participate (OR 1.64), compared to people living in a SES-1 neighbourhood. Attendance was not statistical different between the several CRC-stages. Despite, a stage 4 CRC had an OR of 0.56 on attendance, compared with a stage 1. In addition, when the interaction effect for both independent variables was determined, no statistical differences could be established (Likelihood Ratio test: p=0.24). However, when taken the ORs into account non-attenders, there seems to be a tendency that non-attenders were more likely to live in neighbourhoods with lower SES-scores and had the more unfavourable cancer stages. (Table 4).

Table 4. Results univariate regression analyses on attendance, concerning invitees and significant abnormalities.

	OR (95% CI)	**p-value**	**n**
SES (invitees)			
SES 1	reference	<.01*	21,601
SES 2	1.43 (1.36-1.51)	<.01*	15,117
SES 3	1.50 (1.39-1.62)	<.01*	5,566
SES 4	1.66 (1.58-1.73)	<.01*	30,997
SES (invitees with CRC)			
SES 1	reference	0.05*	151
SES 2	1.64 (1.18-2.26)	0.01*	114
SES 3	1.67 (1.05-2.64)	0.12	45
SES 4	1.56 (1.19-2.05)	0.42	205
Stage			
Stage 1	reference	0.38	198
Stage 2	0.76 (0.43-1.36)	0.36	109
Stage 3	0.80 (0.47-1.38)	0.43	147
Stage 4	0.56 (0.29-1.08)	0.09	61
SES x Stage			
SES 4 x Stage 1	reference	0.24	78

Table 4. Results univariate regression analyses on attendance, concerning invitees and significant abnormalities. **(continued)**

	OR (95% CI)	p-value	n
SES 4 x Stage 2	1.25 (0.49-3.17)	0.64	39
SES 4 x Stage 3	1.12 (0.50-2.49)	0.79	58
SES 4 x Stage 4	0.89 (0.34-2.31)	0.80	30
SES 3 x Stage 1	2.15 (0.57-8.03)	0.26	23
SES 3 x Stage 2	>10.00 (0.00- >10.00)	1.00	9
SES 3 x Stage 3	0.97 (0.18-5.19)	0.97	8
SES 3 x Stage 4	0.48 (0.08-3.11)	0.44	5
SES 2 x Stage 1	3.46 (1.10-10.91)	0.03*	47
SES 2 x Stage 2	1.85 (0.57-6.03)	0.31	27
SES 2 x Stage 3	4.83 (1.06-22.13)	0.04*	32
SES 2 x Stage 4	2.25 (0.26-19.51)	0.46	8
SES 1 x Stage 1	1.45 (0.60-3.56)	0.40	50
SES 1 x Stage 2	0.59 (0.25-1.13)	0.24	34
SES 1 x Stage 3	0.81 (0.36-1.81)	0.60	49
SES 1 x Stage 4	0.64 (0.21-2.00)	0.44	18

SES= social economic status (SES 1: low; SES 4: high), CRC= colorectal cancer
*Statistically significant associated with attendance at the cancer screening programmes

Comparison of the two screening programmes

In total n=38,071 women were invited for both CSPs. Most of these women attended both programmes, n=26,560 (69.8%). Only a small number of women did not participate in any programme, n=1,679 (4.4%). Between the four different subgroups, both 'year of birth' (Kruskal-Walllis: p<.01) and 'neighbourhood SES-score' were statistically different (Likelihood Ratio: p<.01). Women who did not attend the BC-SP but did attend the CRC-SP were the youngest, with a median year of birth of 1954. Non-attenders tended to live more in the neighbourhoods with lower SES-scores. Especially non-attendance at the CRC-SP seemed to be associated with lower a SES-score (BC+, CRC-; SES-score 1= 37.3%, and BC-, CRC-; SES-score 1= 40.7%, compared to BC+, CRC+; SES-score 1= 27.5%.) (Table 5).

Table 5. Combination of the datasets; invited women and their attendance status.

	Total amount of invited women (n=38,071)								
Attendance CSP (+/-)	**BC+ CRC+**		**BC+ CRC-**		**BC- CRC+**		**BC- CRC-**		**Statistical test**
Proportion % (n)	69.8 (26,560)		12.4 (4,721)		13.3 (5,111)		4.4% (1,679)		
Year of birth Median (25-75%)	1953 (1947-1958)		1951 (1947-1954)		1954 (1947-1959)		1951 (1948-1954)		Kruskal-Walllis p<.01
Neighbourhood SES-score	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	Likelihood Ratio p<.01
1	7,289	27.5	1,757	37.3	1,597	31.4	682	40.7	
2	5,704	21.5	922	19.6	1,050	20.6	327	19.5	
3	2,129	8.0	351	7.4	408	8.0	115	6.9	
4	11,373	42.9	1,684	35.7	2,036	40.0	552	32.9	
Unknown	62		7		20		3		

CSP= cancer screening programme, BC= breast cancer, CRC= colorectal cancer, SES= social economic status (SES 1: low; SES 4: high), (+)= attendance, (-)= non-attendance

Discussion

This retrospective observational study, among people eligible for attending the BC-SP and CRC-SP, conducted in a highly urbanised region between 2005 to 2019, delivered multiple insights concerning screening attendance, screening adherence and cancer risks within subgroups. Non-attendance for both CSPs was found in lower SES neighbourhoods and associated with a more unfavourable (late-stage) tumour diagnosis. When combining the results of the two CSPs, our results imply high screening adherence over time. Women who did not participate in both CSPs were older, and more often lived in neighbourhoods with a lower SES-score.

Several studies conducted in the Netherlands did focus on SES as a determinant for screening attendance and/or adherence, and did report the same conclusion: living in a lower SES-area/region/neighbourhood is associated with lower screening uptake.[20-22] Our study thus confirms this 'SES-effect', and shows to remain valid, even within a highly urbanised region. Additionally, our study adds that non-attenders living in a lower SES-neighbourhood, are more often diagnosed with a more unfavourable form of BC, and the same tendency seems to exist for CRCs. In this study we did not look into mechanisms on why people living in lower SES-neighbourhoods developed these more

unfavourable forms of cancer, but in literature factors related to health illiteracy are often mentioned.[23] Just recently, Kregting et al. compared the screening attendance of women at the screening ages of 55/65 years, and concluded that women living in areas with higher population density and lower SES-score were less likely to participated in more CSPs.[24] Three studies conducted in the United Kingdom compared barriers for the CSPs and concluded that women who lived in a more deprived region, participated less in the CSPs.[25-27] Age as a variable, was earlier described in two studies. One did not find any influence,[25] the other reported a lower age to be associated with lesser screening attendance.[26] Within our study we saw a mixed influence of age, depending on the CSP. With respect to screening adherence, we found rather high overall screening attendance rates for both CSPs. The yearly monitoring reports of RIVM show the same high screening adherence on a national level.[13, 14] In terms of cancer risk, we found that men were more likely to be diagnosed with CRC than women, which is consistent with national trends.[14]

By conducting this study, we were able to compare a long-lasting programme with a relatively new programme. We focused on the city of The Hague since we believe, The Hague can be seen as a true 'living lab' to test for differences in screening attendance between different subgroups, due to strong differences between the different neighbourhoods, all well represented by the SES-scores.[28] This also allows our study findings to be directly translated and applied into daily practice. While the segregation between neighbourhoods in The Hague is probably the most evident, we expect our findings to be also applicable for other large cities, as for example Amsterdam and Rotterdam, given their generally similar demographic characteristics.[29-31]

Our study has some limitations that need to be reflected on. Since the CRC-SP is a relative new CPS, we only had access to data of the implementation phase of the CSP, over a period of 4 years. This resulted in relatively little data on the CRC-SP, compared with the data on the BC-SP, and in particular resulted in small CRC numbers. Thereby, one might question the relevance of comparing the data of a CSP in the implementation phase, with a 'steady state' CSP. However, we felt it was relevant to compare the two CSPs at this early stage, as any shortcomings could then be addressed as early as possible. Another limitation has to do with the degree of crudeness of our variables. In the initial study design, we planned to look into several specific characteristics of potential participants and their association with screening attendance. Despite the large number of invited people by the CPSs, adding more patient specific characteristics would possibly lead to identification of individual participants. To avoid this risk, we decided to only look at relatively undetailed patient characteristics, such as: year of birth, age of diagnosis, sex, and neighbourhood SES-scores.

When thinking of clinical relevance and usability of the study findings, our main conclusion is that more effort should be made to engage people living in neighbourhoods with a lower SES-score. Current low-attendance in these areas may lead to a further increasing inequality in cancer survival, in a subpopulation already confronted with several other health-risks and problems. Our study underlines a longstanding hypothesis: people who are possibly the most at risk for the development of an advanced form of cancer, are the less likely to be screened.[32]

Future development therefore should focus on more specific outreach strategies to engage people living in neighbourhoods with a lower SES-score that are at specific risk of non-attendance, as partly earlier was suggest by Woudstra et al.[33] We suggest to encourage healthcare professionals, policymakers and politicians to look into such kind of 'novel solutions'. We also suggest that GPs, or primary health care professionals in general, take on a more prominent role in promoting and educating people on the CSPs. Previous studies showed that GP-involvement has a positive impact on (cervical) screening uptake, in particular for the classic 'hard to reach' subgroups.[34, 35] Especially in deprived areas, people generally trust and have a good long-term relationship with their GP, and primary healthcare centres in these areas are the only available link to enter healthcare and to gain information on health issues.[36] A remaining question would be, how exactly the role of GP practice centres should be improved while avoiding the risk to further increase workload. Perhaps just being enlisted with a primary healthcare centre, and being invited to participate through that centre, could already make a difference.

Conclusion

Non-attendance at both the BC and CRC-SPs tends to be associated with living in a lower SES-score neighbourhood. In addition, non-attenders living in these lower SES-neighbourhoods, were more often diagnosed with the unfavourable forms of cancer, as targeted by the specific CSPs. Since low screening uptake thus contributes to increasing inequalities in cancer survival, future outreach should be focussed on engaging specific groups of people living in lower SES-neighbourhoods carrying the highest risks.

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Contributions
THGB and FLB designed the study, collected, and combined the datasets. Data analysis was undertaken by THGB, supervised by FLB, and in a later stage by LdM and MAGE. THGB drafted the first version of the paper. ORG and MEN helped to interpret the results. All authors reviewed and edited the manuscript.

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BVO

CHAPTER 4

Perspectives on cancer screening participation in a highly urbanized region: a Q-methodology study in The Hague, the Netherlands

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Abstract

Background

The Netherlands hosts, as many other European countries, three population-based cancer screening programmes (CSPs). The overall uptake among these CSPs is high but has decreased over recent years. Especially in highly urbanized regions the uptake rates tend to fall below the minimal effective rate of 70% set by the World Health Organization. Understanding the reasons underlying the decision of citizens to partake in a CPS are essential in order to optimize the current screening participation rates. The aim of this study was to explore the various perspectives concerning cancer screening among inhabitants of The Hague, a highly urbanized region of the Netherlands.

Methods

A Q-methodology study was conducted to provide insight in the prevailing perspectives on partaking in CSPs. All respondents were inhabitants of the city of The Hague, the Netherlands. In an online application they ranked a set of 31 statements, based on the current available literature and clustered by the Integrated Change model, into a 9-column forced ranking grid according to level of agreement, followed by a short survey. Respondents were asked to participate in a subsequent interview to explain their ranking. By-person factor analysis was used to identify distinct perspectives, which were interpreted using data from the rankings and interviews.

Results

Three distinct perspectives were identified: 1). “Positive about participation”, 2). “Thoughtful about participation”, and 3). “Fear drives participation”. These perspectives provide insight into how potential respondents, living in an urbanized region in the Netherlands, decide upon partaking in CSPs.

Conclusions

Since CSPs will only be effective when participation rates are sufficiently high, it is essential to have insight into the different perspectives among potential respondents concerning partaking in a CSP. This study adds new insights concerning these perspectives and suggests several ideas for future optimization of the CSPs.

Background

The Netherlands, as many other European countries, invests considerable time and effort in hosting three population-based cancer screening programmes (CSPs).[1] These programmes focus on cervical, breast and colorectal cancer. CSPs aim to detect cancer in an early or precursor stage and thereby improving survival via early intervention. On average, this approach is assumed to lead to a better prognosis, as well as to fewer and less severe side effects of treatment.[2-5] In the Netherlands, the screening tests of the CSPs are offered free of charge by the government to all citizens of a specific age and gender. The cervical CSP includes women aged between 30-60 and uses a Papanicolaou-smear test, a bilateral mammography is used to screen women between 50-75 years of age on breast cancer. The colorectal CSP is aimed at both women and men aged between 55-75 years, and screening is performed by a faecal immunochemical test. The National Institute for Public Health and the Environment (RIVM) and five regional screening organisations are charged with organizing and coordinating these programmes.[6] Attendance is voluntary and monitored yearly by RIVM.[7-9] Although the three CSPs show many similarities, each CSP has its unique procedures and organization, mainly due to the differences in screening methods.[6]

High participation rates are essential for screening programmes to be (cost-)effective.[10,11] According to the World Health Organization (WHO), at least 70% of the target population should be screened in order to be beneficial on population level.[12-14] Throughout Europe participation in CSPs varies substantially, yet the Netherlands is/was always known for its high screening attendance and adherence.[1] Latest published CSP attendance rates in the Netherlands, before the Covid-19 pandemic (concerning the year 2019), showed rates of 56.0%, 76.0% and 71.8% for the CSPs focused at cervical, breast and colorectal cancer, respectively.[7-9] Although the attendance rates of two programmes are above the recommended rate from WHO, there is an alarming downward trend and wide regional variation in screening uptake. In 2010, the uptake rates of the CSPs for cervical and breast cancer were 65.5% and 80.7%.[7,8] Since the colorectal CSP has only been fully operational since 2019, it is too early to draw any conclusions on trends regarding this screening programme. At the regional level, the four largest cities of the Netherlands are among the regions with the lowest attendance rates, below the minimal effective rate of 70% for all three screening programmes.[15]

In order to improve the attendance rates, it is essential to understand the motivations of citizens to participate in CSPs. A systematic review showed that earlier studies into cancer screening participation have not provided in-depth information on the underlying beliefs and motivations regarding willingness to participate in cancer screening.[16]

Later studies were conducted to reveal the decision processes regarding screening participation,[17,18] but detailed understanding of the perspectives of potential participants remains limited. Furthermore, the underlying beliefs and motives to participate in CSPs could differ between subgroups in the population, for example, between people living in urban and rural regions.[19,20] Since attendance rates in the largest cities of the Netherlands are especially low, we decided to focus on urbanized regions. The aim of this study, therefore, was to explore the perspectives concerning cancer screening uptake among inhabitants of The Hague, a highly urbanized region in the Netherlands. Insight in the mechanisms underlying these perspectives could probably be leveraged or applied to promote participation in non-attenders in high urbanized regions.

Methods

This study was conducted using Q-methodology, a mixed-methods approach designed to provide insight in perspectives on a specific topic in a given population.[21, 22] Q-methodology can be used for a wide range of subjects, and always has to do with the systematic study of subjectivity.[23-26] We conducted the study online due to restrictions following the Covid-19 pandemic.

In brief, respondents were presented with a set of opinion statements on beliefs and motivations for participating in a CSP and were instructed to rank them according to agreement. Qualitative data was gathered by asking respondents to explain their ranking of the statements and by follow-up interviews with several selected respondents. By-person factor analysis was used to identify significant clusters of correlations among the rankings of statements by respondents. The assumption underlying this analysis is that respondents with similar perspectives on participating in CSPs will rank the statements similarly. For each identified factor, a weighted average ranking of the statements was computed, which was the basis for interpretation and description of the factor as a perspective on cancer screening participation. Selected respondents for each of the factors were invited for a follow-up interview to validate the interpretation of the factors and to obtain additional qualitative data for describing the perspectives.[21, 22]

Statement set development

To develop a comprehensive set of statements, representing all the aspects that may be relevant for respondents to express their perspective on the topic, the first two authors (TB, FB) reviewed a large variety of scientific, empirical, and popular literature on motives and beliefs potentially influencing the decision to participate in population-based CSPs. The scientific literature was reviewed systematically and published previously.[16] To structure the statements, and to make sure the set of statements would

be comprehensive, the Integrated Change model (I-Change model, Figure 1) was used as theoretical framework for structuring the development of the statement set.[27] The I-Change model is a health behaviour model, constructed out of several earlier well recognized health behaviour theories, such as: the Health Belief Model, Protection Motivation Theory, Theory of Planned Behaviour and Precaution Adoption Process.[28-31] The I-Change model states that health behaviour is determined by underlying motivations and intentions, and was previously used to study different kinds of health behaviours.[32-35] Since screening attendance can be seen as a (preventive) health behaviour, the elements of the I-Change model provide a useful structure for identifying the aspects that may be relevant for decisions whether or not to participate in a CSP: information, awareness, motivation, ability, intention and barriers. Since predisposing factors (elements) of the I-Change model are more distal factors, more indirectly associated with screening participation, we thought them to be less relevant for including in a Q-study.

Four researchers (TB, FB, MC and VN) developed an initial set of 45 statements based on the collected scientific, empirical, and popular literature. Two external experts were asked to evaluate whether the statement set covered all relevant aspects for the decision to participate in population-based CSPs. Based on their feedback, several adjustments were made; some statements were merged or deleted because they covered similar topics (n=9), some were considered as irrelevant and thus deleted (n=3), and the wording of several statements was revised. Thereafter, we consulted the knowledge institute Pharos (the Centre of Expertise on Health Disparities) to make sure the statements were clear and easily readable for the target population,[36] leading to further reduction of the number of statements (n=2) and minor adjustments to language use. This iterative process resulted in a set of 31 statements. To test the comprehensiveness and clarity of the statement set, a pilot study was conducted among two potential study respondents. Based on their feedback, we finalized the set of opinion statements for the main study.

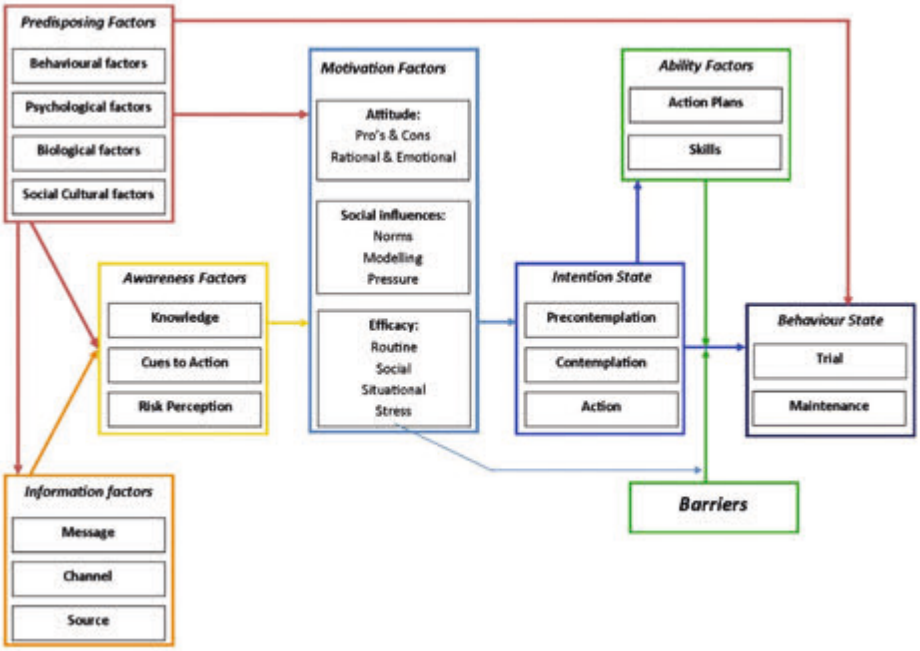

Figure 1. The Integrated Model for Behavioural Change (I-Change Model). The arrows represent the influence between the different factors (referred to as 'elements' in the manuscript)

Data collection

Due to the outbreak of the Covid-19 pandemic we were not able to perform a face-to-face Q-study, as was the initial plan, and therefore we switched to an online data collection approach. We made use of an external research agency (Flycatcher Internet Research) to recruit respondents.[37] The online data collection was effectuated by making use of the Q Method Software tool.[38]

Inhabitants of the city of The Hague, the third largest city of the Netherlands, who were invited for participating in one of the CSPs at least one time, were the target population of this study. The research agency purposively sampled people based on zip-code, sex, and age. In total of 112 Inhabitants of the city of The Hague were invited to participate in this study. We focused on the city of The Hague since we were interested in the perspectives of potential cancer screening respondents living in a highly urbanized region, where uptake rates are generally low. Latest attendance rates (2019) of The Hague were 52%, 64%, 57% for the CSPs at cervical, breast and colorectal cancer, respectively.[39] With respect to the demographic characteristics The Hague is comparable to other large cities in the Netherlands, as for example Amsterdam and Rotterdam.[40-42]

The invitation to potential respondents included some background information about the study and a link to the online software tool. After following the link, respondents reached a website with detailed instructions and information on the study and data use, including regulations regarding anonymity. By clicking on an 'agree and start' button, respondents confirmed to have read and understood the information provided and to take part in the study. Respondents were able to stop participation at any time. In this case, their data was not saved and hence, not included in the study. As it was not possible for respondents to ask for explanation on the ranking process, we provide respondents with extensive clarification materials, both in writing and video before ranking the opinion statements.

During the data collection process, respondents were informed about the study purpose, namely: "We are interested in what you find important when deciding whether or not to participate in a cancer screening programme". Then, they were presented with the set of opinion statements on participating in the CSPs in random order. First, they were asked to read all the statements and to divide them into three piles (i.e., 'agree', 'neutral' and 'disagree') according to the instruction: "To what extent do you agree with the following statements?". Next, they were asked to read them again and place them on a forced-choice sorting grid ranging from 'disagree most' to 'agree most' (see Figure 2), starting with the statements in the 'agree' pile, followed by those in the 'disagree' pile and, finally, those in the 'neutral' pile. Finally, respondents were asked to review the full ranking of the statements and make any last changes, if desired. Then, they were asked about their demographic details (see Table 1). Finally, respondents were asked to explain their ranking of the statements; in particular, they were asked to explain why they placed the specific statements on both end sides of the ranking grid (i.e., columns -4, -3 and +3, +4). After the analysis and initial interpretation of the results, the first author contacted the respondents with the highest factor loadings (i.e., correlation between the ranking of statements by the respondent and the factors) for each factor, to verify the initial interpretation of the factor they were associated with, and to obtain additional qualitative material for finalizing the interpretation and description of the factors. The aim was to interview at least two respondents per factor, so six in total. Respondents then had to leave their contact details in the post-ranking questions. The interviews were audio-recorded after the respondents gave their consent. No data directly leading toward the individual respondent was stored in the audio-file. The interviewed respondents received a €20 gift card for their time investment.

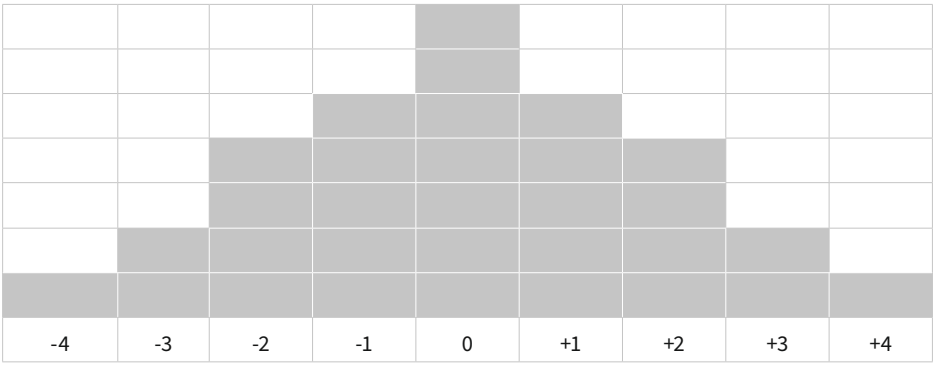

Figure 2. Q-sort grid (9-colum forced choice ranking grid)

Analysis

The data was analysed using KADE version 1.2.0 for MacOS. We excluded respondents of whom the rankings and post-ranking survey answers were in retrospect inconsistent or unclear. This also appeared to be the respondents who completed the ranking exercise very fast, all with a completion time ≤8 minutes (n=6). Furthermore, several responses were excluded based on the answers provided in the post-ranking questions, for example, respondents who indicated that they struggled with the software and had not been able to rank the statements according to instructions. The included respondents completed the raking process with an average time of 25 minutes, with a maximum of 110 minutes. In the analysis, first, a correlation matrix of all pairwise correlations between the rankings of the statements by respondents was computed, which was then subjected to by-person factor analysis to identify groups of respondents with mutually high correlations (using centroid factor extraction, followed by varimax rotation). The resulting factors were interpreted and described as perspectives on cancer screening participation. For each factor, a weighted average ranking of the statements was computed (i.e., the factor array), based on the rankings of the statements by the respondents associated with the factor and their factor loadings. In addition, consensus statements (i.e., those whose rankings did not differ significantly between any pair of factors) and distinguishing statements for each factor (i.e., those whose rankings in one factor differed significantly from those in all other factors) were identified. Where consensus statements are suitable for addressing the amount of agreement of the perspectives, the distinguishing statements are useful for highlighting the differences between the different perspectives. Next, an initial interpretation and description of each perspective was based on the factor arrays and the distinguishing and the consensus statements, supplemented with the qualitative data from respondents whose rankings were associated with that perspective ($p<.05$).

Results

Forty-nine respondents (44%) completed the online Q-study, of which 39 rankings (80% of the respondents) were suitable for analysis. Respondents were mostly female and aged between 50 and 59 years of age. CSP participation was defined as participating at least once in a CSP (i.e., respondents who had experience with attending a CSP). Table 1 shows the demographic characteristics of respondents. Thirty-six respondents (92%) completed all the post-ranking questions, so we had missing supplementary data for three of the 39 analysed rankings. The flowchart of the study population is presented in Figure 3. Afterwards, four post-ranking interviews were conducted. For one factor (perspective 2) none of the respondents left their contact details, so we were not able to perform post-ranking interviews for this perspective. The four interviews lasted about 45 minutes.

Three distinct perspectives on cancer screening participation were identified based on the ranking data collected. These perspectives were sufficiently distinct and clearly interpretable, based on the qualitative data. Together these perspectives explained 54% of the variance in the ranking of statements by the study respondents, 24%, 10% and 20% for factors 1 to 3, respectively. In total, 32 respondents were significantly associated with one of the factors ($p<.05$). Table 2 shows the factor array for each perspective.

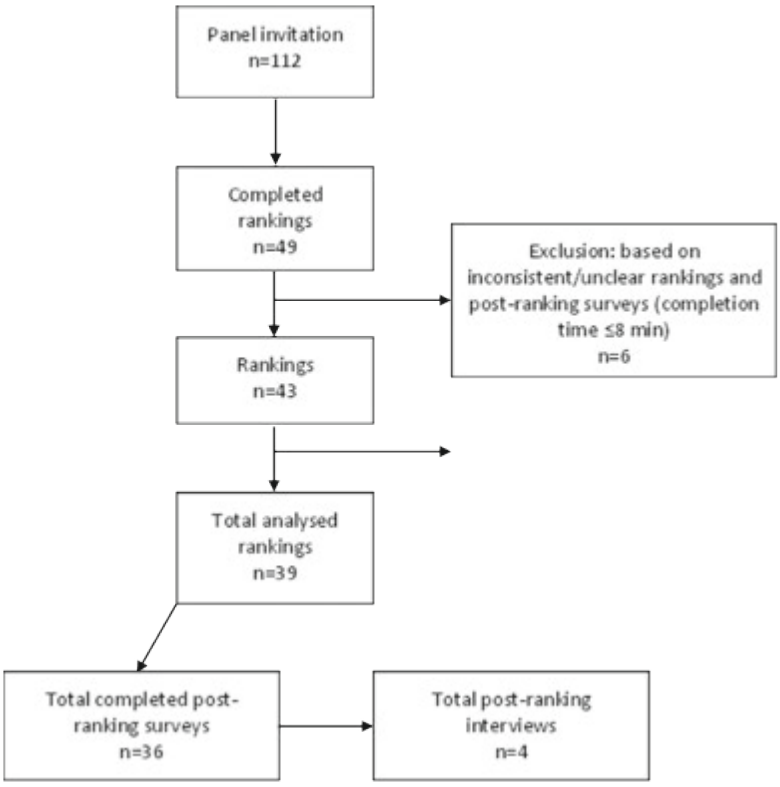

Figure 3. Flowchart on included respondents, rankings of the statement set and qualitative data

Table 1. Characteristics of respondents (n=39)

Characteristics		n	%
Age	30-39	10	25.6
	40-49	3	7.7
	50-59	13	33.3
	60-69	6	15.4
	≥70	4	10.3
	Unknown	3	7.7
Sex	Female	28	71.8
	Male	8	20.5
	Unknown	3	7.7
Household	Alone	9	23.1
	Together (partner/children/roommates)	26	66.7
	Unknown	4	10.3
Children	Yes	25	64.1
	No	9	23.1
	Unknown	5	12.8
Education (highest)	Secondary school	5	12.8
	Secondary vocational education	7	17.9
	University of applied sciences	11	28.2
	University	13	33.4
	Unknown	3	7.7
Religion	No	24	61.5
	Christian	10	25.6
	Other religion	1	2.6
	Rather not tell	1	2.6
	Unknown	3	7.7
CSP participation	Yes	31	79.5
	No	5	12.8
	Unknown	3	7.7

CSP= Cancer Screening Programme

Table 2. Factor arrays; rank scores per statement for each factor

I-Change elements Statements		Perspective		
		I	II	III
Information				
1.	The invitation for the CSPs is clear to me	+2*	+1	+2
2.	I understand the information in the flyer ©	+1	0	+1
3.	The flyer helps me deciding on participating in the CSPs	+1*	+2*	0**
4.	The flyer contains information about the advantages AND disadvantages of the CSPs ©	+1	+1	0
5.	I have sufficient information about the CSPs to make a choice about attendance	+1	+3**	+1
6.	Whenever I have questions about the CSPs I consult my GP	0	+3**	0
7.	I want my GP to invite me for participating in the CSPs	0	0	-1**
8.	I want my GP to provide me with the outcomes of the screening tests	0**	+2**	0**
9.	I want to receive the screening outcome via post mail ©	0	0	+1
10.	I talk about the CSPs with my partner, children, family, and friends ©	+1	+1	0
11.	I would attend an information meeting on the CSPs	0	-1	-2**
Awareness				
12.	As long as a do not have any complaints, I do not want to know whether I have cancer	-3	+1**	-2
13.	There are also disadvantages on participating in a CSP	-1	+2**	-1
14.	I do believe to have a high risk on developing cancer ©	0	0	0
15.	By participating in a CSP I can lower my chance of dying as a consequence of cancer	+1	0**	+2
Motivation				
16.	I am afraid to develop cancer	-1**	-2**	+3**
17.	I think it is important to have a medical check-up now and then, even when I do not have any complaints	+4**	-1**	+2**
18.	I think it is positive that the CSPs are in place	+2**	+4	+4
19.	The opinion of my partner, children, family, and friends on participating in a CSP is important to me	+1**	-1	-1
20.	My faith influences my choice to participate in a CSP ©	-2	-3	-3
21.	Participating in a CSP does NOT match with my faith ©	-3	-3	-4
22.	Within my family we do not talk about cancer ©	-2	-1	-2
23.	By participating in a CSP I am able to do something positive for my health	+3	+1*	+2

Table 2. Factor arrays; rank scores per statement for each factor **(continued)**

I-Change elements Statements	Perspective		
	I	II	III
Intention			
24. I attend the CSPs because I get invited	+2	0**	+1
Ability			
25. I think about possible follow-up studies when deciding to participate in a CSP	-1**	0**	+1**
Barriers			
26. Participating in a CSP takes a lot of time ©	-2	-1	-1
27. I do not participate in a CSP because the follow-up studies cost money	-4**	-2*	-1
28. I have faith in the tests used by the CSPs	+3	+2*	+3
29. None of my peers actually does participate in a CSP ©	-2	-2	-3
30. Due to health problems, I am not able to participate in the CSPs	-1*	-4**	-2*
31. The examinations used in the CPS give me an unpleasant feeling	-1	-2	0**

©= Consensus statement. *p<.05, **p<0.1 versus all other factors.
CSP= Cancer Screening Programme, GP= General Practitioner

Perspective 1

Respondents with this perspective hold a positive attitude towards screening. Having regular medical check-ups, even when feeling well, is considered important (statement 17, rank score +4) and screening attendance is seen as doing sometime positive for your personal health (23,+3). These respondents think it is important CSPs are in place (18,+2) and participate because they are invited (24,+2), the information provided is clear and useful (1,+2; 2,+1; 3,+1; 4,+1; 5,+1), and they trust the testing procedure (28,+3). They also see few disadvantages of participating. The time involved is not a problem for them (26,-2), they are not concerned about potential follow-up testing (25,-1) and any associated costs (27,-4), and they perceive no health (30,-1), or religious objections (21,-3; 20,-2) to participation. Moreover, they do not seem particularly afraid of developing cancer (16,-1; 12,-3) and it is not a taboo topic of conversation in their family (22,-2). In the post-ranking surveys and the interviews, respondents also mainly named advantages of screening attendance. For example, one respondent (ID Z2UT) mentioned: *"Early detection of a possible tumour would lead to earlier treatment, and therefore to better options for cure"*. When potential disadvantages of screening were discussed in the interviews, these were stated as not being relevant enough (ID 2F17): *"Once deviant cells were detected, and as a consequence I had to consult a gynaecologist. Of course, this was not pleasant, and I*

experienced a lot of stress, but the relief afterwards, that it turned out to be good, so I did not have cervical cancer, was much more important. Even though I had a few nights of bad sleep, I would definitely always want to know whether I might have cancer." More than in the other two perspectives these respondents tend to value the opinion of people in their social environment about cancer screening (19,+1), and attending the CSPs was declared to be the social norm (29,-2). "*Among my peers everyone participates with the CSPs. Both my parents and closest friends, all do participate in the CSPs. I actually do not know people who have ethical reasons not to participate."* (ID Z2UT).

We labelled this perspective "positive about participation". Ten respondents were statistically significantly associated with this perspective, of whom eight reported they participated in CSPs, one reported not participating, and one did not report participation status.

Perspective 2

Respondents with this perspective are more thoughtful about screening participation. Although these respondents also think it is good that CSPs are in place (18,+4) and that they can do something positive for their health by participating (23,+1), they feel there also are disadvantages to participating in screening (13,+2). Contrary to the other perspectives, these respondents prefer not knowing whether they have cancer as long as they do not have any complaints (12,+1; 17,-1), and they also have the lowest expectations that participating in screening will lower their risk of dying of cancer (15,0). At the same time, they are least of all afraid of developing cancer (16,-2), compared to the other two perspectives. As one of the respondents explained (ID 1ZCW): *"Without any physical complaints, I do not want to know if a have cancer".* In addition, several respondents mentioned the possibility of a false-positive and/or false-negative test outcome in the answers to the post-ranking questions. These respondents feel they have sufficient information to make a choice on screening participation (5,+3; 3,+2), they trust the testing procedures (28,+2) and do not perceive health (30,-4), religious (20,-3; 21,-3), or other (27,-2; 29,-2; 31,-2; 26,-1) barriers to participation. Distinctive for this perspective is the role these respondents see for their general practitioner (GP) in cancer screening. In case they would have questions about a CSP, they would first of all consult their GP (6,+3) and they also would prefer receiving the outcome of a screening test via the GP (8,+2). One respondent (ID QOIZ) wrote: *"The GP is someone I trust and who is able to provide decent advice on medical issues".*

We labelled this perspective "thoughtful about participation". A total of six respondents were statistically associated with this perspective, of whom five reported they participated in CSPs and one reported not participating.

Perspective 3

Respondents with this perspective think it is good that CSPs are in place (18,+4), that having regular medical check-ups is important, even when feeling well (17,+2), and that they can do something positive for their health by participating in CSPs (23,+2). However, contrary to the other perspectives, these respondents are afraid of developing cancer (16,+3) and dying as a consequence. They disagree with the statements about not wanting to know whether you have cancer as long as you do not have complaints (12,-2) and that there are also disadvantages to participating in CSPs (13,-1). Most of all respondents they consider follow-up testing in their decision (25,+1), and reducing the risk of death an important motivation to participate (15,+2). As one respondent explains (ID IJFC): *"My core motivation for participating in the CSPs is to reduce my chance of dying as a consequence of cancer. I am quite fearful that sooner or later I will get a cancer diagnose. Just the idea of having cancer terrifies me"*. The reason underlying their motivation, also gives them an unpleasant feeling about participation (31,0) (ID IJFC): *"I always find it quite tensive to participate in a CSP. Every time again, I am afraid that they will find something. (…) On the other hand, the fear of a cancer diagnosis out of the blue is even more frightening to me. Therefore, I do participate in the screening programmes"*. These respondents trust the testing procedures (28,+3), and consider the invitation clear (1,+2) and a reason to participate (24,+1). They think the information flyer about screening is not particularly helpful (2,+1; 3,0; 4;0), however, they would probably not attend a meeting to obtain more information about CSPs (11,-2) (ID 50LC): *"I would never go to an information meeting, or something similar (…) Besides, I do not want to talk with strangers on such delicate topics"*. They feel sufficiently informed to decide about participation (5,+1) and at any stage do not see a role for their GP (7,-1; 6,0; 8,0) (ID 50LC): *"I do not need any contact with my GP about the CSPs. When I have questions, I will look them up myself. And whenever I need more information, or when something bad has been identified, I do want to discuss this with a specialist in the hospital (…) The GP's opinion has no added value in this case".*

We label this perspective "fear drives participation". A total of 16 respondents were statistically associated with this factor, of whom 12 reported to participate in CSPs, three reported not participating, and one did not report participation status.

Consensus statements

Several statements were identified as consensus statements (see Table 2), but most of them with scores between +1 and -1, indicating they were not characteristic for the perspectives (or lack of consensus about them within perspectives). Statements 20 and 21 about religion/faith were generally not seen as barriers to screening participation, nor was statement 26 about partaking in CSPs to be time consuming. Moreover, all perspectives disagreed with statement 29 that most peers do not participate in CSPs.

Discussion

The aim of this study was to explore the perspectives concerning cancer screening uptake among inhabitants of highly urbanized regions, where participation rates are particularly low. While earlier studies described general characteristics of (non-)attenders, insight in the underlying beliefs and motivations of potential participants regarding cancer screening participation remained limited.[16-18] This study is the first to investigate these underlying beliefs and motivations with respect to cancer screening participation for all three Dutch CSPs together. This provides us insights into the perspectives towards participation in screening in general. Three perspectives were identified using Q-methodology: *"positive about participation"*, "*thoughtful about participation"* and *"fear drives participation"*. The first and third perspective partly overlap in their inclination to participate in CSPs, but significantly differ in the underlying motivation for participating in the CSPs. The second and third perspectives were most distinct from each other.

Both the respondents of the first perspective *(positive about participation*) and third perspective *(fear drives participation)* are likely to participate in CSPs. In the first perspective the motivation and awareness elements of the I-Change model were found to be central. A positive attitude does seem to be linked directly to screening attendance. In literature, attitude is described to be strongly related with intention, and intention, to be medium-strongly related with screening attendance.[43] An overall positive attitude towards the CSPs has been identified as the default among screening eligible people.[19, 44-45] Together with this positive attitude, respondents of the first perspective participated since it is the social norm, and thereby (probably) also their personal norm. It is known that screening eligible people often feel a kind of moral obligation to attend, and such feelings are recognized as significant predicators for screening attendance.[19, 46] Remarkable was that interviewees with this perspective were not always able to provide correct information on the CSPs and the potential medical follow-up testing. We therefore questioned whether their decision to partake in the CSPs was (always) the result of a well-informed choice, as has been earlier studied by Douma et al., in relation to the publics' opinion on attending in the colorectal CSP.[47] Thereby, is it known that the benefits regarding CSP participation are most often overestimated (and presented).[48, 49] In the third perspective motivation elements of the I-Change model were the most important. Respondents attended the CSPs based on feelings of fear and unpleasantness. Such negative emotions were earlier already described as to both facilitate as deter cancer screening attendance.[50-52] In an earlier study we identified feelings of inconvenience, insecurity and anxiety towards the screening tests and outcomes, as determinants of low or non-attendance.[16] In this study, respondents with the third perspective revealed that an underlying fear, such as worrying to die from

cancer, could also be a motivator for screening attendance. Exclusive for this perspective are the comments of the respondents on all knowing people who actually suffered or died as a consequence of cancer. This implies respondents experienced the effects of a cancer diagnosis directly, and therefore feel more susceptible to be diagnosed with cancer. This is most probably also influencing the risk perception of these people. Several health behaviour modules, including the I-Change model, postulate that risk perception motivates screening attendance. In literature there is no consensus regarding this topic, however most recent studies report on, a small positive association of risk perception and screening attendance.[53-55] A last distinctive component of the third perspective is their tendency to be less open for external influence and guidance. This could be an important issue when trying to reach out to people holding this perspective, for example by healthcare professionals or policy makers.

People within the second perspective (*thoughtful about participation*) appeared to be more hesitant in making a decision about participating in cancer screening. Therefore, they can be considered critical regarding CSP participation. Key in this perspective are the awareness and information elements of the I-Change model. In contrast to the other two perspectives respondents doubted the effectivity of CSPs and think potential consequences of screening (inter alia false-positive and false-negative test outcomes) participation are more important. These finding relate to the protection motivation theory of Rogers, in which response efficacy and response cost are acknowledged as having an effect on screening attendance.[29] Answers in the post-ranking questions suggested respondents were better informed on the possible consequences of the CSPs. This perspective might be related to a need for autonomy as described in a recent study.[56] However, our qualitative data, in particular, revealed that participants think about the potential disadvantages of participating and know that screening is not always conclusive. For this reason, we think our participants are more "thoughtful about participation" than that they have a need for autonomy. Unique in this perspective is the role respondents see for their GP as advisor. Previous studies showed that involvement of primary care leads to an increase of screening attendance rates,[57, 58] in particular among lower socioeconomic and minority groups.[59, 60] This primary care involvement could therefore also be preferred by people who are (more) thoughtful on participation, and thus might be independent of the socioeconomic position in society.

Due to several (practical) choices this study has some limitations. First, a Q-methodology study has an exploratory nature and can be used to identify and describe the main perspectives on a topic in a certain population. The sampling strategy used in Q-methodology studies, is however not informative about how common these perspectives are among people eligible for cancer screening participation in general

(frequency question), nor how the perspectives are associated with the characteristics of respondents, or why specific respondents with the same perspective present different screening behaviour.[61] Such 'frequency-questions' could be examined with surveys,[62] whereas future 'how and why-questions' can be answered by performing additional interviews and focus groups.[63] Second, respondents were recruited from an existing research panel of an external agency. On the one hand this allowed us to conduct the study remotely and thereby guaranteeing full anonymity, whereby respondents did not feel any social pressure during the ranking exercise. On the other hand, it introduced a selection and led to several specific drawbacks. Our sample predominantly contained women, aged between 50 and 69 years, living with a partner, and were higher educated (Table 1). From literature it is known that people with these characteristics are more prone to participate in the CSPs.[16] When taking the general demographics of the screening eligible inhabitants of The Hague into account, one would expect to included: more men, more people living alone, lesser people with children, more people with vocational education or lower, and more people who adhere to a religion.[40] It is possible that additional perspectives would have been identified if more respondents with these more general characteristics had been included in this study. Therefore, we recommend future studies with a similar aim to use a face-to-face sampling approach. Furthermore, the switch to the online data approach may have affected the number of exclusions as issues with the software tool that were not addressed in the explanation materials could not been solved. And, lastly, it was not possible to obtain an interview with the two respondents most strongly associated with each factor directly after they had finished their ranking of the statements, as they could only be invited for this interview after all data was collected and the analysis was finalized. Third, statement categorization by the I-Change model was challenging, especially since the relationship between the components is not always clearly defined.[27, 32] Respondents are not familiar with the subdivision of the I-Change model and could therefore classified some statements differently. However, since we upfront tested our statement set and none of the initial potential respondents, nor the actual respondents, reported to mis significant statements important to their perspective, we believe the I-Change model to be suitable in order to create a comprehensive set of statements.

This Q-methodology study shows that beliefs and motivations towards CSPs are not only different between attenders and non-attenders but can also differ between subgroups of people holding different perspectives. In order to increase awareness and knowledge regarding the CSPs, we therefore suggest tailoring communications to the perspectives of potential participants. This implies that for perspective 1 more attention needs to be paid to providing informing about the CSPs and follow-up medical testing procedures, that for perspective 2 more attention needs to pe paid to the potential disadvantages of

screening, and that for perspective 3 to more education needs to be provided about risks and numbers relating morbidity and mortality. For two of the perspectives in this study, communication channels others than the GP were found to be appropriate. However, for the respondents of the second perspective, who doubted screening attendance and thought about the potential consequences of the screening, information provided by a GP, or a perhaps another trusted primary care health professional, seems essential.

Conclusions

Conducting this study allowed us to explore the perspectives of people living in a highly urbanized region concerning cancer screening participation. Our study identified three perspectives on beliefs and motivations underlying screening attendance. Since CSPs will only be effective when participation rates are sufficiently high, it is essential to have insight into the different perspectives among potential respondents concerning partaking in a CSP. Tailor-made communication strategies for these different perspectives are highly recommended to increase awareness and knowledge regarding the CSPs, and probably should also involve primary care health professionals, at least for a part the population. The findings of this study could contribute to the future optimization of the CSPs.

Abbreviations

CSP: Cancer Screening Programme; RIVM: National Institute for Public Health and the Environment; WHO: World Health Organization; I-Change model: Integrated Change model; GP: General Practitioner.

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Availability of data and materials
The datasets used and/or analysed during the current study is available from the corresponding author on reasonable request.

Authors' contributions
All authors contributed to the design of the study and the interpretation of the data. TB and FB conducted the grey literature search. TB, FB, MC and VN created the statement set for the study. TB performed the pilot study. TB conducted the statistical analysis, supervised by FB and JE. TB conducted the post-ranking interviews. FB checked the qualitative data resulting from the post-ranking interviews. TB drafted the manuscript and FB, MC, JE and VN helped drafting and revising the manuscript. OG and MN give their critical input on the final version of the manuscript. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate
Upfront, this study was approved by the Medical Research and Ethics Committee of the Leiden University Medical Centre (METC Leiden| Den Haag |Delft) (N21.040) and was conducted in accordance with the Declaration of Helsinki. All respondents were informed about the aims of the study, its voluntary nature, and anonymous data usage, before giving consent to participate. Informed consent was obtained from all respondents.

Consent for publication
Not applicable.

Competing interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this study.

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CHAPTER 5

Cervical cancer screening among marginalized women: a cross-sectional intervention study

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Abstract

Background

Many countries organize population-based cervical cancer screening programs (CSP). In the Netherlands, eligible women are invited by mail. Marginalized women living in unstable conditions and homeless women often fail to receive the invitation letter. These women also experience access barriers to regular healthcare. Consequently, despite presumably being at higher risk of developing cervical cancer due to prevalent risk factors, marginalized women are rarely screened for cervical cancer. The aim of the study was to identify the prevalence of (pre)cancerous abnormalities among marginalized women, and subsequently explore invitation approaches to enhance their screening participation.

Methods

A cross-sectional intervention study was conducted in Rotterdam, the Netherlands. Between February and May 2019, marginalized women aged 20-60 years were invited to participate in cervical screening. A participant was considered screen-positive when they tested positive for high-risk human papilloma virus (HR-HPV) and showed cytological abnormalities. Data of the study population were compared with regional data of the Dutch CSP. Various invitation approaches were used to recruit women.

Results

Out of 74 included women, 12 participants (16%) were found screen-positive, against 3.4% in women screened by the Dutch CSP. The prevalence ratio for the study population was 4.4 (95% CI 1.9-8.6) compared with women screened by the Dutch CSP. Using a direct, pro-active approach resulted in participation of 92% of the included women.

Conclusion

Marginalized women have an increased risk of (pre)cancerous cervical abnormalities in screening, compared with women screened by the Dutch CSP. A direct pro-active approach was the most effective to stimulate screening participation. Enhancement of screening uptake for this population needs special effort.

Introduction

Cervical cancer is the fourth most common cancer in women worldwide.[1] The main cause of cervical cancer is a chronic infection with high-risk human papillomavirus (HR-HPV). Although around 80% of the women get infected with this virus, only one percent of the infected women develop cervical cancer.[2] Risk factors for a chronic HR-HPV infection are smoking, a history of chlamydia, herpes, (a history of having) multiple sexual partners, an early sexarche and immune system deficiencies.[3] Mortality from cervical cancer is preventable when detected and treated in an early or precursor stage. Therefore, many countries organize a national cervical cancer screening program (CSP), for early diagnosis.

In the Netherlands, all women between 30-60 years of age are invited to participate in the regionally coordinated national CSP every five years. Invitation is by mail, send to a registered home address. Attendance is voluntary and the primary screening test is free of charge. Women are invited to make an appointment with their general practitioner (GP) for having a cervical smear, or (since 2017) can order a self-sampling HR-HPV-test. Analysis is stepped and starts with a HR-HPV test. In case of a positive test for HR-HPV, a subsequent cytological analysis will be performed.[4] In 2018 61% of all eligible women participated in the Dutch cervical CSP.[5] Despite the availability of a CSP, half of all women that developed cervical cancer were never or insufficiently screened.[6] In the Netherlands, characteristics correlating with low screening uptake are: being born outside the Netherlands, living in an urban region, low socio-economic status (SES), and a younger age.[3,7]

Sex workers living in unstable conditions, homeless women, and undocumented women – from now on referred as: marginalized women – share those characteristics and are often not registered with the municipality, lack a permanent address, or are not registered at all. Therefore, they often fail to receive the invitation letters, or are not invited at all. Moreover, these women face various access barriers to regular healthcare, and they are confronted with other priorities than partaking in preventive services.[8-10] Prior studies have showed how hard it can be to engage marginalized women in screening programs. Even after removing healthcare and financial barriers, 38% of the homeless women would still decline a cervical screening smear.[11] Marginalized women often face multiple risk factors for a chronic HR-HPV infection and consequently, for cervical cancer. A study in the United States of America (US) showed a 4.4 times higher incidence of cervical cancer in homeless women, compared with the average female population, making cervical cancer the third most common type of cancer in this specific population.[12]

There have been several studies on cervical cancer and screening including marginalized women in the US.[11,12] However, to our knowledge, European studies are lacking. Due to the differences between the US and Europe in population, organization of care, and screening for marginalized populations, there is a need for European input on this subject.[8] The study had two specific aims. The first was to identify the prevalence of (pre)cancerous abnormalities among marginalized women. The second was to explore invitation approaches to enhance the screening uptake among this specific group of women in an urban setting in the Netherlands.

Methods

A cross-sectional intervention study among marginalized women was performed in Rotterdam, the Netherlands. Rotterdam is the second largest city of the Netherlands. The study was conducted between February 2019 and June 2019. The study population consisted of women in unstable living conditions, concerning: sex workers, homeless women, uninsured women (in the Netherlands, health insurance is obligatory by law; only a small minority is uninsured, mostly due to the lack of a home address), and undocumented women (women without a residency status). The inclusion criteria were: female sex, age 20-60 years, and the absence of a registered address at a given point in the last five years. Exclusion criteria were: having had a cervical smear in the preceding year, not having a cervix, being incapacitated, being pregnant, having a menstrual period at that specific moment, and having the option to access regular healthcare abroad.

Recruitment of the women took place at homeless shelters, day and night shelters for undocumented people, respite care locations, safe houses for sexual trafficking victims, in brothels and sex worker walk-in houses. The cervical smears were performed by a medical team consisting of a female streetdoctor and a female nurse familiar with the study population. Topics such as contraceptives, sexual trauma and sexual health are part of the expertise of this medical team.

Depending on the local options, either a direct or indirect invitation approach was used for recruiting the women. The direct invitation approach contained a pro-active offer of an immediate cervical smear. This was done during the consultation hours of the streetdoctor or combined with the consultations for sexual transmitted infections (STIs) by sexual health workers. The indirect approach consisted of distributing posters in relevant areas and announcements on a website, with information about the opportunity to have a cervical smear performed. Furthermore, mails were sent to all known care providers or case managers of the population under study, with the option to make an appointment for their client to have a cervical smear.

The screening method used was liquid based cytology sampling. The samples were analysed using both a HR-HPV test (COBAS 6800® HR-HPV, Roche) and cytology (ThinPrep® PAP-test, examined with computer assisted screening on the ThinPrep® Integrated Imager by Hologic) on each sample. The Dutch CSP uses the same laboratory methods.[5] In the Netherlands the Papanicolaou (Pap) classification is used to score the test outcome. A participant was considered being a screen-positive, when they tested positive for high-risk human papilloma virus (HR-HPV) and showed cytological abnormalities (≥Pap-2). This corresponds with the National Health Service Cervical Screening Program of the United Kingdom as: ≥HR-HPV positive and borderline changes in the squamous/endocervical cells, and with the American Bethesda-classification as: ≥ atypical squamous cells of uncertain significance. [13,14]

Participants were informed of their test results by means of consultations, text messages and phone calls; usually directly to the participant, but occasionally to their care providers. Referral to a gynaecologist was done by the streetdoctor, or if present, the own GP. A public health safety-net team served as backup, whenever women needed to be located for follow-up but did not show at their appointment.

Data management

The medical team registered details of the procedure in the routine medical files of the participant. At inclusion the women gave consent to share their medical record for research. For data-extraction, data were anonymized by coding all study participants and removing all information that would enable researchers to trace back the data to a single individual. HR-HPV status and cytological classifications were translated into binary outcomes, respectively negative/positive and normal/abnormal smear. Age (in years) and the inclusion location were extracted as well. The inclusion method was coded as indirect or as direct. Anecdotal reasons for refusal to participate in the study were registered for the few women who declined participation and were willing to the reason. Data were stored and saved in compliance with guidelines of Good Research Practices. Upfront this study was approved by the Ethics Committee of the Leiden University Medical Centre and was conducted in accordance with the Declaration of Helsinki.

Power analysis

The Dutch CSP is coordinated by five regional screening organizations, making screening data available and insightful on specific regions. 'Stichting Bevolkingsonderzoek Zuid-West' is the designated screening organization for Rotterdam concerned with the southwest region of the Netherlands. Of all participating women in the southwest region 3.4% were found to be screen-positive in 2018.[15] A prior study on homeless women presented a percentage of 18% screen-positive women.[11] Using this information a power

analysis was performed on Clincalc.com to determine the size needed for the study population in order to detect a relevant difference in outcome.[16] Using the anticipated incidence of 18%, resulted in a needed sample size of n=22 (α 0.05, β 0.2). When lowering the adjusted rate to a safer prediction and expecting an outcome of 12%, the needed sample size was set at n=53 (α 0.05, β 0.2).

Data analysis

The prevalence of screen-positive women from the study compared with the prevalence rates of the last available regional data from the Dutch CSP in 2018.[15,17] Data were analysed descriptively using counts (percentages), prevalence rates and prevalence ratios (PRs). The prevalence ratios and their confidence intervals (CIs) were calculated by performing binomial tests. The null hypothesis was that the prevalence rate of screen-positive marginalized women, is equal to the prevalence rate of women screened by the Dutch cervical CSP. In Tables 1 and 2 the data are subdivided per age cohorts of 5 years, comparable to the 5-yearly screening.

In order to provide the PR, a calculation was performed excluding and including the women under the age of 30. Additionally, screen-positive women were compared on the basis of their legal-status (undocumented versus documented). For both PR calculations, the regional prevalence rates of screen-positive women by the Dutch CSP were used. These rates are displayed in the Supplementary Table.

To evaluate the various invitations approaches, the number of included participants per approach were counted. All analyses were conducted using IBM SPSS Statistics 25.

Results

In total, 74 women were included in the study, with a mean age of 38.2 year (SD 10.4 years of age). Out of 74 participants, 12 participants (16%) were found to be screen positive. In total 26 participants tested positive on HR-HPV, and fifteen cervical smears returned as abnormal. Figure 1 shows the distribution of the test results of the cervical smears from the women included in the study. In Table 1, the occurrence of HR-HPV and the cytological results per age cohort are presented. Based solely on the current Dutch CSP age-boundaries of 30-60 years, 54 women would be eligible for screening, 8 of which were found to be screen-positive.

Prevalence ratios

Calculating the PR of the included 54 marginalized women (age boundaries 30-60 years), compared with women screened by the Dutch CSP resulted in a ratio of 4.4 (95% CI 1.9-8.6). This indicates that marginalized women, between the age 30-60 years, have an increased risk of 4.4 being screen-positive in comparison with women screened by the Dutch CSP (Table 2a). The additional calculation, which included the women younger than 30 years of age, provided a PR of 4.8 (95% CI 2.5-8.3) (Table 2b).

The additional sub-analysis showed that of the 17 undocumented women, 5/17 (29%) were identified as screen-positives, compared with 7/37 (8%) in the documented group.

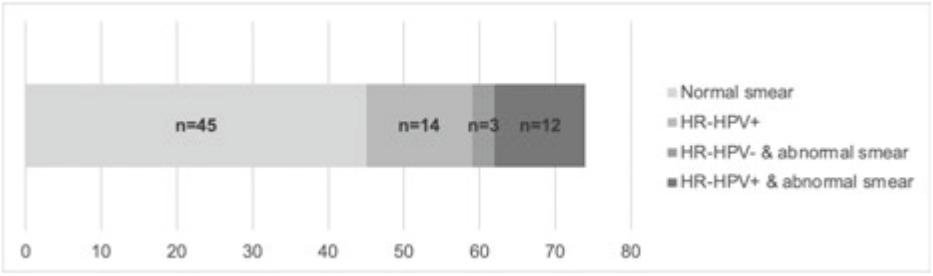

Figure 1: Distribution test results of the cervical smears. HR-HPV= High Risk Human Papillomavirus

Table 1: Occurrence of HR-HPV and cytology of the study population (n=74)

		HR-HPV			**Cytology**			**HR-HPV+ & abnormal smear**
		Count		Percentage HR-HPV+	Count		Percentage of abnormal smears	Count (percentage)
		Negative	Positive		Normal	Abnormal		
Study population (n)		48	26	35%	59	15	20%	12 (16%)
Age cohort	20-25*	1	6	86%	4	3	43%	3 (43%)
	25-30*	10	3	23%	11	2	15%	1 (8%)
	30-35	7	4	36%	8	3	27%	3 (27%)
	35-40	8	2	20%	10	0	0%	0 (0%)
	40-45	8	1	11%	7	2	22%	1 (11%)
	45-50	3	4	57%	6	1	14%	1 (14%
	50-55	10	3	23%	13	0	0%	0 (0%)
	55-60	1	3	75%	0	4	100%	3 (75%)

HR-HPV = High Risk Human Papillomavirus, HR-HPV+ = High Risk Human Papillomavirus positive
*Women in these age cohorts are not screened by the Dutch CSP.

Table 2: Calculations of the prevalence ratios

Table 2a: Prevalence ratio 1. The study population (30-60 years of age) compared to women screened by the Dutch CSP

		Prevalence HR-HPV+ & abnormal smear (A)	Number of women (B)	Expected cases (AxB)	Observed cases (C)	Prevalence ratio ((C/B)/A)
Total women (age 30-60, n=54)		0.034	54	1.84	8	4.4 (95% CI 1.9-8.6)
Age category	30-35	0.076	11	0.84	3	
	35-40	0.045	10	0.45	0	
	40-45	0.032	9	0.29	1	
	45-50	0.029	7	0.20	1	
	50-55	0.022	13	0.29	0	
	55-60	0.014	4	0.06	3	

CSP = Cancer Screening Programme, HR-HPV+ = High Risk Human Papillomavirus positive

Table 2b: Prevalence ratio 2. The study population (20-60 years of age) compared to women screened by the Dutch CSP

		Prevalence HR-HPV+ & abnormal smear (A)	Number of women (B)	Expected cases (AxB)	Observed cases (C)	Prevalence ratio ((C/B)/A)
Total women (age 20-60, n=74)		0.034	74	2.52	12	4.8 (95% CI 2.5-8.3)
Age category	20-30	0.076*****	20	1.52	4	
	30-35	0.076	11	0.84	3	
	35-40	0.045	10	0.45	0	
	40-45	0.032	9	0.29	1	
	45-50	0.029	7	0.20	1	
	50-55	0.022	13	0.29	0	
	55-60	0.014	4	0.06	3	

CSP = Cancer Screening Programme, HR-HPV+ = High Risk Human Papillomavirus positive
*****Women in this age cohort are not screened by the Dutch CSP. Therefore the prevalence rate for age cohors 20-30 was equated to the screen-positive prevalence rate from age cohort 30-35 years of age.

Invitation approaches

The participants of the study were recruited from several locations: 29 participants in homeless shelters, eight participants in a shelter for undocumented women, nine participants in a day shelter for homeless and undocumented people, eight participants in a shelter for sexual human trafficking victims, 15 participants in sex clubs combined with STI screening, and five participants at sex-worker walk-in location combined with STI screening.

Out of the 74 participants, 68 (92%) women were recruited via the direct invitation approach. The remaining six participants were recruited by an indirect invitation approach. Of the indirect approach, five women were recruited through appointments made by their care providers, and one woman chose to participate after reading the website announcement.

Several women declined to participate in the study. Some were willing to tell their reasons, which mainly met one of the exclusion criteria. In a number of cases, still being virgin was mentioned.

Discussion

This cross-sectional intervention study, conducted in a large city of the Netherlands, showed that marginalized women have an increased risk on (pre)cancerous cervical abnormalities compared with women screened by the Dutch CSP, with a PR of 4.4. Subsequently, a direct pro-active approach was found to be the most effective to stimulate screening participation among marginalized women.

The findings of this study are in line with the results of two earlier US-studies among homeless women, showing higher incidence rates of abnormal smears and cervical cancer.[11,12] This emphasizes on the special needs for screening marginalized women on cervical cancer.

The literature called for new and innovative approaches in order to engage homeless women in cervical screening programs.[11] Being pro-active and making use of close care providers seemed crucial to engage in addressing this specific population. During the study peer influence proved invaluable. Several participants became so convinced of the importance of screening they encouraged other women to participate in cervical cancer screening. This mechanism is to be acknowledged as a powerful tool for further enhancing screening uptake among this population; and has been described as being effective among other minority groups.[18,19]

Due to several (practical) choices, the study has its limitations. In order to engage with marginalized women, a flexible expert-based approach is essential at the right time and the right place. But, consequently, a direct comparison of invitation methods was not possible. This since not all the approaches were equally suitable at every location. Furthermore, it is not known how many, and more important which women decided to decline participation and what their characteristics were. Reasons mentioned for not participating, collected during the direct approach, varied widely and mostly involved women who were more hesitant and cautious. A last limitation is that data on the HR-HPV vaccination status of the women was not collected. Participants younger than 21 years of age (n=2) could have received a HR-HPV vaccination; the vaccination program has been in existence in the Netherlands since 2009. In future studies, more participants might be vaccinated for HR-HPV. As this might influence the study results, it should be recorded.

The study included 37 women (50%) who were eligible for the Dutch CSP but did not participate. This raises the question whether there is a necessity to embark on a tailor-made approach for specific high-risk groups within the national CSP. As mentioned in a prior study, involvement of primary care or other relevant care providers for risk groups might enhance screening uptake.[7]

There are several differences between the Dutch cervical CSP and the study. Since special efforts are needed to enhance screening uptake among marginalized women, these differences are highlighted so further studies can be based on 'lessons learned'. Box 1 summarizes suggestions for implementing a cervical screening program for marginalized women.

One of the aims of the study was to remove as many of the access barriers as possible. Marginalized women were invited in a pro-active individual manner, without the necessity of a health insurance. The cervical smear was performed directly at the locations where these women would already be present to work, reside or receive care. Engagement and participation based on trust was shown to be crucial in the study, especially as many women mentioned a history of sexual trauma. The topic of cervical screening was introduced by a close care provider from the location, and this care provider introduced the women to the medical team. The medical team was all female and invested time in gaining the trust of the participant before taking the cervical smear. In the Dutch CSP, the smear is performed by a person's GP. The studied population, however, often does not have guaranteed access to the typically Dutch GP-oriented healthcare system. Therefore, an approach based on creating a safe environment seemed an effective alternative. The study shows that involving peers in educating and raising awareness among the target population will most definitely lead to higher participation rates. The

tailor-made approach for engaging this population in cervical cancer screening is very time-consuming and greatly depends on the availability of a network and the setting, which has proven the major drawback of this approach.

The age boundaries of cervical CSPs do differ between countries, and are under constant review.[14,20,21] Because of the assumption that marginalized women are being exposed to the risk factors for cervical cancer earlier in life, leading to cervical cell abnormalities at a younger age, the age limits for eligible women in the study were extended to the age of 20, instead of 30. A second PR calculation included these younger women and, before calculation, the screen-positive prevalence rate was equated to the prevalence rate from age cohort 30-35 years of age. This since the Dutch CSP is not screening women between 20-30 years of age and therefore no age specific prevalence rates are known. This is most probably an underestimation. HR-HPV infections will be more prevalent among younger women but will most often be transient, and thus will not progress into cervical lesions. HR-HPV testing for women younger than 25 years has a low specificity and creates a risk of over-referral and overtreatment. When screening for (pre)cancerous cervical abnormalities in women below the age of 25, cytology should be the primary screening method.[22] However, including these younger women in the PR calculation, does show an increase of the PR-ratio. This suggests inclusion of women between the age of 25-30 in a high-risk group – such as marginalized women – with an early exposure to HPV, is justifiable and advisable.

Clear arrangements were made with the participating women concerning follow-up and how these results would be reported back. In total 12 participants needed referral to a gynaecologist, which eventually were all managed successfully. Nevertheless, it was crucial to have a back-up municipal safety-net team. One of the 12 referred participants missed out on the second appointment with the gynaecologist, due to a transfer to a safe house in another region. She was traced and referred to a gynaecologist in the other region. Another referred participant did not make an appointment with the gynaecologist due to an emergency admission in a detox facility. After being traced, she needed a new referral. Tracing all the participants who needed a repeat cervical smear after six months as part of the follow-up proved the most challenging. All women could be traced through the public health safety-net team. Future implementation studies should further explore these challenges regarding the follow-up, and most ideally tackle these logistical problems beforehand.

The study included undocumented and European (non-Dutch) women, who are unable to partake in the Dutch cervical CSP. The reason for including these women, was that they are assigned to the care of streetdoctors, and they also face a high prevalence

of risk factors concerning the development of cervical cancer. Without any possibility to return to their homeland for treatment, they will receive the treatment in the Netherlands, with all the attendant costs included. This is of high importance because the findings suggest that undocumented women also have a high risk on (pre)cancerous cervical abnormalities. The number of participants in the study is too low for definitive conclusions, but more research in this specific subpopulation is firmly recommended.

1. Be pro-active as care provider;
2. Provide the cervical smear at the locations where the women work, reside or receive care;
3. Use a trusted care provider on the location for recruitment and the introduction of the program;
4. Use female medical teams;
5. Involve peers: give them a role in educating and raising awareness;
6. Consider screening from a younger age onward, starting at the age of 25 is recommend;
7. Make sure follow-up is guaranteed and explore regionally which organizations can cooperate.

Box 1. Recommendations for implementing a cervical screening program for marginalized women

Conclusion

The current national population-based cancer screening program for cervical cancer is largely missing out on marginalized women. In view of their increased risk, efforts should be made to enhance screening uptake among marginalized women at the cervical CSP. A tailor-made, direct and pro-active invitation approach will most probably be successful to involve marginalized women in cervical screening. In the discussion suggestions and recommendations are offered for future studies. Both researchers and policymakers are invited to use this study for optimizing the current cervical CSPs.

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Disclosure
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Supplementary Table: Prevalence rates of HR-HPV+ & abnormal smears per age cohort of women screened by the Dutch CSP. Regional data from 2018[15]

		Screened	**HPV-HR+**		**HR-HPV+ & abnormal smear**	
		Count (n)	Count (n)	Prevalence	Count (n)	Prevalence
Age cohort	20-25*****	-				
	25-30*****	-				
	30-35	12247	2448	0.20	931	0.076
	35-40	12745	1587	0.12	578	0.045
	40-45	14114	1280	0.09	449	0.032
	45-50	15152	1265	0.08	434	0.029
	50-55	16920	1181	0.07	367	0.022
	55-60	16764	1005	0.06	230	0.014
Total		87942	8766	0.10	2989	0.034

*****Women in these age cohorts are not screened by the Dutch CSP.
HR-HPV+ = High Risk Human Papillomavirus positive, CSP = Cancer Screening Programme

CHAPTER 6

Perceptions and beliefs of general practitioners on their role in the cancer screening programmes in the Netherlands: a mixed-methods study

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Abstract

Background

In the Netherlands, population-based cancer screening programmes (CSPs) are organized aiming at cervical, breast and colorectal cancer. For a CSP to be effective, high participation rates are essential; however, there is an alarming downward trend, including wide regional variation in screening uptake. General practitioner (GP) involvement can have a stimulating effect on screening participation. Current GP involvement is however, limited, varies between the programmes and has changed over time. Unexplored is what GPs think of their role(s) in the CSPs. The aim of this study was therefore to map the perceptions and beliefs of GPs regarding their current and future role in the Dutch CSPs.

Methods

A mixed-methods sequential explanatory study was conducted in the Leiden/The Hague area of the Netherlands, between the end of 2021 and 2022. A questionnaire was developed and distributed among 110 GPs. The aggregated results obtained from the questionnaires served as starting points for conducting semi-structured interviews, with purposefully selected GPs. With this sequential approach we aimed to further enhance the understanding of the questionnaire data and delved into the topics that emerged from the questionnaire responses.

Results

In total, 46 GPs completed the online questionnaire (response rate 42%). Subsequent five semi-structured comprehensive interviews were conducted. GPs indicated that they frequently encounter the CSP in their daily practice and consider it important. They also emphasised it is important that GPs remain closely involved with the CSPs in the future. Nevertheless, GPs also repeatedly mentioned that they are not eager to take on more logistical/organizational tasks. They are however willing to empower CSPs in a positive manner.

Conclusion

GPs were generally positive about the CSPs and their current role within these programmes. Nevertheless, several options were proposed to improve the CSPs, particularly aiming to increase screening uptake among populations in socioeconomically disadvantaged positions. Since it is of utmost importance to screen those who are most at risk of developing the screening-specific tumours, efforts should be made to achieve this goal.

Introduction

The Dutch government invests considerable budgets, time, and effort in hosting three population-based cancer screening programmes (CSPs), aiming at cervical, breast and colorectal cancer (CRC). The goal of these screening programmes (SPs) is to detect cancer in an early or precursor stage. On average, this approach leads to a better prognosis, as well as fewer and less severe side effects of treatment.[1-3] The screening tests of the CSPs are offered free of charge by the Dutch government to all citizens of a specific age and gender. The National Institute for Public Health and the Environment (RIVM) and the national screening organisation (Bevolkingsonderzoek Nederland) are in charge of organizing and coordinating these programmes.[4, 5] Participation is voluntary and monitored yearly by the RIVM.[6-8] Although the three CSPs exhibit many similarities, each CSP has its unique procedures and organization, mainly due to differences in screening methods (see Table 1).

Table 1. Key characteristics of the population-based cancer screening programmes of the Netherlands

	CC-SP	BC-SP	CRC-SP
Since (year)	1979 (pilots from 1976)	1990 (pilots from 1984)	2014 (fully operational since 2019)
Population Age boundaries	30-60	50-75	55-75
Sex	F	F	F & M
Interval (years)	5	2	2
Screening test	HPV-test, if HPV positive then cytology (Pap-smear)	Mammography (bilateral)	Faecal Immunochemical Test (FIT)
General practitioner involvement	Performing pap-smear, discuss outcome, hospital referral[a]	Discuss outcome, hospital referral[b]	None[c]; discuss outcome
Screening outcome	HPV absent, present or unclear (re-testing). When applicable Pap-classification and HPV-typology.	Abnormality absent, abnormality present, not enough information (BI-RADS-code 0-5)	Negative (no examination needed), positive (examination needed), unclear (re-testing)
Financing Invitation, screening test(s) and analyses	Dutch government		
Secondary test(s) and treatment	Standard healthcare, hence depending on one's individual insurance policy		

CC= Cervical Cancer, BC= Breast Cancer, CRC= Colorectal Cancer, SP= Screening programme, F= Female, M= Male, HPV= Human Papillomavirus

[a] From 2017 onward, women can opt to receive a self-sampling test (after being invited). The outcome of the self-sampling test is not automatically shared with the GP due to privacy legislation. Outcomes will only be shared with the GP if it is explicitly stated that the GP is allowed to receive this information. Hence, the GP no longer plays an essential role in this CSP. If HVP is detected, women are recommended to contact their GP to have a smear test taken at the GP practice.
[b] In cases where no abnormalities are detected, the GP will not be involved.
[c] Since 2017, the GP no longer automatically receives the outcome of a FIT. Outcomes will only be shared with the GP if it is explicitly stated that the GP is allowed to receive this information. After a positive FIT patients are encouraged to seek contact with their GP.

High participation rates are essential for a CSP to be effective. According to the World Health Organization (WHO), at least 70% of the target population should be screened in order to be beneficial at the population level.[9-11] Throughout Europe participation in CSPs varies substantially, yet the Netherlands has always been known for its high screening attendance and adherence.[12] The most recent nationally available attendance rates – registered before the COVID-19 pandemic – were 56.0%, 76.0% and 71.8% for the SPs aimed at cervical, breast and CRC, respectively.[6-8] Although the attendance rates of two programmes are above the recommended rate from WHO, there is an alarming downward trend and wide regional variation in screening uptake.[13] In 2010, the uptake rates of the CSPs for cervical and breast cancer were 65.5% and 80.7%, respectively.[6, 7] Since the colorectal CSP has only been fully operational since 2019, it is too early to draw any conclusions on trends regarding this screening programme. The lowest attendance rates are found in the four large cities of the Netherlands and fall, for all three programmes, below the minimal intended rate of 70%.[4] This seems to coincide with a relatively higher incidence and related late-stage diagnoses in the same areas.[14] Hence, efforts should be made to optimize current screening uptake, especially for individuals who currently do not engage in the CSPs.

General Practitioner (GP) involvement is recognized for its ability to influence screening uptake, mostly by stimulating screening participation.[15-18] Within the Netherlands, GP involvement was earlier described as beneficial for the classical, 'hard to reach', subpopulations.[13] Thereby, the Dutch are known for placing trust in and maintaining good long-term relationships with their GPs.[19] Despite these factors, the extent of GP involvement in the CSPs remains limited, varies between the different programmes and has changed over time.[13] Unexplored is what GPs think of their role(s) in the CSPs. This study aims to fill this knowledge gap by mapping the perceptions and beliefs of GPs regarding their current and future role in the Dutch CSPs. With the long-term objective in mind that GP-involvement in the CSPs could potentially boost screening attendance.

Methods

Study design, recruitment of respondents and interviewees, and ethical considerations

We conducted a mixed-methods sequential explanatory study using questionnaires and semi-structured interviews to gain in-depth insight into the perspectives of GPs regarding their role in the Dutch cancer screening programmes (CSPs). This explanatory study is part of an overarching study in which we are trying to identify opportunities to optimize attendance rates for the CSPs.[20]

First, a survey was developed and distributed among GPs by using our Extramural LUMC Academic Network (ELAN). This is a network of GPs in the Leiden – The Hague area of the Netherlands, that aims to improve GP care in the region, including by supporting scientific research.[21] Over 100 GPs are closely linked to ELAN. These GPs were approached via a monthly newsletter between September and December 2021 (for a total of three times) and asked to fill out an online questionnaire. The invitation included background information about the study and a link to the online questionnaire. Second, for the succeeding interviews we again invited GPs via ELAN, but also activated other networks for recruiting GPs. For the interviewed GPs it was not necessary to have completed the previous questionnaire. We initially intended to purposefully select a diverse sample of interviewees within the ELAN GP-network – considering characteristics such as: sex, experience as GP, and neighbourhood (based on reported patient population characteristics) the GP was working in – however, due to time constraints and low response rates we changed to a convenience sample. The interviews were conducted partly face-to-face and partly online (i.e., video calls), based on the GP's preference, between October and December 2022. The interviews were conducted, audio recorded and transcribed by TB, and checked by FB, VN and MC reading the transcripts.

Questionnaire

We developed a questionnaire containing 55 questions in total, on five different topics: (I) the CSPs in the GP-practice in general, (II-IV) the CSPs at cervical, breast and CRC specifically, and (V) three open-ended questions on the (future) role of the GP within the CSPs. Questions were on how often GPs encountered the CSPs in daily practice and on their thoughts concerning the CSPs. Most questions could be answered on a five-point rating scale ranging from strongly disagree to strongly agree. To test the comprehensiveness and clarity of the questionnaire, we piloted the questions among three potential study respondents upfront. Based on their feedback, we altered a few questions with minor language adjustments. The original questionnaire was in Dutch (translated version in the Supplementary File). Aggregated outcomes of the

questionnaire, which were not traceable to individual responders, served as starting points for the interviews.

Interviews

Multiple semi-structured interviews were conducted using a thematic topic list, grounded on the outcomes of the questionnaire. Emerged topics from the questionnaire – described separately in the results section – were: (I) The current role and responsibility of GPs, (II) the informing of GPs (i.e., whether and how GPs are informed by the screening organisation, both on the patient's screening status and screening outcomes), (III) the invitation procedures, (IV) the need for tailor-made strategies for subpopulations, and (V) suggestions for future other optimalisation of the current CSPs.

Analyses

As this study is explanatory, we derived the primary topics from the quantitative phase and utilized the qualitative data gathered from interviews to provide context for the quantitative outcomes. In the results section of this manuscript, the study outcomes are also presented in this sequential order.

Data generated by the multiple-choice questions of the questionnaire are presented descriptively, using counts and percentages. IBM SPSS (version 25) was used for analysing the data. To ensure an adequate number of cases in each category for analysis, we combined and coded the responses 'agree' and 'strongly agree' as 'agreed,' while 'disagree' and 'strongly disagree' were merged and coded as 'disagreed'.

The transcripts, emerged from the interviews, were independently coded and labelled by TB and FB using a partially pre-composed code structure (open coding). Agreement on the codes was also reached between TB and FB. For each main topic, we conducted coding on the interviews to gain insights into how to interpret the quantitative data by incorporating qualitative information. The software Atlas.ti Scientific Software Development GmbH (version 7) was used for data storage, coding, and extraction of quotes for the topics. Quotes (Q) were originally in Dutch and were translated into English for this manuscript. The quotes presented in this paper were chosen based on their eloquence on a particular topic. For an overview of all quotes see Supplementary Table 1.

Results

After an online invitation of 110 GPs, a total of 46 GPs completed the online questionnaire (response rate 42%), with a mean age of 51 years (ranging from 36-68 years). Most of the respondents were female (72%) and had more than 10 years of working experience (85%). Twenty-six percent of the GPs, the largest group, were working in the greater city of The Hague. Most GPs described their population as average regarding age and educational level, and predominantly as having a Dutch cultural background (Supplementary Table 2). Subsequent five semi-structured interviews (convenience sample), ranging from 37-46 minutes, were conducted. The interviewed GPs had comparable characteristics to those of the questionnaire responders (Supplementary Table 3).

The cancer screening programmes (CSPs) were stated as an important and repeating topic in daily practice, and most GPs receive questions regarding the CSPs on a regular basis (Table 2). During the past year, 89% of the GPs received questions concerning the cervical CSP, 70% concerning the breast CSP, and 85% concerning the CRC-SP. Most questions, across all three CSPs, related to the outcomes of the screening test(s) and potential follow-up examinations, with particular emphasis on the self-sampling test for cervical CSP. GPs reported to be most familiar with the cervical CSP, regarding the objective and practice manual of the CSP, and their intended role. Only 69% of the GPs reported being familiar with their role regarding the CRC-SP, compared with 80% for the two other CSPs. Nevertheless, almost all GPs thought that their knowledge and practice policies were sufficient and accurate concerning all three CSPs. Nevertheless, the interviews revealed that GPs, on average, lack specific knowledge on various issues, including when the GP is informed and who is responsible for arranging the referral (Q3, Q21, Q49). Regarding the way GPs discuss and value the CSPs, approximately 80% of GPs indicated that they actively promote patient involvement in CSPs. Most GPs maintain a positive attitude toward patient participation, with 69% expressing the belief that encouraging cancer screening is always the appropriate course of action (Q8, Q16). Only 4% of the GPs occasionally discouraged patients from participating in a CSP. In the interviews it was explained that this occurred when patients struggled with extensive comorbidities or were already involved in (other) intensive medical trajectories. More than half (57%) of the GPs indicated that they mentioned the CSPs sometimes during consultation, even without the patient explicitly asking. From the interviews, it emerged that this was usually related to certain symptoms, such as: vaginal bleeding, a breast lump, or bowel related problems. Conversely, it also occurred that talking about the CSPs served as starting point for discussing other 'intimate' topics (Q16). Sixty-four percent of

the GPs agreed that educating patients on the CSPs is part of their job. Most of the GPs (58% agreed, 16% neutral, 26% disagreed) thought that the final decision to participate in a CSP is an individual choice, and thus should primarily be left with the individual. Although GPs suggested several options to improve the current CSPs, they generally did not feel that the programmes are currently poorly arranged (Q49, Q55 Notably, during all the interviews, the current workload of GPs was repeatedly labelled as high (Q28, Q37, Q45).

Table 2. Quantitative outcomes questionnaire per CSP

	CC-SP	**BC-SP**	**CRC-SP**
Questions during last year	89% (n=45)	70% (n=46)	85% (n=46)
GP familiar with			
Objectives	76% (n=45)	71% (n=45)	72% (n=46)
Practice manual	54% (n=46)	53% (n=45)	54% (n=46)
Role	80% (n=46)	80% (n=45)	69% (n=45)
Sufficient knowledge GP	93% (n=46)	80% (n=44)	82% (n=45)
Accurate practice policy	95% (n=42)	N/A	N/A
In favour of inviting via GP practice	22% (n=41)	17% (n=41)	17% (n=42)
Wanting to know who was invited	54% (n=41)	39% (n=41)	49% (n=43)
Wanting to know who has a positive test	73% (n=40)	83% (n=40)	43% (n=37)
Willingness to inform patients after a positive test	75% (n=40)	78% (n=40)	61% (n=48)

(C)SP= (Cancer) Screening Programme, CC= Cervical Cancer, BC= Breast Cancer, CRC= Colorectal Cancer, GP= General Practitioner, N/A= not applicable

Topic I: Current role and responsibilities of GPs

When discussing their role, the interviewees expressed satisfaction and found it to be fitting. The programmes are seen as important, and for the GPs it makes sense that they are involved, at least for a part (Q14-16). As one interviewee mentioned (Q1): *"As GPs we have to be involved in the screening programmes. The contacts resulting from engagement are eminently suiting GPs. The programmes concern cancer, which always scares patients. This is thus an opportunity for us, where we can make a difference. Patients appreciate it when we are involved when we guide them along the way".* More than once, the CSPs were described as part of 'indicated prevention', and thus as a task for the GP (Q4, Q6). Regarding their wish to stay involved in the CSPs, GPs indicated that they like to stay involved, and in doing so they appreciate the close relationship they have with certain patients (Q2, Q7, Q9, Q10, Q12). When addressing the topic of responsibilities,

GPs concurred that they are not responsible for screening uptake (Q5, Q11). However, in the case of a positive screening outcome for an individual patient, GPs do acknowledge a sense of responsibility. This is especially evident in guiding the patient and composing referral letters (Q13) (where the latter does not apply to the CRC-SP).

Topic II: Informing of GPs

GPs seemed to be divided regarding their preference for knowing the individuals invited by the screening organization. Approximately half of the questionnaire respondents were in favour of knowing this information, and some explicitly wrote this down in the open-ended question section. During the interviews, some stated they want to know all on attenders and non-attenders (GP IV and GP V), whereas others were more hesitant (GP I-III). This is illustrated by quotes 19, 23 and 25: *"I would like to know who did and did not participate. Now I have no clue, and therefore cannot act on it. If I knew, then I would be much better able to proactively engage with people concerning the CSPs"*, 'versus' quotes 18 and 20: *"I am not sure if I want to know when someone has not participated. It remains a patient's own choice. Knowing this can be perceived as intrusive. ... Then, it may no longer feel like a free choice, but much more like coercion…".* Several technical methods have been suggested to better inform GPs on screening attendance and outcomes; such as making use of the GP's IT-systems (Q26), or by an opt-out based invitation system (Q27). By the latter, the interviewee meant that GPs receive information about patients' CSP attendance by default, unless patients explicitly object. In the questionnaire, 73% of the respondents indicated that they want to know who had a positive screening outcome for the cervical CSP, 83% for the breast CSP, but only 43% for the CRC-SP. As became from the interviews, the lower percentage for the CRC-SP may stem from the perception that a positive Faecal Immunochemical Test (FIT, formerly the iFOBT) is considered less serious than a positive outcome in the other two CSPs. In addition, GPs were found to be less willing to inform patients after a positive FIT outcome. Finally, certain GPs interviewed expressed concerns that being aware of individuals who did not participate in the CSPs might result in an increased workload (Q17, Q22, Q24). They believed that this knowledge would entail additional responsibilities, such as actively reaching out to those who did not attend.

Topic III: Inviting via GP-practices

As in the past, screening-eligible people were invited via GP-practices for the cervical CSP, we questioned GPs on this topic. In the questionnaire 63% of the respondents declared they used to invite patients via their GP-practice for the cervical CSP, while 18% reported: 'unknown to me'. Only a minority (20%) of GPs currently favoured inviting patients via GP-practices. During the interviews, none of the GPs appeared to be willing to (re-)start the invitation procedures primarily via GP-practice. Indicated reasons were mostly: lack

of available time, or that their time could be better spent on other things (Q29, Q31, Q34). On the other hand, GPs also realized that the involvement of GP-practices would probably lead to a higher screening uptake (Q28, Q33, Q36). A kind of 'add-on methodology' where GPs can decide, maybe in agreement with the national screening organisation, to also invite patients themselves, so in addition to the general invitation, was considered as a possible positive proposal by all the interviewees. This idea was first introduced by GP I, Q30: "*Everyone is invited by default, but on top, GPs are given a list of high-risk screening-eligible people… You could be more creative than either just the entire invitation via the screening organisation, or via GPs".* And then later named by GP II (Q32): *"What could be done is a kind of 'add-on methodology'. So, in addition to a common basis, something extra can be done on the community-level by GP-practices. Think of a letter, or maybe even a call from the practice".* Such a methodology seems to be in line with Q35, which addressed that screening-eligible people currently do not feel seen individually. Another, less intrusive strategy, would be to send the invitation letter on behalf of the GP, or with an envelope that states that the GP supports the CSPs (Q33, Q36).

Topic IV: Tailor-made strategies for subpopulations/lower SES-neighbourhoods

By the GPs (I, III, V), working in more disadvantaged neighbourhoods, with a relatively lower socioeconomic status (SES), it was extensively discussed that tailor-made strategies are needed for specific subpopulations. As was stated (Q38): *"Given the complexity of participation, it is not surprising that people living in a low SES-neighbourhood and with a non-western migration background are less likely to participate. You have to do it all yourself, read it, understand it etc…".* Several barriers were considered to be especially relevant for people living in the lower SES-neighbourhoods, such as: the lack of (health) literacy, poor education and certain taboos. Furthermore, GPs reported that people living in disadvantaged neighbourhoods often have low trust in everything related to the government (Q44). We found no clear consensus on what these tailor-made strategies should look like (Q39-44). The earlier described 'add-on methodology' however, was thought to be effective increasing screening uptake for socioeconomically disadvantaged populations and was designated as positive by all GPs. Accurate information in several languages, and proactively approaching screening-eligible people were furthermore often mentioned as possibilities (Q39, Q40).

Topic V: Other optimalization opportunities

Numerous other optimalization opportunities for increasing participation were suggested in the open-ended questions of the questionnaire and by the interviewed GPs. Most of the idea's involved solutions as: making use of education videos on smartphones, pictograms, QR-codes and influencers (Q48, Q50, Q51). Furthermore, the waiting room information screen was suggested as a useful tool for informing patient on the CSPs

(Q53). Despite the various technological solutions, the majority of GPs also expressed a consensus that maintaining personal contact with a GP or GP practice should still be possible (Q52). GPs noted that they do not necessarily feel that a GP is required for these interactions. Instead, there was a greater emphasis on the appropriateness of involving a (specialized) practice-based nurse (Q46). Two GPs in particular addressed the funding concerning the CSPs and prevention in general (Q45, Q47, Q57): "*… the budget for primary care will truly have to increase substantially. We … actions within the system could then be funded much more easily".* Other suggestions involved (more) cooperation at both the regional as national level (Q56), and the training of medical students (Q58). One suggestion concerned the CRC-SP in particular. Multiple GPs observed that patients with a positive FIT are much more worried and anxious, than patients with positive outcomes at the other two CSPs. Therefore, they suggested that deeper clarification is needed on the meaning of the FIT for the public. This message should at least contain that a positive FIT, does not (immediately) equal CRC (Q54).

Discussion

This mixed-methods study aimed to map the role of GPs in the Dutch cancer screening programmes (CSPs), indicate that the CSPs are a regular topic during consultation hours and that GPs in general have a positive attitude towards the CSPs, and towards screening participation. GPs are most often consulted regarding the cervical CSP and the CRC-SP, and most questions are related to the outcomes of the screening tests and related follow-up examinations. The current role of GPs is generally evaluated as appropriate by GPs, and they would like to remain involved in the CSPs. GPs are not in favour of inviting screening-eligible people via their practices, or taking on more logistical/organizational tasks, but are willing to empower the CSPs. GPs agreed that they want to be informed on all positive test outcomes, but there was no consensus on knowing the participation status of all, nor all screening outcomes. Several options were proposed to improve the CSPs, particularly aiming to increase screening uptake among populations in socioeconomically disadvantaged positions.

To our knowledge, this is the first study to map in-depth the role of the GP regarding all three Dutch CSPs, and then specifically concerning perceptions and beliefs that GPs have about their role(s) and optimalization possibilities. Most of the current literature focusses usually only on one of the CSPs and GP involvement, related to screening uptake and/or GP attitudes. The findings of our study are consistent with these prior studies. As our findings indicate that GPs generally exhibit a positive attitude toward the CSPs, and they possess the ability to influence screening attendance rates.[15-18, 22-24] In addition, we found that GPs are aware of and willing to ensure that individuals with a potentially higher risk

of developing the screening-specific tumours, who often live in relatively disadvantaged lower SES-neighbourhoods, participate in the CSPs. There is evidence in the literature that GPs are able to increase screening participation among people at higher risk, which was mostly achieved by approaching and inviting people selectively.[25, 26]

GPs were found to be most familiar with the cervical CSP, which is not surprising, since current GP involvement is most prominent in this CSP.[5] GPs seemed to be especially interested in CSP aiming at breast cancer, as they were most interested in knowing who had an abnormal mammogram and were most willing to discuss positive screening outcomes with patients themselves. This is likely related to how serious positive screening outcomes are valued by GPs. Earlier research described that GPs value a positive FIT outcome much less serious, than a positive mammography outcome,[27] as was also stated by several GPs included in our study. GPs appeared to be less familiar with the CRC-SP, which is most likely related to the novelty of the programme.[5] A study focused on the CRC-SP concluded that GPs should take on a 'guidance-role' concerning possible false-positive CRC screening outcomes.[28] Responding GPs in our study explicitly stated that they like such a 'guidance-role', and do see this as a GP's task. We therefore believe that such a guidance role of GPs could be applied to the entire portfolio of the CSPs.

Regarding our study there are certain issues which need to be reflected on. First, our questionnaire yielded a response rate of 42%, which is comparable with the results of other questionnaires searches among physicians.[29] With (online) questionnaires, there is always a potential risk of selection bias.[30] In our case, it could be that GPs who consider the CSP important participated in our study. However, as the results of the interviews align with the results of the questionnaire, we believe that we managed to minimize this risk. Second, during the interviews, we noticed that several GPs sometimes lacked parts of necessary background information to answer certain questions. For instance, most GPs assumed that they would always be informed when a patient had a positive FIT result; which is not the case (see Table 1). As described earlier, this constitutes an outcome of our study; yet it also impedes a more profound exploration of certain topics. For forthcoming studies, it could be crucial to consider that the average GP may not possess a comprehensive understanding of the organization of the CSPs. Third, during the interviews, it emerged that GPs had not always thoroughly considered their reasons for wanting certain information. For example, they regularly indicated that they wanted to know all on who had been invited, as well as on the outcomes of all screening tests. However, when we further probed into what they intended to do with this information, clear answers were not always provided. Fourth, for this study, we used a f convenience sample, due to logistical and time-related issues. Although most interviews yielded about the same answers, we cannot state that we achieved data saturation, as is often aimed for

in qualitative studies.[31] Future (qualitative) studies are thus needed to clarify the above issues, which could also analyse possible differences in GP-specific characteristics related to outcomes. Lastly, as we conducted our study with GPs in (highly urbanised areas of) the Netherlands, our conclusions are primarily valid for Dutch GPs. GP involvement in the CSPs is however, not unique for the Netherlands,[15-18, 22, 24, 30, 32, 33] therefore we believe that interested readers (e.g., healthcare professionals and policymakers) from other (European) countries could also benefit from the insights gained from this study.

Based on the results of this study, we are confident that the future role of GPs can be optimised. One of the most cited concepts in the interviews was the idea of an 'add-on methodology' to increase current screening uptake, which might be particular suited for the more deprived neighbourhoods. This is in line with a more proactive, population/neighbourhood/community-oriented primary care approach and fits into the description of structured Population Health Management.[34] Such an 'add-on methodology' can be organised as a proactive tool, aiming to prevent adverse health events resulting from missing early screening opportunities in populations specifically at risk. A tool like this also responds to the concept of 'trust' in primary care and pays attention to people as individuals. Moreover, positive endorsement can be promoted by a GP practice. Another important, and recurring issue in the interviews was the currently increasing workload of GPs.[35] In our view, the prospect of getting even busier hinders potential innovations in primary care. This phenomenon is not desirable given all the challenges in the current healthcare landscape. We would therefore advocate that new innovations to optimise current CSPs should be implemented only in close consultation with GPs.

For the nearby future, we would like to challenge the national screening organisation, together with GP-practices, to determine whether such an 'add-on methodology' can be rolled out in several neighbourhoods, and to evaluate whether this approach is indeed effective for increasing current attendance rates among screening-eligible people, ideally for those at highest cancer risks. Considering the results of this study, it would be logical to establish a pilot study in the greater city of The Hague. The hope is that if GPs are more involved in the CSPs, they can especially educate and motivate people with potentially higher pre-existing risks of developing cancer to get screened. In this regard, attention must also be given to communication from GPs to potential participants, as it is known that the way of communicating influences perceptions on the CSP.[36] In this context, consideration can also be given to shared decision-making tools, where thought should be given to what can help involve individuals who are currently not participating in the CSPs. Recent research suggests that shared decision-making tools appear to be particularly useful for people belonging to socially disadvantaged groups. A prerequisite hereby is that there is sufficient time available for the consultation.[37] Ultimately, it is most

important to screen those with the highest risk of developing the screening-specific tumours.

Conclusion

Our study indicated that the cancer screening programmes (CSPs) are a regular topic during consultation hours and that GPs judge this as a topic in which they like to stay involved. GPs are not eager to take on more logistical/organisational tasks but are willing to positively empower the CSPs and especially targeting subpopulations at highest risk. Several suggestions emerged from our study to further optimise the CSPs. A targeted proactive primary care approach was suggested as a desirable option.

Abbreviations

CRC: Colorectal Cancer; CSP: Cancer Screening Programme; ELAN: Extramural LUMC Academic Network; FIT: Faecal Immunochemical Test; GP: General Practitioner; RIVM: National Institute for Public Health and the Environment; SES: Socioeconomic Status; SP: Screening Programme; Q: Quotes; WHO: World Health Organization.

Ethics approval and consent to participate

Upfront, this study was approved by the Medical Research and Ethics Committee of the Leiden University Medical Centre (METC Leiden| Den Haag |Delft) (N21.040) and was conducted in accordance with the Declaration of Helsinki. All respondents and interviewees were informed about the aims of the study, its voluntary nature and anonymous data usage, before giving consent to participate. Prior to conducting the interviews informed consent was obtained of participating GPs.

Consent for publication

Not applicable.

Data availability

The datasets generated and/or analysed during the current study are not publicly available due to the size of the data and the qualitative nature of the data but are available in modified format from the corresponding author on reasonable request. Survey results are also available from the corresponding author upon reasonable request.

Competing interests

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this study.

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Authors' contributions
All authors contributed to the design of the study and the interpretation of the data. TB, FB, VN and MR developed the questionnaire. TB performed the quantitative analysis in SPSS, supervised by FB. The interviews were conducted and transcribed by TB, and checked by FB, VN and MC reading the transcripts. Coding and labelling of the transcripts were independently done by TB and FB, agreement on the codes was reached between TB and FB. TB drafted the manuscript and FB, VN, MC helped drafting and revising the manuscript. OG and MN give their critical input on the final version of the manuscript. All authors have read and approved the final version of the manuscript.

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Supplementary Tables

Supplementary Table 1. Quotes resulting from the interviews (n=5)

Topic	Number	GP	Quote
Topic I	Q1	I	As GPs we have to be involved in the screening programmes. The contacts resulting from engagement is eminently suiting GPs. The programmes are concerning cancer, which always scares patients. This is thus an opportunity for us, where we can make a difference. Patients appreciate it very much when we are involved, and when we guide them along the way. This should also be part of a GP's natural interest.
	Q2	I	It is important that a GP personally calls if a screening outcome is showing abnormalities. For patients it is a 'bad news call', women (people) are shocked by that. I think, that we as GPs should have these kind of conversations. Thereby, it is also handy; so we can keep track of our patients.
	Q3	I	It would help, though, to have even more clarity on what is expected of you as a GP with regard to the CSPs. Especially since it changes over time.
	Q4	I	We are talking about indicated prevention, this simply is part of the GP's job.
	Q5	I	I never really felt responsible for the CSPs, or at least not concerning the execution of the programmes. The initiative does not lie with the GP; it could only be, as maximum, a shared responsibility to meet certain targets. Then you will have to formulated a target together first; what do you want the minimum uptake to be?
	Q6	II	In my opinion indicated prevention, such as: smoking cessation, reducing obesity and cancer screening, is part of the range of tasks of a GP. This also makes sense since we know our patients and thus know on who we should focus.
	Q7	II	I want to be close to my patients. I like that, therefore I also decided to become a GP. For me it does not feel like an extra task to make an phone call regarding a positive CSP outcome. Patients really appreciate this too. It makes the work fun. So it is positive from two sides.
	Q8	III	I try to motivate patients, and if the screening outcomes return positive, then that they also participate in the follow-up tests. Most people are scared after getting a positive test-outcome.
	Q9	III	In my opinion, the CSPs are in essence not part of a GP's job. It is fine to be indirectly involved, but this is also enough. We already have so much other things to do. I would much rather leave this to others.
	Q10	III	Regarding the guidance of patients after an oncological diagnosis it very much depends on the patient to what extent I am involved. That is really tailor-made. But very often I am involved. I also really consider that as a task for myself, and for GPs in general.

Supplementary Table 1. Quotes resulting from the interviews (n=5) **(continued)**

Topic	Number	GP	Quote
	Q11	III	I am not responsible for ensuring people to participate. There also should not be any pressure either. If there would be any pressure, GPs will immediate quit cooperating.
	Q12	IV	I call patients myself when I am informed on a positive screening outcome. A (practice-based) nurse could also do this, but it is nice to take the lead in this as GP. It is an important outcome after all. I also like doing this. As a GP, you have a relationship of trust. It is about important things and it is really nice for patients to discuss this with someone they know. That familiar face just helps.
	Q13	IV	Whether people participate or not, therefore I am certainly not responsible. That is an individual choice. But as soon as there is a positive outcome and thing needs to be done (referral, guidance etc.), it also becomes a responsibility of the GP.
	Q14	V	We cannot afford, doing nothing in terms of prevention.
	Q15	V	Of course prevention is part of a GP's job. In fact, it should be part of every consultation.
	Q16	V	I personally think discussing the CSPs is important. Mostly I recommend patients to participate in the CSPs. I also use this topic to talk about sexual health, intimate topics etc. So for me, it serves as a starting point for several issues.
Topic II	Q17	I	It is nice to know whether someone has, or has not, participated in the CSPs, including the screening outcomes. However, it remains a bit of a question what to do with this information. It would take a lot of energy if GPs had to start calling/inviting/motivating everyone who did not participate in the CSPs. On the other hand, it could make sense if the programmes really prove to be very effective, in terms of decreased cancer mortality.
	Q18	I	Things are a bit complicated, as non-attender you have not been able to give consent, whether your GP is allowed to know your participation status. So regarding privacy legislation several things should be sorted out.
	Q19	II	I do think I always want to know if a patient has a positive test. Especially when you are a practice owner and know your patients well. You can use this knowledge during your consultations. The context is very important and as a GP you can act on this.
	Q20	II	I am not sure if I would want to know when someone did not participate. It remains a patient's own choice. Knowing this can be perceived as intrusive. I think it is not right when a patient decides to not participate, the GP then gets this messages and then contacts the specific patient. Then it may no longer feel like a free choice, but much more like coercion.

Supplementary Table 1. Quotes resulting from the interviews (n=5) **(continued)**

Topic	Number	GP	Quote
	Q21	III	Strange, you would expect that we as GPs have insight in all positive outcomes. In any case, I would like to know this. Then I am also able to monitor patients and maybe discuss the outcome when that specific patient comes by.
	Q22	III	I would not necessarily want to know who did not participate. Because if I know this, then I probably have to do something with this information.
	Q23	IV	I think we would like to have insight in all screening outcomes. Thus from all who participated. This would help us during consultation and in our relation with our patients.
	Q24	IV	I would be interested to know who did not participate, but actually I have never really thought about it before. I do think it will cost a lot of energy, if we then also have to do something with this information. So if, for example, we are expected/supposed to approach all the non-attenders. The time is just not there. If there is someone who can take over, then it might be interesting.
	Q25	V	I would like to know who did and did not participate. Now I have no clue, and therefore cannot act on it. If I knew, then I would be much better able to proactively engage with people concerning the CSPs.
	Q26	V	I want there to be a pop-up in my electronic patient management system. This year patient X will be invited for this CSP. Then I will able to check if they have participated and if not, I can discuss it with them. At present, I do not think it will be too much of an added workload. I would like to give it a try.
	Q27	V	I would like to see that on all surveys, patients can very clearly tick a box to share their attendance information with their GP. Or perhaps even better, vice versa. That such consent is basically regulated, unless...
Topic III	Q28	I	GPs are not waiting for more work, that is for sure. You would have to be well into the numbers to determine whether the invitation should be running via GPs (again). However, if the effect that the GPs can achieve is significant, that in, let say certain practices it saves half in terms of attendance, then, at least you should consider it. It should be a possibility if it is not running adequately in other ways.
	Q29	I	As a practice, we could start inviting potential participants ourselves (again). But then, at first it would require an estimate of how much effort this would be. You could also setup some extra assistance, which then also should be paid for.
	Q30	I	As an example: Everyone is invited by default, but on top, GPs are given a list of high-risk screening-eligible people whom you want to include in particular. You could be more creative than either just the entire invitation via the screening organisation, or via GPs.

Supplementary Table 1. Quotes resulting from the interviews (n=5) **(continued)**

Topic	Number	GP	Quote
	Q31	II	I do not think it is a good idea for GPs to start inviting. Because that is another extra task, besides, it means that we as GPs then have to take responsibility for this invitation procedures. This just has to run super smooth. We cannot have invitations not being sent, just because of some IT-failures. Or someone might not have changed their address and therefore did not receive an invitation.
	Q32	II	What could be done is a kind of 'add-on methodology'. So in addition to a common basis, something extra can be done on the community-level by GP practices. Think of a letter, or maybe even a call from the practice
	Q33	III	If you invite yourself as GP, you will probably get higher screening attendance rates. If people get a letter from an organisation they do not know, especially here in the neighbourhood, they very easily throw it away. There is a lack of trust, so to say. There is a lot of suspicion and distrust of what the government is and does. If the letter comes via the GP, or it says on the letter, "this letter is from your GP" then that will probably lead to a higher uptake.
	Q34	IV	I am not in favour of inviting myself. Right now it is well organised. We just do not have the energy and time. We already have enough things to do.
	Q35	V	People do not feel they are individually seen right now. That is also why they do not participate. This is a pity, because it could so easily be organized differently; i.e. by involving us as GPs more. We have also seen this with programmes aimed at cardiovascular risks and diabetes. If you provide individual attention, that will work. People appreciate it when they are looked after. People respond and flourish when you give them attention.
	Q36	V	I think it matters who sends the invitation letter. So whether it comes from a neutral organization/government, or via us, as GPs. This will have an effect on the screening uptake. In the past, we were involved in the invitation procedures, that worked incredibly well. It is a shame that that is no longer possible now.
	Q37	V	It is true, nowadays we have been appointed a lot of other tasks. Before, it was easy to be involved in the CSPs, but maybe now not anymore. This is also a political choice, what do we as a society want a GP to do? In addition, GPs are current busy because of the 'Purple Crocodile'. If only we could get rid of that, we would have time again to tackle really important issues. There is a desire for GPs to work more on prevention, look also at the Integral Prevention Agreement, but now it is hardly doable for us.
Topic IV	Q38	I	Given the complexity of participation, it is not surprising that people living in a low SES-neighbourhood and with a non-western migration background are less likely to participate. You have to do it all yourself, read it, understand it etc. You may wonder whether sufficient instructions are provided. There has been very little attention to enlighten this problem.

Supplementary Table 1. Quotes resulting from the interviews (n=5) **(continued)**

Topic	Number	GP	Quote
	Q39	II	Information in other languages is essential; but, I think it already exists. This should be included with the invitation(s).
	Q40	II	You could choose to go more into the neighbourhoods, to talk with people, and to activate peers more. Only of course, if low attendance is really perceived as a problem.
	Q41	III	There is not just a silver bullet, you will have to aim for different things. It often starts with proper education. In addition, there are probably also many other barriers that need to be addressed.
	Q42	III	In our neighbourhood, there is a curious paradox. On the one hand we see people who are very carcinophobic and hypochondriac, yet on the other hand, they seldomly participate in the CSPs. As GPs, we could respond to that quite well, if we were better engaged. Better screening uptake is in all our interests.
	Q43	IV	I do not believe anything has to change with respect to the invitation letter or procedure. I cannot remember a patient consulting me on these matters.
	Q44	V	In this neighbourhood, there is a distrust of everything which has to do with the government. People here also think: "government you have nothing to do with my 'intimate' health". Those people then do not participate. I could really act on this as a GP. For many people here in the neighbourhood, the GP is still quite important. It matters what the doctor says. There are also people who do not participate because they do not like the tests, or because they are afraid they will not perform them in the right manner. I could really respond to this kind of barriers/believes.
Topic V	Q45	I	It would show political decisiveness to ensure that you can get by as a GP with a practice of, let say, 1.200 patients. Then, you will have time to do a lot of things and then these kinds of preventive tasks can be added much more easily. But then the budget for primary care will really have to increase substantially. We do not need to earn more as GPs, but actions within the system could then be funded much more easily.
	Q46	I	Within the practice, you could also appoint an assistant to specifically deal with the CSPs. This person could then answer questions about the CPS, perform Pap-smears, etc. Instruction videos in different languages would help too. However, the option to come to the practice, and to speak to someone should always remain possible.
	Q47	I	The GP is an easily accessible healthcare professional for a lot of people, and that is nice too. As a GP, you should also be able to continue like this, you should have time do provide these contacts. If there is a bit of extra funding for counselling potential participants, that would be really nice and would fit within current primary care.

Supplementary Table 1. Quotes resulting from the interviews (n=5) **(continued)**

Topic	Number	GP	Quote
	Q48	I	These days, I believe more and more in the possibilities of technology. Everyone has a smartphone. Everyone can watch films on it. This opens endless possibilities. More thought should be given to this.
	Q49	II	Actually, I do not think it is badly arranged now. Also the amount of GP involvement seems appropriate. What is however remarkable is the differences between the three CSPs. Why cannot just the screening organisation always make the referral, for example. Why do we as GPs still have to sit in between?
	Q50	II	I think language is often way too difficult. Language in itself can be a big problem. Written language is for many people difficult. There is a reason why 'thuisarts.nl' already has lots of videos. Besides, you should really use pictograms; and QR-codes for quick access to videos.
	Q51	II	Influencers on social media really make a differences these days, why not involve them?
	Q52	II	I think there are a lot of people who would like to talk with a healthcare professional about participating in the CSPs. GP practices would be a good place for that. It is often not just about facts and figures, but very often about trust. That is precisely where the GP (practices) can facilitate.
	Q53	III	Where you could do this in the GP's waiting room, by making use of the waiting room screen. That is an excellent place for education. Short, powerful, clear, straightforward, that works. We have had waiting room videos for years and really noticed that people learn something via this screen. People do need knowledge, but you have to really tailor it. The waiting room is pre-eminently a place where people can absorb medical information.
	Q54	III	Regarding the CRC-SP. I wonder if it is sufficiently clear to patients that this is not a test directly for cancer, but much more for its precursors. I would like people to be less shocked by the outcome. Nowadays, people are instantly worried they have cancer.
	Q55	IV	For now, most things are just fine. So then we should not want to change much. I am satisfied with how things are arranged.
	Q56	V	What I miss is cooperation. Everyone is always talking about this word. Also for the screening on cancer, it would help if healthcare providers and organizations cooperate. GPs, community centres, municipal health services, everyone is doing something, but not as a whole. We are working alongside each other. They/we are all little islands. Everyone is "helping", but who is really doing something? Where does the patient really benefit from in the end? In addition, we as GPs are really not valued properly by the current politics/government. We could really help, but are ignored. People will participate if we as GPs ask them to. In the process, this also undermines the credibility of the entire healthcare system.

Supplementary Table 1. Quotes resulting from the interviews (n=5) **(continued)**

Topic	Number	GP	Quote
	Q57	V	I would opt that health insurers collectively put 10% into a fund. This money could then be used to set up nationwide prevention projects.
	Q58	V	Finally, I really hope that we will educate the new medical students differently. Teach them about prevention.

GP= General Practitioner, (C)SP= (Cancer) Screening Programme

Supplementary Table 2. Characteristics of the questionnaire respondents (n=46)

		n	%
Age (years)	Mean: 51 (min-max: 36-68)	46	
Contractual hours	Mean: 37 (min-max: 20-60)	45	
Sex	Female	33	72
	Male	13	28
Experience as GP (years)	0-2	1	2
	3-5	2	4
	6-10	4	9
	10-19	20	44
	≥20	19	41
Location of practice (city/village)	The Hague	12	26
	Noordwijk/Leidschendam	10	22
	Alphen aan de Rijn	7	15
	Leiden	6	13
	Delft	5	11
	Zoetermeer	4	9
	Hoofddorp	2	4
Patient population (description)			
Age-range	Old (≥65 years) overrepresented	9	20
	Average distribution (all ages)	31	69
	Young (≤35 years old) overrepresented	5	11
Education	Higher education (university of applied sciences) overrepresented	8	18
	Average distribution	28	62
	Lower education (≤secondary vocational education) overrepresented	9	20
Cultural background*	Predominantly Dutch	32	74
	Predominantly from Western	4	9
	Predominantly from non-Western	7	16

GP= General Practitioner
*for definition see the survey attached as supplementary file (page 12)

Supplementary Table 3. Characteristics of the interviewed respondents (n=5)

		n	%
Sex	Female	3	60
	Male	2	40
Experience as GP (years)	0-5	1	20
	6-19	1	20
	≥20	3	60
Patient population (description)			
Age	Elderly (≥65 years) overrepresented	1	20
	Average distribution	3	60
	Young people (≤35 years old) overrepresented	1	20
Education	Higher education (university of applied sciences) overrepresented	1	20
	Average distribution	3	60
	Lower education (≤secondary vocational education) overrepresented	1	20
Cultural background*	Predominantly Dutch	3	60
	Predominantly from Western	0	0
	Predominantly from non-Western	2	40

GP= General Practitioner
*for definition see the survey attached as supplementary file (page 12)

Supplementary File (Questionnaire)

The general practitioner and the population-based cancer screening programmes
On experiences, wishes & ideas

Dear general practitioner, dear colleague,

The Health Campus The Hague is investigating how the current population-based cancer screening programs (CSPs) can be optimized. This because it appears that fewer and fewer people are participating in the CSPs.[1-3] For information on the overarching study, see the website: Screening the CITY

As a general practitioner you currently have varying tasks regarding the CSPs aiming at cervical, breast and colorectal cancer. We would like to ask you some questions about these different tasks. In addition, we would like to know whether you feel that certain aspects should be changed when it comes to your role as a GP regarding the CSPs.

We developed a short questionnaire and would like you to fill it out. Within 10-15 minutes you are able to share your experiences, wishes & ideas with us. Naturally, the information will be treated with confidentially and processed anonymously. Afterwards, we will publish the results on our website and use them for a scientific manuscript. We hope you are willing to fill out the questionnaire. As you will understand, the more completed questionnaires, the better the results will reflect on the collective thinking.

Thank you in advance for your cooperation.

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Also on behalf of the other members of the research team:
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1. Rijksinstituut voor Volksgezondheid en Milieu. Landelijke Evaluatie & Monitoring Bevolkingsonderzoeken. https://www.rivm.nl/
2. Bevolkingsonderzoek Zuid-West. Jaarverslag 2019. https://www.bevolkingsonderzoeknederland.nl/media/1442/jaarverslag-2019_def.pdf
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List of abbreviations

CSP	Cancer screening programme
BC-SP	Cancer screening programme aiming at breast cancer
CC-SP	Cancer screening programme aiming at cervical cancer
CRC-SP	Cancer screening programme aiming at colorectal cancer
FIT	Faecal Immunochemical Test (screening test CRC-SP)
GP	General Practitioner
hrHPV	High risk human papillomavirus
NHG	Dutch College of General Practitioners
Pap-test	Papanicolaou test (screening test CC-SP)

Below are a number of statements and questions. Please choose the answer most applicable to your situation in each case. We would like you to complete all statements and questions. Comments and remarks can be made on the last page.

I. The CSPs in the general practice

Following are a number of statements and questions about to which extent you deal with the cancer screening programmes (CSPs) on a daily basis. In each case, please choose the answer that best suits your situation.

1. Patients come to the GP-practice (to me as GP and/or to the practice assistants) with questions about the CSPs.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

2. The questions I get about the CSPs are (multiple answers possible):
   ◯ mostly on the CSP aimed at cervical cancer (CC)
   ◯ mostly on the CSP aimed at breast cancer (BC)
   ◯ mostly on the CSP aimed at colorectal cancer (CRC)
   ◯ not applicable; I don't get any questions about the CSPs

3. In the past year, have you encouraged patients to participate in the CSPs?
   ◯ yes
   ◯ no

4. In the past year, have you advised patients against participating in the CSPs?
   ◯ yes
   ◯ no

5. Do you ever bring up the CSPs without a patient explicitly asking about these programmes?
   ◯ yes
   ◯ no

Following are a number of statements on the several tasks you have as a GP. Please choose the answer that best suits you.

1. I think providing information about the CSPs is part of my job as GP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

2. I think I should encourage participation in the CSPs.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

3. I feel that I should leave the choice to participate in the CSPs mainly with the patient.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

4. I feel I should only discuss the CSPs when the patient has specific questions regarding the screening programmes.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

II. Specific questions about the CSP aiming at cervical cancer

Following questions concern your role and that of the practice assistant(s), regarding the CSP aiming at cervical cancer (CC-SP). In each case, please choose the answer that best suits you.

1. In the past year, have you (or any of your practice assistants) had any questions about the CSP aiming at CC?
   ◯ yes
   ◯ no; you can proceed to question 3

2. What were the questions about (multiple answers possible):
   ◯ the invitation
   ◯ participation in the CSP
   ◯ the risk of developing cervical cancer
   ◯ the outcome of the (screening) test
   ◯ the self-test
   ◯ follow-up examinations
   ◯ participation at the follow-up examinations

Following statements are about your experiences with the CSP aiming at cervical cancer (CC-SP). Please choose the answer that best suits you.

3. I am well informed about the content and objectives of the CC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

4. I am aware of the NHG practice manual on the CC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

5. I know what my role is regarding to the CC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

6. I have sufficient knowledge to explain about the CC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

7. In the practice where I work, we (GPs and practice assistants) know how to perform PAP-tests according to the CC-SP guidelines.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

Following questions and statements are about your vision of the CSP aiming at cervical cancer (CC-SP). Please choose the answer that best suits you.

In the past, invitations to participate in the CC-SP were sent via GP practices. The national participation rate was at the time higher.

8. Were women in your practice actively invited to participate in the CC-SP in the past?
   - ◯ yes
   - ◯ no; you can proceed to question 10
   - ◯ unknown to me; you can proceed to question 10

9. Since women are no longer invited via GP practices, I noticed that fewer women are participating in the CC-SP.
   - ◯ strongly disagree
   - ◯ disagree
   - ◯ neutral
   - ◯ agree
   - ◯ strongly agree

10. I (again) would like to have the possibility to invite women for the CC-SP.
    - ◯ strongly disagree
    - ◯ disagree
    - ◯ neutral
    - ◯ agree
    - ◯ strongly agree

11. I want to know which of 'my' patients were invited for the CC-SP.
    - ◯ strongly disagree
    - ◯ disagree
    - ◯ neutral
    - ◯ agree
    - ◯ strongly agree

For the CC-SP, the possibility of using the hrHPV (high-risk human papillomavirus) self-test exists since 2017. As a result, it is no longer necessary for women to have a smear test taken at the GP practice, but women can independently test for hrHPV. The GP does not receive the outcomes of a self-test .This is in the context of privacy legislation. If hrHPV is found with the self-test, a woman is advised to have a smear taken at the GP practice. This smear is then cytologically assessed.

12. As a GP, I always want to know if a patient has taken a self-test as part of the CC-SP.
    - ◯ strongly disagree
    - ◯ disagree
    - ◯ neutral
    - ◯ agree
    - ◯ strongly agree

13. When women receive a positive screening outcome, I want to be able to inform them myself.
    ◯ strongly disagree
    ◯ disagree
    ◯ neutral
    ◯ agree
    ◯ strongly agree

Depending on the outcomes of the screening test, the GP is still involved by partaking a control smear after 6 months, or by referring the women to a gynaecologist for follow-up examinations.

The GP will always be informed about outcomes emerging from the follow-up examination(s).

III. Specific questions about the CPS aiming at breast cancer

Following questions concern your role regarding the CSP aimed at breast cancer (BC-SP). In each case, please choose the answer that best suits you.

1. Have you had any questions about the BC-SP in the past year?
    ◯ yes
    ◯ no; you can proceed to question 3

2. What were the questions about (multiple answers possible):
    ◯ the invitation
    ◯ the invitation interval (actual since Covid-19)
    ◯ participation in the CSP
    ◯ the risk of developing breast cancer
    ◯ the outcome of the (screening) test
    ◯ follow-up examinations
    ◯ participation at the follow-up examinations

Following statements are about your experiences with the CSP aiming at breast cancer (BC-SP). Please choose the answer that best suits you.

3. I am well informed about the content and objectives of the BC-SP.
    ◯ strongly disagree
    ◯ disagree
    ◯ neutral
    ◯ agree
    ◯ strongly agree

4. I am aware of the NHG practice manuals on the BC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

5. I know what my role is regarding the BC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

6. I have sufficient knowledge to explain about the BC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

Following statements are about your vision of the future regarding the CSP aiming at breast cancer (BC-SP). Please choose the answer that best suits you.

7. I want to know which women from my practice, have been invited for the BC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

8. I want to be able to invite women for the BC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

As GP, you will be involved in the BC-SP when follow-up examinations are needed as a result of the mammograms. As GP you need to refer the specific women to a hospital for further analysis. This may be because the X-rays are not conclusive, or if the X-rays show abnormalities.

9. As a GP, I always want to know if a patient has had a mammogram as part of the BC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

10. When women gets an abnormal screening outcome, I want to be able to inform them myself.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

The GP will always be informed on the outcomes following the follow-up examination(s).

IV. Specific questions about the CSP aiming at colorectal cancer

The following questions are about your role at the CSP aiming at colorectal cancer (CRC-SP). Please choose the answer that best suits you.

1. Have you had any questions about the CRC-SP in the past year?
   ◯ yes
   ◯ no; you can proceed to question 3

2. What were the questions about (multiple answers possible):
   ◯ the invitation
   ◯ participation in the CSP
   ◯ the risk of developing colorectal cancer
   ◯ the outcome of the (screening) test
   ◯ follow-up examinations
   ◯ participation at the follow-up examinations

The following statements are about your experiences with the CSP for colorectal cancer (CRC-SP). Please choose the answer that best suits you.

3. I am well informed about the content and objectives of the CRC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

4. I am aware of the NHG practice manuals on the CRC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

5. I know what my role is regarding the CRC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

6. I have sufficient knowledge to explain about the CRC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

Following question and statements are about your vision on the future of the CSP aimed at colorectal cancer (CRC-SP).Please choose the answer that best suits you.

7. I would like to know who participated in the CRC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

8. I would like to be able to invite patients for the CRC-SP myself.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

Since January 2017, GPs are no longer automatically notified on the outcomes of the FIT; the primary screening test for the CRC-SP. This is in the context of privacy legislation. Participants must give explicit consent for sharing information regarding the FIT. In case of a positive FIT outcome, a patient receive an appointment for follow-up testing by the screening organization. Patients are advised to contact their GP if they receive a positive FIT outcome.

9. Were you aware of this change?
   ◯ yes
   ◯ no

10. As a GP, I always want to know whether a patient has submitted an FIT as part of the CRC-SP.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

11. As a GP, I always want to know if a patient had a positive FIT.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

11. When patients from my practice receive a positive screening outcome, I want to be able to inform them myself.
   ◯ strongly disagree
   ◯ disagree
   ◯ neutral
   ◯ agree
   ◯ strongly agree

The GP will always be informed about outcomes following the follow-up examination(s)

Descriptive characteristics

Finally, a few questions about you as a GP, and the place where you work.

1. What is your year of birth?

2. What is your gender?
   ◯ male
   ◯ female

3. What kind of professional appointment do you have?
   ◯ practice owner
   ◯ employed GP (at a permanent practice)
   ◯ acting general practitioner

4. What are the first 2 digits of the zip code where you work as a GP? (if you are an acting GP, please enter the postcode of the practice where you most often work)

5. How many years of work experience do you have as a GP?
   ◯ 0-2
   ◯ 3-5
   ◯ 6-10
   ◯ 10-20
   ◯ 20+

6. On average, how many hours per week do you work (contract hours)?

7. How would you describe your patient population with respect to age distribution?
   ◯ elderly (≥65 years) overrepresented
   ◯ average distribution
   ◯ young people (≤35 years old) overrepresented

8. How would you describe your patient population with respect to level of education?
   ◯ higher education (university of applied sciences) overrepresented
   ◯ average distribution
   ◯ lower education (≤Secondary vocational education) overrepresented

9. How would you describe your patient population with respect to cultural background?
   ◯ predominantly from a Dutch background
   ◯ predominantly from a Western-migration background. (Countries in Europe, North America, Oceania, Indonesia and Japan; excluding Turkey)
   ◯ predominantly from non-Western migration backgrounds. (countries in Africa, Latin America and Asia (excluding Indonesia and Japan) or Turkey)

V. Open questions

1. Do you have any general comments regarding this questionnaire?

2. Do you think GPs should have a role regarding the CSPs? If so, how do you think that role should look like?

3. Are there any other things you would like to add which have a relation with the CSPs, and/or could possibly be of additional value to our research?

Thank you very much for your participation!

CHAPTER 7

General discussion

The overall aim of this thesis was to identify cues that may contribute to optimizing the current attendance rates of the cancer screening programmes (CSPs) in the Netherlands, with a focus on the potential role of primary care. We hypothesised that the CSPs that currently handle a 'one-size-fits-all' approach, with a limited role for primary care and general practitioners (GPs), should shift to a more targeted approach for subpopulations at relatively higher risk, with sophisticated involvement of primary healthcare providers and healthcare centres to support such a new approach. In this final chapter, the study findings are outlined and discussed in relation to each other. First the key findings of the studies in this thesis will be presented. Then, we will look back at the case of the Janssen family and discuss the methodological considerations of this thesis. Thereafter, the implications of our findings and recommendations for future research will be discussed. Finally, the overall conclusion based on this thesis will be presented as a reflection on our hypothesis.

Main findings

Reviewing the literature in **Chapter 2**, shows that thus far published studies tend to describe the well-known and general characteristics of (non-)attenders, but rarely provide in-depth information on other factors that may influence participation. Non-influenceable determinants as a non-Western migration background, living in a highly urbanised area and with a lower socioeconomic status (SES) background, were most often described as being associated with low(er) cancer screening attendance. Our findings in **Chapter 3** also suggest that non-attendance at the cancer screening programmes (CSPs) aiming at breast and colorectal cancer in a highly urbanised area, is linked to living in lower SES-neighbourhoods. Additionally, it is associated with a more unfavourable tumour-stage at diagnosis. In **Chapter 4** we present evidence that beliefs and motivations towards the CSPs and CSP attendance are not only different between attenders and non-attenders, but can also differ between subgroups of people holding different perspectives. We identified three different perspectives. Responders holding one specific perspective – those doubting screening attendance and anticipating the potential consequences of the screening results – were in particular open to receive information provided by a general practitioner (GP), or another trusted primary healthcare provider. **Chapter 5** can be seen as a 'proof of concept' study, in which we showed that a targeted proactive primary care approach for a subpopulation at relatively higher risk on the development of (in this case: cervical) cancer, is needed – sometimes even essential – to enhance screening. In **Chapter 6** we concluded that GPs are generally positive about the CSPs and are willing to positively empower the CSPs. The GPs involved suggested several options to improve the current CSPs, especially to increase screening uptake for populations in a socioeconomic or otherwise socially disadvantaged position.

The story of the Janssens family – The Answers

In his search for answers the GP found that it would still be wise for Sarah to participate in the cervical cancer screening programme (CSP). Furthermore, he understands that participating in a CSP can also have some potential harms. He learns that deciding on participation in a CSP is not always an easy choice, and that some people are not capable of deciding on participation, because they lack certain knowledge, or experience certain kinds of (access)barriers. The GP experiences that his role is different between the different programmes and varied over the course of preceding years. The GP's quest for information yields the following results.

For many people cervical cancer is linked to being sexually active. While this is not completely untrue, prominent and persistent misinterpretation of the association may discourage people from attending the cervical CSP.[1] Regarding the human papillomavirus (HPV) vaccination campaign, similar effects have been described.[2] To a certain extent, Sarah is right that she is less likely to be infected with HPV if she has had one and the same boyfriend for a long time. Nevertheless, the virus may be contracted by her boyfriend long before or during their relationship, wherefore it still would be best for Sarah to get screened on HPV.[3]

Even if Sarah was vaccinated for HPV, it would be wise for her to participate in the CSP, since vaccinating is not 100% effective.[3] Luckily HPV-testing can be done easy and quick via a self-sampling test, which has been validated to be used by every woman and nowadays is seen as an equal alternative,[4] or by getting a Pap-smear done at a GP-practice.[5] Earlier the Dutch Health Council advised to send the HPV self-sampling test along with the invitation as standard.[6] Recently this advice was adopted by the minister of Health. These days only women who are invited for the very first time (at 30 years of age) receive a self-sampling test immediately with the invitation. From the second invitation onwards, women can ask for the self-sampling test, or it will be sent along with the reminder letter after 12 weeks.[7]

The rationale behind the CSPs is that participation will lead to overall early-stage cancer diagnoses, better treatment options and a better outcomes. The harms of the CSPs are however lesser known; not only by the public, but also by some healthcare providers. [8, 9] Potential harms of attending the CSPs can be best summarized as: (I) overdiagnosis and overtreatment; (II) false-positive screening results; (III) underdiagnosis and undertreatment, caused by a false-negative screening result, and (IV) causing certain physical and psychological side-effects, due to the used screening test(s).[10]

Given these harms, there are numerous reasons why people refrain from participation. The GP in this case however, also finds out that deciding on CSP attendance is not always a matter of purely rational decision-making.[11-14] Similar to John's situation there are many people who do not understand the invitation or do not have a clue about the CSPs at all. In this regard, our GP develops the opinion that primary/GP-care has a pivotal role in providing guidance and information for potential participants concerning the CSPs.

Because the GP believes that John may have a higher risk of developing colorectal cancer, he contacts the family.

Methodological considerations

In this thesis all three Dutch cancer screening programmes (CSPs) are examined and discussed, taking the differences and similarities of the programmes into account, over a longer period of time. The presented studies in this thesis can all be regarded as building blocks that improve the evidence needed for the *Screening the CITY* project, in which we aimed to explore and resolve specific problems that come up in highly urbanized areas when the CSPs were implemented and seem to be underused.

The individual studies conducted in this thesis employed a diverse range of research methodologies and focused on different study populations. By utilizing varied research methodologies and study populations, we intended to overcome potential limitations of each sub-study, as discussed in each chapter. In two studies (see Chapter 2 and 4), we made use of the Integrated Change Model as a comprehensive theoretical framework to enhance our understanding of screening participation.[15, 16]

Some of the studies in the *Screening the CITY* project were conducted different than originally intended. This was mainly due to the outbreak of the COVID-19 pandemic and its associated effects. At the peak of the pandemic the CSPs were temporally suspended, and over the course of the pandemic, screening organisations understandably prioritized other pressing matters over facilitating scientific research.[17, 18] This led to several modifications to our studies, and had in particular impact on the studies described in Chapter 3 and 4.

Concerning the research presented in **Chapter 3** we encountered an issue where we were unable to access the data on cervical CSP. Consequently, we were unable to combine data on all three cancer screening programmes in the city of The Hague. It transpired that the data on this screening programme resided within a separate data

infrastructure, which was not readily accessible for research purposes at the time. This fragmentation – where collections of data are scattered across various locations, resulting in numerous datasets distributed across multiple servers – hinders the possibility of interconnection and smooth exchange of data, but appears to be not unique concerning our study.[19] Furthermore, the original idea for this study was to enrich our datasets – containing information on individuals' participation status and cancer incidence rates – with supplementary data from Statistics Netherlands (CBS; Centraal Bureau voor de Statistiek) to obtain a more comprehensive understanding of determinants affecting cancer screening attendance. Unfortunately, not all parties involved agreed to share their data, so we were not allowed to set up straight forwardly pseudonymized data linkage procedures as we had originally planned. From literature it appears to be a recurring challenge in Dutch studies, where data linkage problems appears to be commonly encountered.[20, 21] The General Data Protection Regulation (AVG; Algemene Verordening Gegevensbescherming) is then mostly cited, which would not allow re-use and/or data linking.[21] This is regrettable, since from the perspective of (I) the patient, (II) the researcher, (III) the quality assessor, but also (IV) the healthcare professional, there are multiple arguments why linking, sharing and re-using of (medical) routinely collect data is desirable.[22] With regard to the data retrieval and linkage issues, the Netherlands underperforms when compared with other countries in Europe.[23, 24] For patients, sharing of data would contribute to better individual care, as in this way, all caregivers involved are aware of the patient's latest condition. Patients are often convinced that every healthcare provider is aware of their complete medical record (even between different healthcare institutions or during out-of-office care) and are surprised when this turns out not to be the case. For researchers and quality assessors, linking, sharing, and re-using of data would offer them a chance to gain clearer insights into care processes. For healthcare professionals, the linking, sharing, and re-using of health data would allow them to provide better care and probably saves a lot of frustration. Due to overinterpretation of privacy rules patients may encounter health care providers who do not have access to medical records others produced and are therefore not aware of a patients' medical history, which is not desirable.

An illustrative example demonstrating the benefits of reutilizing existing routine collected data in a smart manner, is the recently released atlas by the Netherlands Comprehensive Cancer Organisation (IKNL; Integraal Kankercentrum Nederland) that provides insight into incidence rates of certain tumours in certain areas in the Neterlands.[25] This is actually what we also had in mind with the sub-study described in Chapter 3, but then with a focus on the different neighbourhoods in the city of The Hague. In an ideal world we would redo the study described in Chapter 3 with a pseudonymized individual procedure that links the cancer registry data, to data of Statistics Netherlands and routinely collected

electronic medical record data from GPs. This would enable us to gain a more detailed insight of the determinants that influence attendance and non-attendance concerning the CSPs, currently lacking as we showed in Chapter 2. In ideal circumstances we would like to have information on the living environment of the screening-eligible people, and gain information on someone's profession, house value, family composition and financial situation. Furthermore, we would like to have insight in several medical characteristics, such as medical history, family history, medication, and substance use. In addition, would we be interested in the frequency of general practitioner (GP) visits, and maybe also recent health measurements (such as vital parameter, and for example body mass index as indicators of overall health). The challenge with all these variables is that the data, especially when combined, must not be traceable back to individuals.

For the future, non-commercial information systems should become available that allow free data linkage, sharing, and re-using (routine) data in primary care. A recent report by the ministry of Health, Welfare and Sports suggested that they are currently investigating how certain, more privacy sensitive data, can be (re)used for certain specified aims.[26]

For the study described in **Chapter 4** our original plan was to proactively recruit screening-eligible individuals and conduct a face-to-face Q-methodological study in selected lower socioeconomic status (SES) neighbourhoods. However, due to the COVID-19 pandemic and the associated safety concerns, people were hesitant about leaving their homes, unable to replace this completely with adequate remote facilities, and the government advised minimizing contact with others and staying at home. Consequently, we had to find alternative approaches to reach and include participants. This ultimately did result in an online panel for recruitment, with pros and cons regarding the selection of panel members. By leveraging an existing research panel, we were able to include a considerable number of individuals. However, it is important to acknowledge that employing an online panel introduced a selection bias. As the study progressed, it became evident that our sample primarily consisted of individuals who held, on average, more positive views towards the CSPs and their participation. Therefore, we cannot deny the possibility that other perspectives would have emerged if we had been able to include screening-eligible individuals with different characteristics.

The studies presented in Chapters 5 and 6 can be considered exploratory in nature. To improve the robustness of our study findings, additional study inclusions would have been necessary. For **Chapter 5** this would mean more marginalised women should be included and screened. As described, we view this study as a 'proof of concept'. Municipal health services (GGD; Gemeentelijke Gezondheidsdienst) in The Hague, Rotterdam, and Amsterdam are currently exploring how they can utilize the findings from our study to

enhance the health of marginalized women in these cities. Regarding our findings in **Chapter 6** it would be interesting to see whether the results would differ if new or more interviews were conducted with GPs practicing in (more) rural regions of the Netherlands.

Implications for researchers, clinicians, and policymakers

The studies presented in this thesis can yield various implications for different stakeholders involved in the field of the Dutch cancer screening programmes (CSPs). In the following sections, I will delve into our findings, outlining their specific relevance for researchers, clinicians (GPs and other primary healthcare providers), and policy makers.

Implications for researchers

In the preceding chapters, comprehensive recommendations for further research have been provided based on the individual studies conducted. The main common denominator is that we showed that still more detailed information is needed on screening-eligible individuals residing in lower socioeconomic status (SES) neighbourhoods. People living in these lower SES-neighbourhoods happen to be at a higher risk of developing screening-specific tumours, wherefore potentially the greatest health benefits can be achieved in these subpopulations. Although our research showed interesting findings concerning differences, future researchers should look further into these issues. Appropriate methodologies suitable for people with lower SES are needed to make that possible. For this purpose collaboration with a knowledge institute like Pharos is highly recommendable.[27] Building upon the findings in Chapter 5 and existing international literature, it is strongly advocated to make use of proactive, face-to-face strategies to engage with individuals in low(er) SES-neighbourhoods.[28, 29]

A related recommendation would be that future researchers take factors as '(low) literacy' and 'health illiteracy' into account. As we highlighted in Chapter 2 these factors seem to be of high importance when it comes to screening attendance. Here it is worth mentioning that currently in the Netherlands, 2.5 million individuals (aged ≥16 years) have low literacy skills, and one in four (25%) Dutch people possess limited health skills.[30] Both low literacy as health illiteracy are known to be more prevalent among those with lower educational attainment, elderly, and migrants.[31, 32] In addition are these issues known to have a burden on health outcomes, among others also on the incidence of cancer.[33] Knowing this, the new changes to the cervical CSP (for instance sending self-tests) might be less appropriate for people who have low literacy levels, possess low health literacy skills. It is precisely among these groups that you hope to optimize the attendance rates but might not benefit at all from the innovations in the CSP. Subsequent and related are also cultural factors, as a recent study among Moroccan-Dutch women clearly showed.

Included women were asked about their attitude regarding the cervical CSP, and it turned out that they became more positive regarding the screening programme after seeing a culturally sensitive educational video to facilitate informed cervical cancer screening decisions.[34]

Furthermore, future researchers should look into some relatively small modifications, such as altering the envelope, or the invitation letter by including a text stating, such as: "The message is positively endorsed by your GP". Subtle adjustments like these might already have large positive impact on the attendance rates, without having to invest to much effort, and should therefore be considered in future studies. Finally, as a last suggestion and thus far unexplored in our studies, integrating all three CSPs together may have unknown benefits. It might be profitable and convenient for women to receive an invitation for all three CSPs simultaneously. Combining the three CSPs might contribute to providing women with comprehensive information and facilitating their participation in screenings to the fullest extent possible.

Implications for clinicians: GPs and (other) primary healthcare providers

As a positive note to be mentioned, is that our findings highlight the enduring high appreciation and trust that the public places in primary care and in GPs. In these post-COVID-19 pandemic times this is in contrast with another notion, that public trust in (medical) science seems to be declining.

Two important points for medical professionals 'in the field'. First, clinicians are able to influence the attendance rates of the CSPs. Second, GPs are in the position and capable of ensuring that individuals with higher risks do participate in the CSPs; this follows both from our sub-studies, but is also earlier described in several publications.[35-37] Clinicians therefore should realize that it matters how they speak, feel and decide upon the CSPs. They can really make a difference concerning cancer screening participation. Thereby, engagement in a CSP is not a purely rational matter. It is shaped by practical, emotional, cultural, and religious factors.[38] This further emphasises the significance of fostering and enlarging the role of primary healthcare providers within the CSPs.

For multiple studies, especially the one described in Chapter 3, we tried to make use of routine care – and registry data that are already present in the electronic health records (EHRs) of general practices. However, during our studies we encountered a common problem, which is that medial data are somewhat poorly coded and underused in current EHRs. As reuse of EHR-data will probably become more important in the nearby future, to reduce patient selection in research and for population health management purposes, greater emphasis should be placed on the value of correct coding of medical information

during the medical training and EHR systems should be further improved in supporting the coding facilities during routine care. An earlier study examining the quality of cancer registration in primary care, based on International Classification of Primary Care (ICPC) codes,[39] revealed that approximately 40% of cancer cases cannot immediately be recognized in the coded registrations, and almost half of the cases is coded prematurely and based on hypothesis, resulting in false positive cancer diagnoses.[40, 41] In that respect, there is still much to be gained in terms of proper coding, while also inadequate coding support that the EHRs still present to the users, should be reduced.

A last recommendation for GPs and primary healthcare providers has to do with the advice they are providing screening-eligible people who have questions about the CSPs. What we have noticed is that many people, and the majority of healthcare providers we have spoken to, hold rather positive views on the CSPs.[9, 42, 43] However, screening can also have certain harmful effects. Since clinicians are primarily concerned with the health of their patients, a good understanding of the pros and cons of the CSP is essential and physicians should be able to provide patients with complete and accurate information. In daily practice most significant negative effects of the CSPs are the amounts of overdiagnosis and overtreatment.[44, 45]

Implications for policymakers

For policymakers, import recommendations align with the recommendations for researchers. The need to allocate more efforts towards individuals residing in socioeconomically deprived neighbourhoods is imminent. These individuals often face various health-related challenges and preventive research participation is not typically a priority for them. Additionally, they may lack awareness of existing preventive programmes, as for the CSPs.[12, 46-49] It is essential, both for the well-being of individuals and the society as a whole, that screening-eligible individuals in lower SES-neighbourhoods actively participate in these programmes, also when taking the associated disease-related health costs into account.[50, 51] The findings presented in Chapter 5 highlight the importance of exploring new invitation approaches to engage marginalized women in the CSPs.

Then, concerning the policymakers of the Dutch College of General Practitioners (NHG; Nederlands Huisartsen Genootschap) a more definite stance when it comes to advising patients on their participation in the CSPs would be welcome. Despite years of thinking, reading, and researching the CSPs, it remains challenging to provide clear information and subsequent guidance on cancer screening participation. While the politically correct approach would be to leave the full decision with the individual, in reality this is not a fair option. Despite we are in the middle of the zeitgeist of shared decision making,

it is also known that this concept is not always ideal, nor is it feasible for everyone.[52] In the current guidelines it is stated that GPs should be supportive towards the CSPs. Unfortunate, even well-intentioned GPs, may still find it difficult to offer accurate and honest information to screening-eligible individuals regarding the CSPs.[53] Just, given the complexity and sensitivity of the topic, NHG should adopt a clearer position on screening participation, and should provide GPs with appropriate information which is open and honest. In return this will empower GPs to deliver more nuanced education to screening-eligible individuals about the CSPs, and in the long run will thus optimize cancer care.

Lastly, derived from our research two unexplored ideas might inspire future policymakers. First, the possibility of implementing an 'opt-out' system for sharing screening attendance data of individuals with the GP-practices might help to target primary care interventions. This approach would ensure that GP-practices receive essential CSP information by default unless patients actively choose to opt out. By knowing the attendance screening status of their patients, GPs and other primary healthcare providers are better fit to aid their patients. Second, discussing our research abroad, colleagues wondered why in the Netherlands we do not have a dedicated primary healthcare provider, physicians or nurse, specifically trained to address women's primary care needs. This concept, similar to the 'frauenarzt' model in Germany, might create a space where female patients can have confidential discussions about women's health, including the CSPs and screening participation.[54] This might be especially effective to reach women with an immigrant background. Implementing such a role might provide an ideal setting for addressing women's health concerns and promoting participation in the screening programmes.

Future perspectives

The studies presented in this thesis can – and hopefully will – be used to think about the future of the population-based cancer screening programmes (CSPs) in the Netherlands. In the next section three questions are addressed to discuss on how, if and when the current CSPs of the Netherlands could be enhanced.

What do we expect from primary care?

As is widely known and underlined by the studies in this thesis, a strong primary care is crucial for the healthcare system in the Netherlands. General practitioners (GPs) and other primary healthcare providers have become increasingly busy lately, especially since the range of tasks kept expanding and the demand on healthcare services increased. As a result anno 2023 many GPs complain of a high workload, and GPs are at risk of (prematurely) quitting their jobs.[55] There should be a public debate about what 'we' (read as: the society) expect from primary care and our GPs. Such a debate should

include a discussion on the specific health tasks and roles GPs and GP-practices should have. Thereby it should be discussed what kind of role we see for GPs with respect to prevention programmes, such as the CSPs.

As this thesis shows, GPs are in the position as well as both capable and willing to play a substantial part in the CSPs, and it appears that some patients, or at least a certain group of patients, also prefer greater involvement of GPs. In previous literature it was described that screening-eligible people appreciate contact with their GP when it comes to participating in cancer screening.[56] If 'we' consider cancer screening participation to be of significant importance, then 'we' should ensure that GPs and GP-practices are able to empower the CSPs. Recent studies stated that GPs are interested in taking a more active role in preventative healthcare, yet the broader appeal for greater emphasis on prevention is not being adequately addressed.[57,58] What might help is that GPs themselves speak up and declare even more prominently what they are able and willing to do, and what not.[59] Given our studies, our understanding from daily practice and international literature, we strongly believe that primary healthcare providers can play a key role in the optimalisation of the current CSPs.

Thereby I hope that the concept of 'trust' in the healthcare system and healthcare professionals returns, which might also contributes to a reduction and emphasis on filling out all paperwork, the so called famous 'Paarse Krokodil' (Purple Crocodile).[60]

What do general practitioners want?

Over the past few years we have spoken to many GPs and asked GPs them what they need in order to empower the CSPs in the future, they roughly responded with three answers: I) more GPs are needed, II) GP-practices should become smaller, i.e. fewer patients per GP, and III) better/more funding is needed for the entire (primary care) healthcare system.

It can be said that the government has been working on increasing the number of GPs for years. Nevertheless, it still does not seem easy to educate more GPs, especially in the more peripheral areas of the Netherlands. The workload remains high, and additionally there is an issue of a significant shortage of support staff for GPs continues to persist.[61,62] Therefore, a significant challenge emerges for various stakeholders in primary care, as well as for society at large.

The National General Practitioners Association (LHV; Landelijke Huisartsen Vereniging) has been arguing for a long time for smaller number of registered patients per GP-practice and stated that a norm practice should consist of about 1800 patients.[63] Although the practice size per GP has indeed decreased in recent years – from 2350 patients in 2006, to

2095 patients in 2023 – we are still far from 1800 patients enlisted per GP (fte).[64] Recently, the LHV has signed the Integral Care Agreement (IZA; Integraal zorgakkoord),[65] in which there are certain positive notes that might benefit both GPs and patients concerning the CSPs. The most concrete example here is that GPs get more time per patient (Meer Tijd Voor de Patient). Extended consultations seem essential in order to inform and guide patients adequately also with respect to the CSPs.

Regarding the last point, it is a bit difficult to be optimistic. Healthcare costs have been rising for decades, and so far no unequivocal solution seems to have been found to solve this problem.[66] It might be useful to think about paying for health and keeping the population healthy, and thus focusing more and more on prevention. Which leads us to the next question.

What about prevention?

In addition to the public debate on the role of the GP, the role of (primary) prevention is an issue for GPs. When it comes to cancer, there is a lot more that could and should be done to prevent cancer (see also the introduction of this thesis). Most logical steps would be to create more public awareness about cancer risk factors and promoting healthy lifestyle choices. When looking at the numbers, currently only about 1.8% of the total of healthcare costs are spend on population-wide preventive and public healthcare.[67] We are willing to spend a significant amount of money on extremely expensive medications and treatments, but there is scarce funding available for the prevention of common diseases. Fortunately, the public opinion regarding this seems to be changing.[68-70] Where the Netherlands rated in the top three healthiest countries of the world, only a few decades ago. 'We' have now dropped to the 30th place.[71] This is the next challenge for politics. Since 2018 there has been a prevention agreement, hopefully this will contribute to a healthier Dutch population in the long run.[72]

Cancer screening based upon Population Health Management principles

Anno 2023, one might wonder if the current population-based cancer screening programmes (CSPs) are still best suited to reduce the burden of the screening-specific tumours for the population as a whole. As stated in the introduction, the WHO declared (based on the Wilson and Jungner criteria) that the benefits of participating in a screening programme should outweigh the potential disadvantages of the screening programme.[73] In the current situation there however appears to be a prevailing inclination wherein the advantages at the population level appear to surpass the potential drawbacks at the individual level. Given the findings of our studies presented in this thesis we believe it is

about time to think on how the current CSPs can be optimized in such a way that both efficiency and effectiveness of programmes are increased, whereby individual harms ideally get further diminished. Introducing Population Health Management principles into cancer screening might help to achieve this goal.

Defining Population Health Management

Population Health Management (PHM) can be defined as a healthcare strategy that shifts its attention from individual patients to specific at-risk population groups in order to address the current challenges within the healthcare system.[74, 75] Given the mounting difficulties in Western countries to deliver cost-effective, accessible, and high-quality healthcare, it appears that adopting this approach is becoming increasingly essential.[76, 77] While current literature contains multiple definitions on PHM, we would like following the master programme in The Hague, by defining PHM as: *"A proactive management of a population at risk for adverse health outcomes; through a variety of individual, organizational and cultural interventions to improve patient, clinical and financial outcomes, based on risk stratified needs assessment of the population; supported by a comprehensive governance infrastructure".*[78] In order to pursuit PHM, the aims of the Quadruple Aim are often mentioned. These are: (I) to improve population health, (II) to provide better quality of care, (III) to ensure that healthcare provider experiences improve, and (IV) to reduce the (overall) healthcare costs.[79]

In order to understand the above-mentioned definition, the concept of 'risk stratification' might need some clarification. It refers to a methodical evaluation of a patients' profile, in order to assign an individual risk score. This established risk profile can then serve as the basis for delivering tailored healthcare to both the individual and the larger population based on their respective risk levels.

Population Health Management building blocks in this thesis

Although individual studies have already been briefly summarized at the start of this chapter, it might help to now rethink about these findings within the definition of PHM in mind. It then becomes clear that the studies within the thesis can also be regarded as PHM building block for CSPs in the Netherlands.

In Chapter 2, several characteristics are described that could be used for risk stratification. Chapter 3 highlights the importance of involving individuals residing in low socioeconomic status (SES) neighbourhoods in screening examinations. Here specific tailormade interventions are most likely needed in order to engage these people within the CSPs. In Chapter 4, we demonstrate the desire among potential participants to receive further support and guidance from primary healthcare providers. Subsequently,

Chapter 5 explores potential strategies for addressing unique barriers faced by a small, in particular, high-risk subgroup in participating in a CSPs. Lastly, Chapter 6 reveals that primary healthcare providers (GPs) themselves are inclined to be (more) involved in the current CSPs, hence potentially serving as key enablers for incorporating PHM principles within the screening programmes.

As the studies within this thesis show, we believe that the current CSPs could benefit from making use of PHM principles, in which primary healthcare providers are given a more prominent and proactive role. As the studies in the thesis are all conducted in highly urbanised regions of the Netherlands, it would make sense to see if a pilot-study can be set-up within this region. Effective integration of PHM principles should be done in close collaboration with the national screening organization, primary healthcare provider organizations, and ideally with some level of political support.

For risk stratification I envision a prediction tool, based on characteristic out of the Electronic Health Records (EHR) that provide insight into the degree of risk an individual faces concerning one of the screening specific tumours, similar to the frailty index score for the elderly.[80]

Conclusion

This thesis provides additional evidence that the current population-based cancer screening programmes (CPSs) of the Netherlands could be further optimized, in particular regarding the screening uptake of people living in highly urbanized and/or low(er) socioeconomic status (SES) neighbourhoods. Our findings suggest that non-attendance in these lower SES-neighbourhoods is associated with more unfavourable, relatively late-stage, tumour diagnosis. Given that participation in cancer screening is not solely based on rational decision-making, primary healthcare providers could play an important role in educating and advising individuals who are eligible for participation in the CPSs. We found that both screen-eligible people and general practitioners (GPs), support the idea of a more targeted GP-involvement in the CSPs. Based on the findings of this thesis, we recommend that a proactive primary care approach would be suitable to enhance the current cancer screening uptake, with the ultimate goal to screen (sub) populations who are highest at risk of developing the screening-specific tumours.

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CHAPTER 8

Summary

Currently, the Netherlands has three population-based cancer screening programmes (CSPs). These are the CSPs aiming at cervical, breast, and colorectal cancer. Potential participants are invited based on their age and gender to participate in these screening programmes. The primary screening methods – respectively the Pap smear/self-sampling test, bilateral mammography, and the faecal immunochemical test (i.e., stool test) – are offered free of charge to all residents registered and living in a Dutch municipality. It is known that the success of a screening programme is highly depends on the percentage of invitees who actually participate in the screening programme. According to the World Health Organization (WHO), at least 70% of invitees need to participate, without preselection, for a screening programme to be effective at the population level.

Looking at the attendance rates in the Netherlands (the latest available data is from 2022), we can conclude that the national numbers are still reasonably high; with percentages of 54.8% for the cervical cancer screening programme (CC-SP), 72.5% for the breast cancer screening programme (BC-SP), and 70.6% for the colorectal cancer screening programme (CRC-SP). However, this does not mean that the attendance rates cannot be further enhanced or that there are no further challenges regarding the attendance rates of the current screening programmes.

For years, the CC-SP has faced low attendance when we take the threshold of 70% participation into account. Additionally, there is a clear declining trend visible in the attendance rates of all three screening programmes over a period of several years. Hereby it should be noted that it might still be too early to draw this conclusion for the CRC-SP; the introduction of this screening programme dates back to 2014, and it has only been fully operational since 2019. Furthermore, significant regional differences exist in the attendance rates of the screening programmes, with particularly low rates in the major cities of the Netherlands – Amsterdam, Rotterdam, The Hague, and Utrecht. Finally, some general practitioners have informed us that they notice potential participants who might benefit the most from participating in the screening programmes are currently the least inclined to participate in the screening examinations.

Although these challenges are not unique to the Netherlands, we have chosen to focus specifically on the Dutch context in this thesis. We have focused on a multicultural urban environment, as the accessibility and inclusivity of the screening programmes seem to be under pressure here. The overarching goal of this thesis is to contribute to the future optimalization of the current Dutch screening programmes, with particular emphasis on the role of primary care (including general practitioners).

Key findings of this thesis

Although various studies have been conducted on the different factors influencing participation in the Dutch population-based cancer screening programmes (CSPs), there was no systematic literature review systematically describing, ranking, and analysing all these factors. In **Chapter 2**, we therefore begin with a systematic review in which we describe all literature published up to February 2018 regarding the characteristics of both participation and non-participation in the screening programmes. For this purpose, we searched all known and relevant electronic databases, including PubMed, Cochrane Library, and PsycINFO. Additionally, we utilized the so-called grey literature (e.g., reports from the National Institute for Public Health and the Environment (RIVM) and the national screening organisation (Bevolkingsonderzoek Nederland)). To organize all identified characteristics, we used the Integrated Change model (I-Change model) by De Vries et al. This is a model from health psychology that incorporates elements from various widely used and valued theories of health behaviour, such as the Health Belief Model, the Protection Motivation Theory, the Theory of Planned Behaviour, and the Precaution Adoption Process Model. Through this literature study, we were able to identify knowledge gaps. This study thereby formed the basis for this thesis.

The main findings arising from this study are that the previously published studies primarily tend to describe the general characteristics of (non-)attendance and (non-) attenders, but that they rarely provided in depth information on other factors of (non-) participation. We found that classic – often non-influential factors – such as socioeconomic status (SES), country of birth, and place of residence are most frequently reported and investigated in their relationship to participation in the screening programmes. Low SES, non-Western migration background, and living in an urban environment were strongly correlated with lower participation in the screening programmes. Additionally, we found that younger women and men (of course only applicable for the colorectal cancer screening programme) are less inclined to participate. Finally, we found some indications that general practitioners may be able to influence the attendance rates of the screening programmes. The I-Change model proved to be a useful tool in mapping the current knowledge about participation in the screening programmes.

In **Chapter 3**, we describe a retrospective data study to further understand which potential participants are less likely to participate in the CSPs in the city of The Hague and what risks (in terms of tumour outcomes) this entails. Due to limitations in data availability, we had to focus on the screening programmes targeting at breast cancer (BC-SP) and colorectal cancer (CR-CSP). Although it is unfortunate that we could not examine all three CSPs collectively, this did give us a unique opportunity to compare a

long-standing CSP with a relatively new one. We utilized databases from the national screening organisation (Bevolkingsonderzoek Nederland) (supplemented with specific regional data via Bevolkingsonderzoek Zuid-West) and linked them to databases from the Netherlands Comprehensive Cancer Organisation (IKNL). In this study, over the period from 2005 to 2019, we were able to elucidate (at an aggregated level) who did/did not participate in the BC-SP and CRC-SP, and who ultimately was/was not was diagnosed with of one of the screening-specific tumours. For our analyses, we compared two subgroups: potential participants who did (participation >50% after invitation) and did not (participation ≤50% after invitation) participate in the screening programmes over the period.

The main findings from this study are that non-participation in the screening programmes can be directly linked to residing in a low socioeconomic status (SES) neighbourhood. Moreover, non-participation is also associated with a less favourable tumour outcome – relatively advanced tumour outcome – at the time of diagnosis. Therefore, non-participation in the screening programmes is potentially concerning and problematic, especially for certain subpopulations. When we combined the data from both screening programmes, it became clear that the majority of women do participate and generally do so consistently over time. Also, from the combined datasets, it emerged that women who did not participate in either screening programmes over time were more likely to reside in lower SES-neighbourhoods. Based on these findings, we believe that there is a need for the development of future strategies that engage specific subgroups more effectively in the screening programmes. The city of The Hague, with all its multicultural facets, proved to be an excellent setting for conducting this type of research. This is primarily due to the significant differences that exist between the various neighbourhoods in the city, which are adequately represented by the SES-scores.

In **Chapter 4**, we present a Q-methodology study (Q-study) on the beliefs and motivations of potential participants residing in the city of The Hague regarding participation in the CSPs. The idea behind this study was to clarify what is important to potential participants when they think/decide about participating in the screening programmes. A Q-study is a 'mixed-methods' methodology, particularly used to gain insight into prevailing perspectives on specific subjects within certain populations. Due to the COVID-19 pandemic outbreak, we conducted our Q-study online using an existing research panel. In a Q-study, respondents are presented with a set of statements that they must rank based on their beliefs within a predetermined framework. These rankings (one ranking per participant) thus form the quantitative data. Subsequently, factor analysis is conducted to identify significant clusters of correlations. The assumption is that respondents with similar perspectives will rank the statements in similar ways. The qualitative data is

formed by respondents providing explanations for their rankings. In our study, we also interviewed selected respondents after they completed their rankings. We identified three different perspectives. The first identified perspective was labelled as 'positive about participation'. These are the people who typically always participate in the screening programmes. They have a positive attitude towards the screening programmes, and respondents indicated that participation in the screening programmes is part of their (social) norm. Interestingly, the interviewed respondents with this perspective could not always provide correct information about the screening programmes, particularly not about the medical follow-up tests. Therefore, we questioned whether their decision to participate in the screening programmes is the result of a deliberate, well-informed choice. The second perspective was labelled as 'thoughtful about participation'. People with this perspective were found to be more hesitant about participating in the screening programmes. They more often doubted the effectiveness of the screening programmes and considered the potential consequences of screening (including false-positive and false-negative results) more important. These respondents were generally better informed about the potential consequences of the screening programmes. Unique to this perspective is the role that respondents see for their general practitioner/primary care provider(s) as advisors. The third perspective was labelled by us as 'fear drives participation'. These people mostly participate in the screening programmes, but this is mainly due to feelings of fear and discomfort. Most respondents with this perspective knew people who had actually suffered from or died from the consequences of cancer. Respondents may have felt more vulnerable to being diagnosed with cancer themselves. People with this perspective were less open to external influence and guidance.

The main findings from this Q-study are that beliefs and motivations about the screening programmes not only differ between participants and non-participants, but also can differ between subgroups of people with different underlying perspectives. We believe that it is meaningful to adjust communication about the screening programmes to the perspectives of potential participants. For people belonging to perspective 1 (positive about participation), more attention should be paid to providing information about the screening programmes and the medical follow-up tests. For perspective 2 (thoughtful about participation), more attention should be paid to the potential drawbacks of screening. For perspective 3 (fear drives participation), more attention should be paid to the risks (and numbers) associated with participation in the screening programmes. For two of the perspectives in this study, communication channels outside of primary care seem suitable. However, for respondents belonging to the second perspective, who are doubtful about participating in the screening programmes, it appears that they value information provided by a general practitioner or other trusted primary care provider.

In **Chapter 5**, we demonstrate the importance and effectiveness of a specific invitation strategy for vulnerable subpopulations. Therefore, we consider this study a 'proof of concept study'. In the city of Rotterdam, we conducted a cross-sectional intervention study, inviting marginalized women to participate in a screening study for cervical cancer. For this study, women were considered marginalized if they had not received, or could not receive, invitation letter(s) for the cervical cancer screening program (CC-SP) due to their living conditions. Our study focused on sex workers in unstable conditions, homeless women, and women without official documentation. In total, we were able to collect samples from 74 women for this study. The collected samples were analysed for both the presence of high-risk human papillomavirus (hrHPV) and cytological abnormalities. In doing so, we intentionally deviated from the standard practice within the current CC-SP. We compared the results of the samples we collected with regional prevalence data from women who had participated in the CC-SP. We obtained this data through the national screening organisation, region South-West (Bevolkingsonderzoek Zuid-West).

The main findings from this study are that marginalized women seem to have a four times higher risk of hrHPV infection with cytological abnormalities compared to women screened through the CC-SP. Additionally, through this study, we demonstrated that a direct proactive approach is by far the most effective way to reach marginalized women. In our study, 92% of all women were included for participation in the study through this proactive approach. Based on this study, we believe that much more attention should be paid to vulnerable women without stable housing in relation to the development of (precursors to) cervical cancer.

Since our earlier studies suggested that primary care providers might play an important role in optimizing participation rates of the CSPs, in **Chapter 6**, we focused on general practitioners (GPs) and surveyed them about their current role regarding the CSPs and whether they believe it should be different. For this purpose, we conducted a stepped 'mixed-methods' study by first developing a questionnaire and distributing it among GPs. Subsequently, we interviewed a selected number of GPs using semi-structured in-depth interviews to interpret the data resulting from these questionnaires.

The main findings from this study are that GPs generally hold a positive view of CSPs and their role therein. Furthermore, GPs indicated their willingness to further support and reinforce the CSPs. However, they clearly stated their reluctance to take on (additional) logistical and organizational tasks. A proactive neighbourhood-based approach emerged as one of the possible options to optimize the current screening programmes. In this regard, GPs emphasized the need to pay more attention to involving people residing in low socioeconomic status (SES) neighbourhoods. The most innovative idea to achieve

this was the concept of an 'add-on methodology', whereby GPs/general practices themselves selectively invite patients, as a supplement to the general invitation for participation in the CSPs. The most positive effects are likely to be expected when GPs select patients whom they assess to be at (higher) risk of developing one of the screening-specific tumours.

Conclusion

The studies described in this thesis provide additional evidence that the current Dutch population-based screening programmes (CSPs) can be further optimized, particularly concerning the participation of potential participants from highly urbanized and low socioeconomic status (SES) neighbourhoods. Our findings suggest that non-participation in the CSPs in these low SES-neighbourhoods is associated with more unfavourable, relatively advanced, tumour outcomes. Given that the decision to participate in a CSP is not solely based on rational decision-making processes, primary care providers could play an important role here. This would primarily involve informing and advising potential participants who are hesitant about participating in CSPs. In this thesis, we describe that both potential participants and general practitioners support the idea that primary care should be more involved in the invitation process of the CSPs. Based on our findings, we therefore recommend implementing a proactive, risk-based invitation strategy from primary care regarding the invitation process of the current CSPs.

APPENDIX

Nederlandse samenvatting
Dankwoord
Curriculum Vitae
Bibliography and PhD coursework

Nederlandse samenvatting

Nederland heeft momenteel drie bevolkingsonderzoeken naar kanker (bvo's). Dit zijn de bvo's naar baarmoederhals-, borst- en darmkanker. Potentiële deelnemers worden op basis van hun leeftijd en geslacht uitgenodigd om deel te nemen aan deze screeningprogramma's. De primaire screeningsmethoden – respectievelijk het uitstrijkje/de zelfafnametest, een bilaterale mammografie en de fecaal immunochemische test (i.e. ontlastingstest) – worden kosteloos aangeboden aan alle inwoners geregistreerd en woonachtig in een Nederlandse gemeente. Bekend is dat het succes van een bvo afhankelijk is van het percentage genodigden dat daadwerkelijk deelneemt aan het screeningprogramma. Volgens de Wereldgezondheidsorganisatie (WHO) dient tenminste 70% van de genodigden deel te nemen, zonder voorselectie, wil een bvo effectief zijn op populatieniveau.

Wanneer we kijken naar de opkomstcijfers in Nederland (de laatst beschikbare gegevens komen uit 2022), dan kunnen we constateren dat de nationale cijfers nog redelijk op niveau zijn; met percentages van respectievelijk 54,8% voor het bvo naar baarmoederhalskanker (bvo-BMHK), 72,5% voor het bvo naar borstkanker (bvo-BK) en 70,6% het bvo naar darmkanker (bvo-DK). Dit betekent echter niet dat de opkomstcijfers niet verder kunnen worden verbeterd of dat er geen verdere uitdagingen zijn met betrekking tot de opkomstcijfers van de huidige bvo's.

Zo heeft het bvo-BMHK al jaren te maken met een te lage opkomst wanneer we de grens van 70% deelname hanteren. Daarnaast is er een duidelijk dalende trend zichtbaar in de opkomstcijfers van de drie bvo's over een tijdsperiode van meerdere jaren. Hierbij dient wel de kanttekening gemaakt te worden dat het voor het bvo-DK misschien nog te vroeg is om deze conclusie te trekken; de invoering van dit bvo dateert uit 2014 en pas sinds 2019 is dit bvo volledig operationeel. Verder is het zo dat er aanzienlijke regionale verschillen bestaan tussen de opkomstcijfers van de bvo's, waarbij deze met name in de grote steden van Nederland – Amsterdam, Rotterdam, Den Haag en Utrecht – laag zijn. Tot slot hebben enkele huisartsen ons laten weten dat zij merken dat potentiële deelnemers die mogelijk het meeste baat zouden kunnen hebben van deelname aan de bvo's, op dit moment het minst geneigd lijken om deel te nemen aan de screeningsonderzoeken.

Hoewel deze uitdagingen niet uniek zijn voor Nederland, hebben we ervoor gekozen om ons in dit proefschrift specifiek te richten op de Nederlandse context. Daarbij hebben we ons gericht op een multiculturele grootstedelijke omgeving, aangezien de toegankelijkheid en inclusiviteit van de bvo's juist hier onder druk lijkt te staan. Het overkoepelende doel van dit proefschrift is om een bijdrage te leveren aan de toekomstige

optimalisatie van de huidige Nederlandse bvo's. Hierbij hebben we in het bijzonder naar de rol van de eerstelijnsgezondheidszorg (waaronder huisartsen) gekeken.

Belangrijkste bevindingen van dit proefschrift

Hoewel er al diverse studies zijn verricht naar de verschillende kenmerken die van invloed zijn op deelname aan de Nederlandse bevolkingsonderzoeken naar kanker (bvo's), bestond er nog geen systematisch literatuuroverzicht waarin al deze kenmerken systematisch beschreven, gerangschikt en geanalyseerd zijn. In **Hoofdstuk 2** beginnen we daarom met een systematische review waarin we naar alle literatuur die verschenen is tot februari 2018, aangaande de kenmerken van zowel deelname als niet-deelname aan de bvo's beschrijven. Hiervoor hebben we gezocht in alle bekende en relevante elektronische databases, o.a. PubMed, Cochrane Libary en PsycINFO. Daarnaast hebben we gebruik gemaakt van de zogeheten grijze literatuur (o.a. rapporten van het Rijksinstituut voor Volksgezondheid en Milieu (RIVM) en Bevolkingsonderzoek Nederland). Om alle geïdentificeerde kenmerken te ordenen maakten we gebruik van het Integrated Change model (I-Change model) van De Vries et al. Dit is een model uit de gezondheidspsychologie dat elementen bevat uit verschillende veelvuldig eerder gebruikte en gewaardeerde theorieën over gezondheidsgedrag, zoals het: Health Belief Model, de Protection Motivation Theory, de Theory of Planned Behaviour en het Precaution Adoption Process Model. Door middel van deze literatuurstudie waren wij in staat om kennislacunes te identificeren. Deze studie vormde daarmee ook de basis voor dit proefschrift.

De belangrijkste bevindingen voortkomend uit deze studie zijn dat de tot dan toe gepubliceerde studies zich voornamelijk richten op de algemene kenmerken van (niet-) deelname en (niet-)deelnemers, maar dat het ontbreekt aan gedetailleerde kennis aangaande kenmerken van niet-deelnemers aan de bvo's. Zo vonden wij dat de klassieke – veelal niet-beïnvloedbare factoren – als sociaaleconomische status (SES), geboorteland en woonplaats het vaakst zijn gerapporteerd en onderzocht in hun relatie tot deelname aan de bvo's. Hierbij blijken een lage SES, een niet-westerse migratieachtergrond en wonen in een stedelijke omgeving sterk gecorreleerd te zijn met een lage(re) deelname aan de bvo's. Daarnaast vonden we dat jongere vrouwen en mannen (uiteraard alleen van toepassing op het bvo naar darmkanker) minder geneigd zijn om deel te nemen. Tot slot, vonden we reeds enkele aanwijzingen dat huisartsen mogelijk instaat zijn om de opkomstcijfers van de bvo's te beïnvloeden. Het I-Change model bleek een nuttig hulpmiddel te zijn bij het in kaart brengen van de huidige kennis over deelname aan de bvo's.

In **Hoofdstuk 3** beschrijven wij een retrospectief dataonderzoek om nader in beeld te brengen welke potentiële deelnemers minder geneigd zijn om deel te nemen aan de bvo's in de stad Den Haag en welke risico's (gekeken naar tumor uitkomsten) dit met zich meebrengt. Door beperkingen in de beschikbaarheid van data hebben wij ons hierbij moeten richten op de bvo's naar borstkanker (bvo-BK) en darmkanker (bvo-DK). Hoewel het jammer is dat we niet naar alle drie bvo's in gezamenlijkheid hebben kunnen kijken, gaf ons dit wél een unieke kans om een langlopend bvo te vergelijken met een relatief nieuw bvo. Wij hebben gebruik gemaakt van databases van Bevolkingsonderzoek Nederland (aangevuld met specifieke regionale gegevens via Bevolkingsonderzoek Zuid-West) en deze gelinkt aan databases van het Integraal Kankercentrum Nederland (IKNL). In deze studie hebben we, over de tijdsperiode 2005 tot 2019, inzichtelijk kunnen maken (op geaggregeerd niveau) wie er wel/niet deelnamen aan de bvo's-BK en -DK, en wie er uiteindelijke wel/niet werden gediagnosticeerd met een van de screening specifieke tumoren. Voor onze analyses vergeleken we een tweetal subgroepen: potentiële deelnemers die *wel* (deelname in >50% na uitnodiging) en *niet* (deelname ≤50% na uitnodiging) deelname aan de bvo's over de tijdsperiode.

De belangrijkste bevindingen voortkomend uit deze studie zijn dat het niet-deelnemen aan de bvo's direct gelinkt kan worden aan het woonachtig zijn in een lage sociaaleconomische status (SES)-wijk. Daarbij is niet-deelname tevens geassocieerd met een minder gunstige – relatief vergevorderde – tumoruitkomst ten tijde van de diagnose. Daarmee wordt niet-deelnemen aan de bvo's dus potentieel kwalijk en problematisch; in het bijzonder voor bepaalde subpopulaties. Ten tijde dat we de data van beide bvo's combineerde, werd duidelijk dat het merendeel van de vrouwen wél deelneemt en dit doorgaans ook consistent over de tijd doet. Ook uit de gecombineerde datasets bleek dat de vrouwen die over de tijd niet meededen aan beide bvo's, vaker woonachtig zijn in de lagere SES-wijken. Op basis van deze bevindingen menen wij dat er behoefte is aan de ontwikkeling van toekomstige strategieën die specifieke subgroepen meer betrekken bij de bvo's. De stad Den Haag, met al haar multiculturele facetten, bleek bij uitstek geschikt om dit type onderzoek te verrichten. Dit komt met name door de aanzienlijke verschillen die er bestaan tussen de verschillende wijken in de stad, welke adequaat gerepresenteerd worden door de SES-scores.

In **Hoofdstuk 4** presenteren wij een Q-methodologie studie (Q-studie) over de overtuigingen en motivaties van potentiële deelnemers die woonachtig zijn in de stad Den Haag met betrekking tot deelname aan de bvo's. Het idee achter deze studie was om helder te krijgen wat voor potentiële participanten van belang is wanneer zij nadenken/beslissen over deelname aan de bvo's. Een Q-studie is een 'mix-methods' methodologie, welke in het bijzonder wordt gebruikt om inzicht te verkrijgen in de

heersende perspectieven over specifieke onderwerpen binnen bepaalde populaties. Door de uitbraak van de COVID-pandemie hebben we onze Q-studie online uitgevoerd met behulp van een bestaand onderzoekspanel. Bij een Q-studie wordt aan de respondenten een set van stellingen overhandigd die zij dienen te rangschikken op basis van hun gedachtengoed binnen een vooraf bepaald kader. Deze rangschikkingen (per deelnemer één rangschikking) vormen zo de kwantitatieve data. Hierna volgt dan een factoranalyse om significante clusters van correlaties te identificeren. De veronderstelling is dat respondenten met vergelijkbare perspectieven de uitspraken op vergelijkbare manieren rangschikken. De kwalitatieve data wordt gevormd doordat respondenten een toelichting geven op hun rangschikking. In onze studie hebben we bovendien enkele geselecteerde respondenten na afloop van hun rangschikking geïnterviewd. Wij identificeerden drie verschillende perspectieven. Het eerste geïdentificeerde perspectief hebben we geduid als 'positief over deelname'. Dit zijn de mensen die eigenlijk altijd deelnemen aan de bvo's. Ze hebben een positieve houding ten opzichte van de bvo's en de respondenten gaven aan dat deelname aan de bvo's onderdeel is van hun (sociale) norm. Opmerkelijk was dat de geïnterviewde respondenten met dit perspectief, niet altijd correcte informatie konden geven over de bvo's, en dan met name niet over de medische vervolgtesten. Wij vroegen ons daarom af of hun beslissing om deel te nemen aan de bvo's het resultaat is van een weloverwogen, goedgeïnformeerde, keuze. Het tweede perspectief hebben we geduid als 'twijfelend over deelname'. Mensen met dit perspectief bleken meer aarzelend te zijn over deelname aan de bvo's. Ze twijfelden vaker over de effectiviteit van de bvo's, en vonden de potentiële gevolgen van screening (o.a. vals-positieve en vals-negatieve uitslagen) belangrijker. Deze respondenten waren over het algemeen beter geïnformeerd over de mogelijke gevolgen van de bvo's. Uniek voor dit perspectief is de rol die respondenten zien voor hun huisarts/eerstelijnszorgverlener(s) als adviseur. Het derde perspectief werd door ons geduid als 'angst drijft deelname'. Deze mensen bleken veelal deel te nemen aan de bvo's, maar dat kwam met name door gevoelens van angst en ongemak. De meeste respondenten met dit perspectief kenden mensen die daadwerkelijk leden of waren overleden aan de gevolgen van kanker. Respondenten voelden zich daarbij mogelijk meer kwetsbaar om zelf met kanker gediagnosticeerd te worden. Mensen met dit perspectief bleken minder open te staan voor externe invloed en begeleiding.

De belangrijkste bevindingen voortkomend uit deze Q-studie zijn dat de overtuigingen en motivaties over de bvo's niet alleen verschillen tussen deelnemers en niet-deelnemers, maar dat deze ook kunnen verschillen tussen subgroepen van mensen met verschillende onderliggende perspectieven. Hierbij menen wij dat het zinvol is om de communicatie rondom de bvo's aan te passen aan de perspectieven van potentiële deelnemers. Voor mensen die behoren tot perspectief 1 (positief over deelname) zal er meer aandacht

moeten komen voor het verstrekken van informatie over de bvo's, en de medische vervolgonderzoeken. Voor perspectief 2 (twijfelend over deelname) moet meer aandacht worden besteed aan de potentiële nadelen van screening. Voor perspectief 3 (angst drijft deelname) zal er meer aandacht moeten worden geschonken aan de risico's (en cijfers) die verband houden met deelname aan bvo's. Voor twee van de perspectieven in deze studie lijken communicatiekanalen buiten de eerstelijnsgezondheidzorg geschikt te zijn. Echter, voor de respondenten behorende bij het tweede perspectief, en die dus twijfelen aan deelname aan de bvo's, blijkt dat zij juist waarde hechten aan informatie die verstrekt wordt door een huisarts of een andere vertrouwde eerstelijnszorgverlener.

In **Hoofdstuk 5** laten we zien hoe belangrijk en effectief een specifieke uitnodigingsstrategie voor kwetsbare subpopulaties kan zijn. Deze studie beschouwen we daarom als een 'proof of concept studie'. In de stad Rotterdam hebben wij hiervoor een zogeheten cross-sectionele interventiestudie uitgevoerd, waarbij we marginaliserende vrouwen hebben uitgenodigd om deel te nemen aan een screeningsonderzoek naar baarmoederhalskanker. Voor deze studie werden vrouwen als gemarginaliseerd beschouwd als zij geen uitnodigingsbrief(en) hadden ontvangen, of konden ontvangen, voor het bvo naar baarmoederhalskanker (bvo-BMHK) als gevolg van hun leefomstandigheden. Onze studie richtte zich hierbij op sekswerkers in onstabiele omstandigheden, dakloze vrouwen, en vrouwen zonder officiële papieren. In totaal hebben wij bij 74 vrouwen uitstrijkjes kunnen afnemen voor deze studie. De uitgevoerde uitstrijkjes werden geanalyseerd op zowel het voorkomen van hoog risico humaan papillomavirus (hrHPV), als op cytologische afwijkingen. Hiermee weken wij bewust af van hetgeen gangbaar is binnen het huidige bvo-BMHK. De uitslagen van de door ons verrichte uitstrijkjes vergeleken we met regionale prevalentiedata van vrouwen die deel hadden genomen aan het bvo-BMHK. Deze data verkregen wij via Bevolkingsonderzoek Zuid-West.

De belangrijkste bevindingen voortkomend uit deze studie zijn dat marginaliserende vrouwen een vier keer zo hoog risico lijken te hebben op een hrHPV-infectie met cytologische afwijkingen in vergelijking met vrouwen die gescreend worden door het bvo-BMHK. Daarnaast hebben wij middels deze studie kunnen aantonen dat een directe proactieve benadering verreweg het meest effectief is om gemarginaliseerde vrouwen te bereiken. In onze studie werd namelijk 92% van alle vrouwen op deze, proactieve, manier geïncludeerd voor deelname aan de studie. Naar aanleiding van deze studie menen wij dat er veel meer aandacht moet komen voor kwetsbare vrouwen zonder vaste woon- en verblijfplaats in relatie tot de ontwikkeling van (voorstadia van) baarmoederhalskanker.

Omdat uit onze eerdere studies naar voren kwam dat mogelijk juist eerstelijnszorgverleners een belangrijke rol zouden kunnen spelen bij de optimalisatie van de opkomstcijfers van de bvo's, hebben wij ons in **Hoofdstuk 6** gericht op huisartsen en hen bevraagd over hetgeen zij vinden van hun huidige rol ten aanzien van de bvo's, en of ze vinden dat deze anders dient te zijn. Hiervoor hebben we een getrapte 'mixed-methods' studie uitgevoerd door eerst een vragenlijst te ontwikkelen en deze te verspreiden onder huisartsen. Vervolgens hebben we een aantal geselecteerde huisartsen geïnterviewd, middels semi-gestructureerde diepte-interviews, om de data voortkomend uit deze vragenlijsten te duiden.

De belangrijkste bevindingen voortkomend uit deze studie zijn dat huisartsen over het algemeen positief zijn over de bvo's en hun rol daarin. Verder gaven huisartsen aan dat ze bereid zijn om de bvo's verder te ondersteunen en te bekrachtigen. Hierbij gaven ze echter wel duidelijk aan niet (nog) meer logistieke en organisatorische taken op zich te willen nemen. Een proactieve wijkgerichte benadering kwam naar voren als een van de mogelijke opties om de huidige screeningprogramma's te optimaliseren. Hierbij benadrukten huisartsen de noodzaak om meer aandacht te besteden aan het betrekken van mensen die woonachtig zijn in lage SES-wijken. Het meest innovatieve idee om dit te realiseren was het concept van een 'add-on methodologie', waarbij huisartsen/huisartsenpraktijken zelf patiënten gericht uitnodigen, als aanvulling op de algemene uitnodiging voor deelname aan de bvo's. De meest positieve effecten kunnen hierbij waarschijnlijk verwacht worden wanneer huisartsen zelf patiënten selecteren waarvan zij inschatten dat deze een (hoger) risico lopen op de ontwikkeling van (een van) de screening specifieke tumoren.

Conclusie

De studies beschreven in dit proefschrift leveren aanvullend bewijs dat de huidige Nederlandse bevolkingsonderzoeken (bvo's) verder geoptimaliseerd kunnen worden. Dit met name wanneer we kijken naar de deelname van potentiële participanten uit sterk verstedelijkte en lage sociaaleconomische status (SES)-wijken. Onze bevindingen suggereren dat niet-deelname aan de bvo's in deze lage SES-wijken geassocieerd is met meer ongunstige, relatief vergevorderde, tumoruitkomsten. Gegeven het feit dat de beslissing om deel te nemen aan een bvo niet louter gebaseerd is op rationele besluitvormingsprocessen, zouden eerstelijnszorgverleners hier een belangrijke rol in kunnen spelen. Dit zal dan met name gaan over het informeren en adviseren van potentiële deelnemers die twijfelen over deelname aan de bvo's. In dit proefschrift beschrijven wij dat zowel potentiële deelnemers als huisartsen het idee ondersteunen dat de eerstelijnsgezondheidszorg meer betrokken moet worden bij het uitnodigingsproces van bvo's. Gebaseerd op onze bevindingen raden wij dan ook aan om een proactieve, risicogerichte, uitnodigingsstrategie vanuit de eerstelijnsgezondheidszorg in te zetten aangaande het uitnodigingsproces van de huidige bvo's.

Dankwoord

Het is zover, mijn proefschrift is af! Op deze plek wil ik een aantal mensen bedanken die hier een bijdrage aan hebben geleverd.

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Mede-AIOTHO's, onze trajecten zijn niet altijd eenvoudig, maar ze zijn zeker altijd uitdagend. Als wij ervoor zorgen dat we de problemen binnen de huisartsgeneeskunde samen aanvliegen, dan ben ik ervan overtuigd dat het goed gaat komen.

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PER ASPERA AD ASTRA

Curriculum Vitae

Thomas Hendrikus Gerardus Bongaerts was born on March 8, 1989 in Maastricht, the Netherlands. After graduation from secondary school (VWO Atheneum, Porta Mosana College) in 2008, he started studying Psychology at the University Maastricht. After obtaining his propaedeutic exam in 2009, he was selected (decentrale selectie) to study Medicine at the University of Groningen. Throughout the bachelor's phase, he was an active member of various committees and boards, including the KNMG-district Groningen and IFMSA-Groningen. By then he was already interested and involved in conducting research (Junior Scientific Masterclass) and education (Basiskwalificatie Onderwijs voor Studenten). In 2012 he obtained his bachelor-degree with 'honours'. During the second year of his master's program, he moved abroad for over more than a year to complete multiple clerkships at the Sint-Elisabeth hospital in Curaçao, and the Diakonessenhuis in Paramaribo, Suriname. In 2015 he returned to the city of Groningen and obtained his medical degree in December of that year. In the beginning of 2016 he started his medical career with a residency at the department of paediatrics in the Martini Hospital Groningen. After working for over a year, he subsequently moved to Delft and became a medical intern at the cardiology department of the Reinier de Graaf Gasthuis. After almost two years of clinical work he started as researcher at the Health Campus The Hague at the end of 2017. In March 2018, this led to a combined trajectory of PhD research with the training to become a general practitioner. Under supervision of prof. dr. Mattijs Numans, dr. Frederike Büchner and dr. Onno Guicherit, he investigated how to optimize the current uptake of the population-based cancer screening programmes in the Netherlands, with a focus on the potential role of primary care. The results of the PhD trajectory are described in this thesis and presented at several (inter)national conferences. During his employment he was involved in teaching medical students and nurses in training, and in parts of the education for the Leiden University College and the Population Health Management master. Furthermore, he worked as an out-of-hours acute physician for different nursing homes in the Leiden/The Hague area via GeriCall, and was he an active member of the education committee of the LOVAH (Landelijke Organisatie Van Aspirant Huisartsen). At the time of writing, he is in the process of completing his training to become a general practitioner at Huisartsenpraktijk Ottengraf in Leidschendam. He resides in The Hague with his fiancée, Laura Bloemer, and their son Olivier. In August, they expect their second child.

Bibliography and PhD coursework

Scientific publications in this thesis

Bongaerts THG, Büchner FL, Nierkens V, Crone MR, Guicherit OR, Numans ME. Perceptions and beliefs of general practitioners in the cancer screening programmes in The Netherlands: a mixed-methods study. *BMC Primary Care, provisionally accepted.*

Bongaerts THG, Büchner FL, de Munck L, Elferink MAG, Guicherit OR, Numans ME. Cancer screening participation within a highly urbanized region in the Netherlands: comparing the breast and colorectal cancer screening programmes of The Hague. *BMC Open,* June 2023.

Bongaerts THG, Büchner FL, Crone MR, van Exel J, Guicherit OR, Numans ME, Nierkens V. Perspectives on cancer screening participation in a highly urbanized region: a Q-methodology study in The Hague, the Netherlands. *BMC Public Health,* September 2022.

Bongaerts THG, Ridder M, Vermeer-Mens JCJ, Pukkel JJ, Numans ME, Büchner FL. Cervical Cancer Screening Among Marginalized Women: A Cross-Sectional Intervention Study*. International Journal of Women's Health,* May 2021.

Bongaerts THG, Büchner FL, Middelkoop BJC, Guicherit OR, Numans ME. Waarom mensen niet deelnemen aan oncologische bevolkingsonderzoeken. *Huisarts & Wetenschap,* August 2020.

Bongaerts THG, Büchner FL, Middelkoop BJC, Guicherit OR, Numans ME. Determinants of (non-)attendance at the Dutch cancer screening programmes: A systematic review. *Journal of Medical Screenin*g, October 2019.

Other scientific publications

Bongaerts, THG. Syndroom van Tietze (hfdst. 149). *Kleine kwalen in de huisartspraktijk,* December 2023.

Bongaerts, THG. Huilbaby's (hfdst. 15). *Kleine kwalen bij kinderen,* December 2021.

Sjoerdsma MH, **Bongaerts THG,** van Lente L, Kamps AWA. Nurse-driven Clinical Pathway Based on an Innovative Asthma Score Reduces Admission Time for Children. *Pediatric Quality and Safety*, September 2020.

Bongaerts, THG. Opkomst oncologisch bevolkingsonderzoek kan beter. *Huisarts & Wetenschap,* August 2018.

Wesseling W, **Bongaerts THG**, Hoogerbrugge A, Ridder M, Numans ME, Koot MH. Preventief onderzoek naar baarmoederhalskanker: Het perspectief van ongedocumenteerden vrouwen.

Presentations at (inter)national conferences

Perspectives on cancer screening participation in a highly urbanised region: a Q-methodology study in The Hague, the Netherlands. *NAPCRG Annual Meeting 2023, San Francisco, United States of America (poster presentation)*

Perceptions and beliefs of general practitioners in the cancer screening programmes in The Netherlands: a mixed-methods study. *Ca-PRI conference, 2023, Oxford, United Kingdom (oral presentation)*

Cancer screening participation within a highly urbanised region in the Netherlands: comparing the breast and colorectal cancer screening programmes of The Hague. *Ca-PRI conference, 2023, Oxford, United Kingdom (oral presentation)*

Perspectives on cancer screening participation in a highly urbanised region: a Q-methodology study in The Hague, the Netherlands. *Ca-PRI conference, 2023, Oxford, United Kingdom (poster presentation)*

Screening baarmoederhalskanker onder gemarginaliseerde vrouwen: Nog veel winst te behalen! *LOVAH wetenschapsdag, 2022, Utrecht, the Netherlands (oral presentation)*

Nominated for the *SBOH Academiseringsprijs 2022* (top 3, national)

Opvattingen over deelname aan de oncologische bevolkingsonderzoeken: een online Q-studie. *NHG-wetenschapsdag, 2022, The Hague, the Netherlands (oral presentation)*

Cervical cancer screening among marginalised women: Lessons learned from a pilot study in the Netherlands. *Ca-PRI conference, 2020, Oxford, United Kingdom (oral presentation) (cancelled due to the Covid-19 pandemic)*

Optimalisatie van de bevolkingsonderzoeken in Den Haag: een Population Health Management benadering. *NHG-wetenschapsdag, 2019, Nijmegen, the Netherlands (oral presentation)*

Identifying determinants of (non-)attendance at cancer screening programs. *NAPCRG Annual Meeting 2018, Chicago, United States of America (poster presentation)*

Differentiële opkomst in de landelijke kankerscreening programma's. *NHG-wetenschapsdag, 2018, Amsterdam, the Netherlands (oral presentation)*

Overview of attendance and differences at the national cancer screening programmes in the Netherlands. *Ca-PRI conference, 2018, Groningen, the Netherlands (oral presentation)*

Overview of teaching activities

Teacher: Festina Lente zorg, 2021 – 2024 *(training for nurses with a focus on oncology)*

Guest lecturer: Panel Mangement, 2023 (*Population Health Management, master students, Leiden University)*

Guest lecturer platform kwalitatief onderzoek: Workshop Q-methodology, 2022 (*Leiden University Medical Center)*

Master thesis supervision Wietske Wesseling (medical student), 2021. Thesis title: *Kennis over en interesse in screening op baarmoederhalskanker onder ongedocumenteerde vrouwen in Nederland.*

Teacher: Lijn Samenwerking, Gezondheidsbevordering en Leiderschap jaar *(Medicine, third year students, Leiden University Medical Center)*

Guest lecturer: Non-communicable diseases. Cancer and Cancer Screening, 2018 – 2022. *(Leiden University College, bachelor students)*

Master thesis supervision Roosje Basri (medical student), 2018. Thesis title: *Deelname verschillen en context bij het bevolkingsonderzoek naar baarmoederhalskanker in Den Haag.*

Teacher: Start tot Arts, 2018 – 2019 *(Medicine, first year students, Leiden University Medical Center)*

Overview of graduate training activities and courses

Basic Course Regulations and Organization for Clinical Researchers recertification (BROK), 2022 *(Nederlandse Federatie van Universitair Medische Centra, Utrecht, the Netherlands)*

Q-Methodology, 2021 *(Erasmus School of Health Policy & Management, Rotterdam, the Netherlands)*

Clinical Epidemiology, 2018 *(Leiden University Medical Center, Leiden, the Netherlands)*

Werkconferenties LUMC/Health Campus Den Haag 2018 – 2022 *(Health Campus The Hague, The Hague, the Netherlands)*

Interfacultair Overleg Huisartsgeneeskunde, 2018 *(Leusden, the Netherlands)*

Open iterview & qualitative data for PhD's, 2018 *(Graduate School LUMC, Leiden, the Netherlands)*

Population Health Management: Fundamentels, 2018 *(Health Campus The Hague, The Hague, the Netherlands)*

Population Health Management: Advanced Panel Management in Health Care, 2018 *(Health Campus The Hague, The Hague, the Netherlands)*

Population Health Management: Risk Stratification, 2018 *(Health Campus The Hague, The Hague, the Netherlands)*

Speed Reading, 2018 *(Graduate School LUMC, Leiden, the Netherlands)*

Population Health Management: Advanced Governance and Health Economics, 2018 *(Health Campus The Hague, The Hague, the Netherlands)*

Medical Business Projects Rotterdam, project: Thuis Hemodialyse, 2018 *(Department of Nephrology, Maasstad Ziekenhuis, Rotterdam, the Netherlands)*

Basic Course Regulations and Organization for Clinical Researchers (BROK), 2018 *(Nederlandse Federatie van Universitair Medische Centra, Utrecht, the Netherlands)*

Basic Methods and Reasoning in Biostatistics, 2018 *(Graduate School LUMC, Leiden, the Netherlands)*

Population Health Management: Governance, 2017 *(Health Campus The Hague, The Hague, the Netherlands)*

Population Health Management: Responsible Data Analysis, 2017 *(Health Campus The Hague, the Netherlands)*

Epidemiology: An Introduction, 2017 *(Leiden University Medical Center, Leiden, the Netherlands)*

PhD Introductory Meeting (including the workshop Scientific Conduct for PhDs), 2017 *(Graduate School LUMC, Leiden, the Netherlands)*