Thea Beate Brevik

Ph.d.-avhandlinger i helse- og sosialfag 2022:4

Educational interventions on breast and cervical cancer screening

Educational interventions on breast and cervical cancer screening

Thea Beate Brevik

En avhandling levert til Høgskolen i Molde - Vitenskapelig høgskole i logistikk og Høgskulen i Volda for graden Philosophiae Doctor (ph.d.)

Ph.d.-avhandlinger i helse- og sosialfag 2022:4

Høgskolen i Molde - Vitenskapelig høgskole i logistikk og Høgskulen i Volda

Molde 2022

Thea Beate Brevik

Educational interventions on breast and cervical cancer screening.

2022

Ph.d.-avhandlinger i helse- og sosialfag 2022:4

Høgskolen i Molde - Vitenskapelig høgskole i logistikk og Høgskulen i Volda
Postboks 2110
6402 Molde,
www.himolde.no

Postboks 500,
6101 Volda
www.hivolda.no

Avhandlingen kan bestilles fra bibliotekene ved Høgskolen i Molde eller Høgskulen i Volda

biblioteket@himolde.no

skranke@hivolda.no

Trykking: Høgskolen i Molde

ISBN: 978-82-7962-319-9

ISSN:2535-2822

Contents

Acknowledgement

The present work was carried out at the Faculty of Health Sciences and Social Care at Molde University College. I have also received funding from the Research and Development Unit at Møre and Romsdal Hospital Trust and from the Norwegian Research School of Global Health at NTNU. I would like to thank the organizations for the funding and for their support.

I have been privileged to have Professor Stål Bjørkly as my principal supervisor and Professor Petter Laake and Dr. Ameli Tropé as my co-supervisors. It has been an honor to learn from and work with these excellent supervisors. I am inspired and truly impressed by their immense knowledge in their research fields and their unstinting willingness to share their knowledge, experience, and network with others.

I want to thank the International Agency for Research on Cancer (IARC) for hosting me as a PhD fellow for one year. I am deeply grateful to Dr. Partha Basu and his colleagues at the Early Detection, Prevention, and Infection Branch for their enthusiastic involvement in my project and for including me in their important projects on cancer screening. I would like to express my sincere gratitude to Dr. André Carvalho for being a brilliant supervisor. I am truly impressed by his expertise, dedication, and engagement. I would like to offer my special thanks to Isabel Mosquera Metcalfe, Li Zhang, Lara Calegari, and Adam Todd for all their insightful comments and suggestions. There is no doubt that their knowledge, ideas, and constructive (and critical) comments have increased the quality of this work. I would like to extend my sincere thanks to IARC's Education and Training Program and the Summer School for offering brilliant training courses.

I would also like to thank my colleagues at Molde University College and at Molde Hospital for unwavering support and encouragement. I would like to offer my special thanks to Professor Knut-Willy Sæther for our discussions on religious barriers -- which led to a paper on taking religious fatalism seriously in cancer screening education. A special thanks to my fellow PhD students for all the fruitful discussions.

Finally, I can honestly say that no one has been more important to me than my husband. I am forever grateful for his remarkable optimism, encouragement, and patience.

Abbreviations

CIN	Cervical Intraepithelial Neoplasia
CI	Confidence Interval
EU	European Union
FE	Fixed Effect
HBM	Health Belief Model
HIC	High-Income Country
HPSR	Health Policy and Service Research
HPV	Human Papillomavirus
IARC	International Agency for Research on Cancer
I^2	I square
κ	Cohen's Kappa coefficient
LMIC	Low- and Middle-Income Country
PAHO	Pan American Health Organization
Pap test	Papanicolaou Test
PICO	Population, Intervention, Comparator, and Outcomes
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-analysis
RCT	Randomized Controlled Trials
RD	Risk Difference
RE	Random Effect
RoB	Risk of Bias
RR	Risk Ratio
USA	United States of America
VIA	Visual Inspection after Application of Acetic Acid
WHO	World Health Organization

Key definitions

Key definitions on cancer screening

Cancer

Cancer is a generic term for a large group of diseases that can affect any part of the body (1). One defining feature of cancer is the rapid creation of abnormal cells that grow beyond their usual boundaries and that can then invade adjoining parts of the body and spread to other organs (metastasis) (1). *Pre-cancer* is a condition that may, or is likely to, become cancer (2).

Cancer screening

Screening means examining asymptomatic individuals for findings that are suggestive of a specific cancer or pre-cancer (1). When abnormalities are identified during screening, further diagnostic tests follow and eventually treatment if needed (1).

Screening program

Cancer screening programs are screening performed in the framework of a publicly mandated program. To be considered a *program* there must be a commitment from the government to provide the screening services to the eligible population as defined by laws, statutes, regulations, or official notifications (3). The screening programs must define the eligible population, the screening test, and the screening interval (3).

Screening participation rate

Screening participation rate is a quality indicator in screening programs (3) and is measured as:

$$\frac{\text{Number of individuals screened out of the invited}}{\text{Number of indivduals invited}} \times 100$$

Test sensitivity and specificity

The *test sensitivity* describes how well a test can detect a specific disease in people who actually have the disease (true positive) (2). *Specificity* refers to the percentage of people who test negative for a specific disease among a group of people who do not have the disease (true negative) (2).

Key definition on inequality

High-, middle-, and low-income countries

The World Bank assigns the world's economies to four income groups based on the gross national income per capita in current United States dollars ($) (4). In 2020, countries were divided into the following four groups: low income (less than $1,046), lower-middle income ($1,046 - 4,095), upper-middle income ($4,096 - 12,695), and high income (more than $12,695).

Health inequality

Health inequality is the generic term used to designate differences, variations, and disparities in the health achievements of individuals and groups (5). The term *health inequality* is very closely aligned with *health disparities* (5), which are not simply differences between groups, but rather differences that are avoidable, unfair, unjust, and result from systemic and potentially remediable differences in one or more aspects of health across socially, demographically, or geographically defined populations or population subgroups (6). Broadly defined, health disparities may be evident in any group of people who systematically experience social and/or economic obstacles to health and healthcare (6).

Cancer inequality

Cancer inequalities are the systematic differences in cancer outcomes (for example, in cancer incidence, mortality, and survival) that exist between and within countries (5-6). Cancer inequalities between countries may be due to a combination of individual and contextual factors, such as culture, geography, politics, policies, societal structure, and economic structure (6). Disparities in cancer outcomes are largely linked to ethnicity and race, socioeconomic status, disability, sexuality, and geographical differences in availability of and access to high-quality care (5-6).

Disadvantaged population

Cancer disproportionately affects the most disadvantaged individuals and groups (5-6). *Disadvantaged populations* include any situation in which a population is in a lower position than others in terms of gender/sex, race/ethnicity, education, occupation, socioeconomic status, place of residence, and personal characteristics associated with discrimination (7).

Socioeconomic position

Socioeconomic position reflects a complex set of social and economic factors, often imperfectly correlated with one another. Socioeconomic position is usually measured by the level of educational attainment, the household income, the occupational classification, and sometimes by the home residence (6).

Ethnicity and race

Terms related to race and ethnicity are often used interchangeably, without clear and unified definitions. The National Institute of Cancer uses the following definitions: *Ethnic group* is defined as a group of people who share a similar culture (beliefs, values, and behaviors), language, religion, ancestry, or other characteristics that are often handed down from one generation to the next (2). The group members may come from the same country or live together in the same area. Examples of ethnic groups include Hispanics and Han Chinese (2). *Race* is used to describe a group of people who share similar biological, physical, or genetic characteristics, such as skin, hair, and facial features (2). Examples of races include Blacks and Caucasians (2). In cancer outcomes, residual disparities by race and ethnicity remain after adjustment for socioeconomic status (6). In this PhD thesis, I have used only the same terms describing race that were used in the source material being referred to.

List of articles

Article 1

Brevik, Thea Beate; Laake, Petter & Bjørkly, Stål (2020). Effect of culturally tailored education on attendance at mammography and the Papanicolaou test. Health Services Research. ISSN 0017-9124. 55(3), s. 457–468. Doi: 10.1111/1475-6773.13271.

Article 2

Brevik, Thea Beate; Trope, Ameli; Laake, Petter & Bjørkly, Stål (2021). Does women's screening history have any impact on mammography screening attendance after tailored education? A systematic review and meta-analysis. Medical Care. ISSN 0025-7079. 59(10), s. 893–900. Doi: 10.1097/MLR.0000000000001576.

Article 3

Brevik, Thea Beate; Calegari, Lara; Mosquera, Isabel Metcalfe; Laake, Petter; Maza, Mauricio; Basu, Partha; Todd, Adam; Carvalho, Andre (2022). Training health providers to administer visual inspection after application of acetic acid (VIA) as a screening test for cervical cancer: A systematic review of essential training components. Submitted to the International Journal of Gynecology and Obstetrics.

Summary

One of the most important aspects of cancer screening from a health system perspective is the substantial inequality in screening access and participation -- between continents, countries, and social groups of society. Women's opportunities to participate in breast and cervical screenings are not equally distributed. In this PhD project, we aimed to explore educational interventions on breast and cervical cancer screening. Most HICs offer breast and cervical cancer screening services, but ethnic minority women have low participation rates and are defined as a disadvantaged group requiring special attention. Although tailored educational interventions are considered a key approach to increasing the screening participation of these women, the effectiveness of these interventions remains unknown. In most LMICs, cervical cancer screening services are offered, but these services are only available for certain women. Educational interventions hold a key position in enhancing cervical cancer screening access and participation in LMICs because the screening programs depend on high quality training of health providers. However, it remains unknown to what extent health providers are trained or how well the training guidelines are adhered to.

The objectives of this PhD project were to

1) determine the effectiveness of culturally tailored educational interventions on screening attendance at mammography and the Pap tests among ethnic minority women;
2) explore whether women's screening histories impact screening attendance after tailored education;
3) and examine essential training components in cervical cancer screening programs implemented in low-resource settings.

In our first study, we conducted a systematic review, searching for articles published in five databases from inception to 2018. Randomized controlled trials (RCT) of culturally tailored educational interventions for ethnic minority women in Western countries were investigated for a meta-analysis. RCTs that assessed attendance at mammography or the Papanicolaou test (Pap test) were eligible for inclusion. Study characteristics and results were extracted separately by two reviewers, and independent raters assessed risk of bias by using Cochrane Collaboration's tool. Data were combined in a meta-analysis by using random effects models,

and heterogeneity was estimated by using I^2-statitics. We identified seven RCTs (N = 4,246 women) eligible for inclusion on mammography attendance, and four RCTs (N = 1,750 women) on Pap test attendance. The effect of culturally tailored educational interventions on attendance at mammography was an increase of 18% (RR = 1.18, 95% CI, 1.09-1.28, p < 0.001), with low heterogeneity (I^2 = 30.0, p = 0.237), and a 54% increase at Pap test (RR = 1.54, 95% CI, 1.14-2.09, p = 0.005), with substantial heterogeneity (I^2 = 75.9%, p = 0.001). We found that culturally tailored educational interventions may increase attendance of ethnic minority women at breast and cervical cancer screenings. These results must be interpreted within the limitations set by the low number of studies and substantial heterogeneity for the Pap test.

In our second study, we conducted a systematic review, searching for articles published in five databases from inception to 2020. RCTs of educational interventions tailored to ethnic minority women that measured screening attendance were eligible for inclusion. Data extraction and risk of bias assessment were performed independently by two reviewers. Data were combined in a meta-analysis by using random effects models and heterogeneity was estimated by using I^2-statitics. We identified six studies (N = 3,521 women) eligible for inclusion on mammography attendance. Tailored education increased attendance at mammography by 54% among never-screened women (RR = 1.54, 95% CI, 1.24-1.91, p < 0.001), with low heterogeneity (I^2 = 27.1%, p = 0.231), and by 26% among ever-screened women (RR = 1.26, 95% CI, 1.11-1.43, p < 0.001), with low heterogeneity (I^2 = 35.5%, p = 0.213). Although these findings must be interpreted with caution, the findings suggested that women's screening history is an important and ignored variable that affects how effective tailored education is on screening attendance.

In our third study, we conducted a systematic review, searching for articles published in PubMed, Embase, and Web of Science between the years 2006 and 2021. Studies on cervical cancer screening that used VIA and that trained health providers with any level of health education were included. The outcome of interest was the reporting of the training components. We performed a narrative synthesis of the included studies. We developed a framework to conceptualize seven essential training components and applied that framework to determine how training courses had been carried out in different settings. We identified 14 primary studies eligible for inclusion, including 2,847 trained health providers and 406,611 screened women. We found that most training courses lasted 5 to 7 days and included

theoretical education, practical skill development, and competence assessment. It was unclear how visual aids and training in client counselling and quality assessment were integrated in the courses. Extended on-job training was provided through supervision, feedback, and refresher training. This study showed that international training recommendations are feasible to implement in real settings. By providing illustrating examples, we showed how the training components had been carried out in different clinical settings. These examples can be helpful for clinicians and stakeholders who want to implement or scale up a cervical screening program.

The results of this PhD thesis contribute to a better understanding of educational interventions on cancer breast and cervical cancer screening. Our results, combined with findings from other studies, suggest that tailored educational interventions can be considered for further implementation in clinical practice. Defining evidence-based interventions is a necessary first step in the implementation of effective strategies in the healthcare system. Evidence-based healthcare can provide access to core and higher-quality information on what works, resulting in a higher likelihood of successful programs being implemented, more efficient use of resources, and reduced health inequality. Further knowledge is needed about how tailored educational interventions can be systematically and successfully implemented into healthcare services. By applying the principles of implementation science, tailored educational interventions can move from research to practice.

1 Introduction

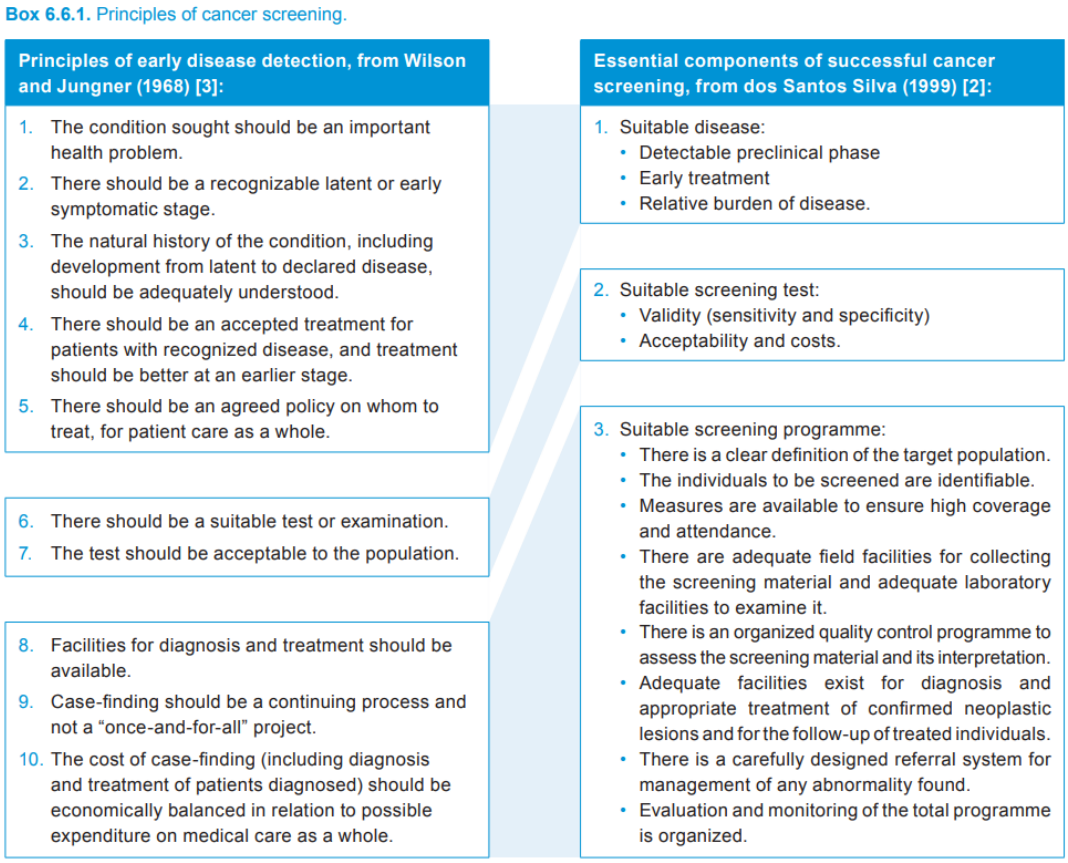
1.1 Principles of cancer screening

Cancer is a leading cause of death worldwide, ranking as the first or second leading cause of death in 134 of 183 countries and as third or fourth in an additional 45 countries (6). Between 30% and 50% of all cancers can currently be prevented by avoiding risk factors and implementing existing evidence-based prevention strategies (1). The cancer burden can also be reduced through early detection and appropriate treatment and care of patients who develop cancer (1). Early detection of cancer is achievable either by earlier diagnosis in symptomatic patients or, for some cancers, by systematic screening of asymptomatic individuals (6). Cancer screening aims to identify individuals with findings suggestive of a specific cancer or precancer before they have developed symptoms (1). When abnormalities are identified during screening, further diagnostic tests follow and, if needed, referral for treatment (1). The primary objective of cancer screening is reduction of mortality (6).

Organized cancer screening is a health service performed in the framework of a publicly mandated program (3). To be considered a *program*, there has to be a commitment from the government to provide the screening services to the eligible population as defined by laws, statutes, regulations, or official notifications (3). In such cases, the eligible population, the screening test, and the screening interval must be defined and mechanisms for monitoring and supervision should be implemented (3). Figure 1 summarizes the principles of early detection and the essential components of successful cancer screening (6). After decades of research and development, only screening programs for cervical cancer, breast cancer, and colorectal cancer have been successfully implemented and evaluated (6).

Figure 1

Principles of Cancer Screening (6)



The two main types of cancer screening programs are population-based screening programs and opportunistic screening programs -- although the definitions of these are not consistent across studies (6). A *population-based screening program* is designed and managed at a central level to reach most of the population at risk according to a national screening policy (3). Population-based screening may be implemented nationwide (preferably) or regionally and is expected to be highly organized, with mechanisms to identify the eligible individuals and to send personal invitations to attend screening (3). Screening activities outside of a population-based screening program are known as *opportunistic screening*. Opportunistic screening settings can present different levels of organization and coordination, but an important aspect of them is that the participation will rely on self-referral or recommendations from health providers (3). In general, population-based screening programs are preferred over opportunistic screening because of increased coverage, improved cost–effectiveness, and improved equity (6). Screening participation and coverage rates are essential quality and performance indicators for screening programs, and from a health system perspective, it is

important to monitor these indicators to identify trends and potential needs for strategic interventions (3). According to the World Cancer Report, achieving relatively high screening coverage and participation rates will reduce health inequality (6).

1.1.1 Inequalities in cancer screening

One of the most important aspects of cancer screening from a health system perspective is the substantial inequality in screening access and participation -- between continents, countries, and social groups of society. Screening programs are in general far more complex and resource-intensive than early diagnosis approaches (1). Certain quality assurance guidelines propose more than 40 quality indicators per screening program, which illustrates why the standard of cancer screening programs are difficult to meet in most low- and middle-income countries (LMICs) (6). For instance, screening programs depend on highly trained health personnel, who are limited in many LMICs. Overall, sub-Saharan Africa has a very low physician-to-population ratio of about 18 per 100,000, compared with the ratios of India (60 per 100,000), Brazil (170 per 100,000), and France (370 per 100,000) (6). Additionally, screening service itself is extremely resource demanding. In Europe, the 55 million screening tests used per year costed alone more than €500 million per year (6). This illustrates why the many triumphs in cancer prevention, early diagnosis, and screening in recent decades have occurred predominantly in high-income countries (HICs), where health systems' infrastructure and capacity are well established (5-6).

Disparities in cancer outcomes are attributable to an opportunistic model of access to cancer prevention and early detection, which poorly serves both advantaged and disadvantaged groups (6). Organized population-based screening programs are more effective in reducing health inequality, especially differences in survival in a target population (6). European studies have shown an inverse relationship between screening coverage and cervical cancer incidence and mortality (6). However, this relationship is less clear in regions without population-based screening, such as Latin America, where screening coverage has increased but recall attendance after positive screening results remains low (6). Barriers preventing implementation of cancer screening programs include lack of infrastructure, inadequate training and expertise, inequitable distribution of services in urban versus rural areas, and poverty (8). Sociocultural influences, such as use of traditional medicines, can also work against the development of population-based cancer screening programs (8).

Low screening participation among certain social groups contributes to the lack of mortality reduction in LMICs and to the higher mortality in socially disadvantaged populations in HICs (6). Data on trends in cancer mortality and cancer screening participation generally show more favorable trends among people with higher socioeconomic positions, both in HICs and in LMICs (5-6). These differential trends can be explained by the fact that individuals with higher socioeconomic positions tend to benefit more from cancer prevention interventions and to have earlier detection and better treatment (6). All this is because privileged individuals have better access to healthcare services, greater health literacy, fewer financial barriers to healthcare, and lower severity of co-morbidities compared with individuals from lower socioeconomic strata (5-6).

Low education, low income, being uninsured, and living in rural versus urban areas are all factors associated with lower levels of participation at screening (6;8;9). For example, women in the USA with incomes of less than 139% of the federal poverty level were less likely to have had a recent mammogram or Pap test, compared with women with incomes above 400% of the federal poverty level (6). Insured women were found to be more than twice as likely to undergo mammography screening than those uninsured (55% vs. 22%) (6). Women living in rural areas have the lowest screening rates, both in HICs and LMICs (6;8). In Argentina, the cervical cancer mortality rate was four times higher in the province of Jujuy (15/100,000) than in the city of Buenos Aires (4/100,000) (10). In China, the higher cancer mortality seen in rural areas compared with urban areas has been explained by a lack of awareness among rural residents about cancer prevention and a lower willingness to participate in cancer screening programs, even if the screening is provided free of charge (6). A meta-analysis of 28 studies found the same tendency: Screening participation was higher among the urban population than in the rural population in Australia, the USA, and Canada (8).

Ethnic and racial minorities are defined by the World Health Organization (WHO) as a disadvantaged group in cancer screening (6). Although there can be a substantial overlap between inequalities related to socioeconomic status verses race or ethnicity, there are generally residual disparities by race and ethnicity even after controlling for socioeconomic status (6). In addition to socioeconomic barriers, ethnic minority women can face additional barriers to cancer screening. A systematic review of 180 studies on breast and cervical cancer screening among immigrant women in the USA identified a variety of barriers to screening at the personal and system levels (11). Lack of knowledge, low health literacy, and limited

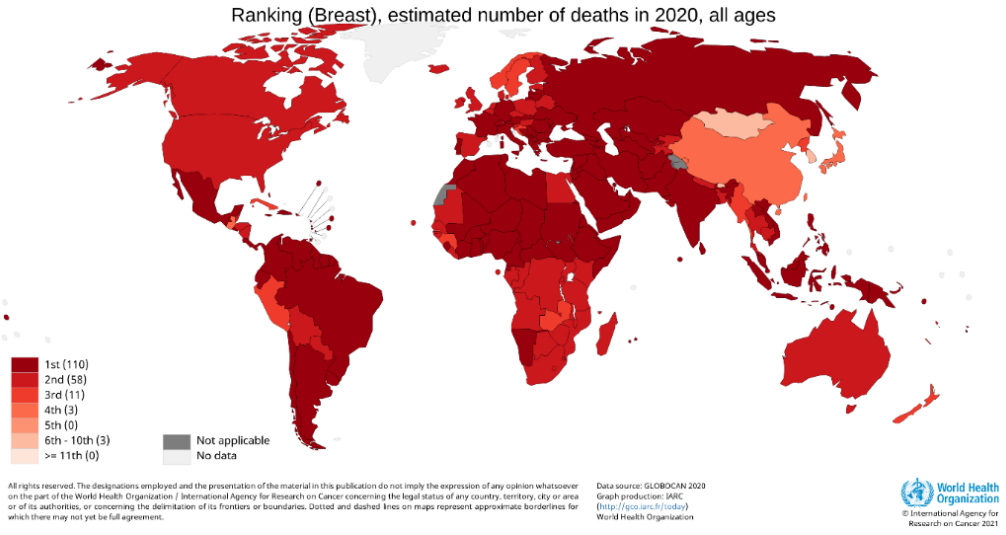
language proficiency were found to correspond to lower attendance at screening (6;8;11). One of the most prevalent system barriers to cancer screening is the lack of translation or interpreter services in healthcare systems (11). Moreover, cultural and religious understandings can influence women's decisions on attending screening (8;11). For instance, fatalism has for decades been identified as a barrier to cancer screening attendance (12). A systematic review of 11 studies on the relevance of fatalism among Latinas (in Mexico and in the USA) found that 64% of the women reported a statistically significant association between fatalism and non-use of cancer screening services (13). Due to some religious and cultural beliefs, immigrants have reported being embarrassed by the idea of discussing or exposing their private body parts during a medical consultation, especially if examined by a male physician. Some immigrant populations have also expressed mistrust in healthcare systems, governmental institutions, or research (11).

1.2 Breast cancer screening

Breast cancer is the most diagnosed cancer in women and a leading cause of cancer death in women globally (6). In 2020, there were an estimated 2.2 million new cases of breast cancer and 685,000 deaths from breast cancer worldwide (14). Breast cancer ranks as the leading cause of cancer death in 110 countries (14) (Figure 2). Breast cancer in men is a very rare disease, with incidence rates of about 1% of those for women (8). Male breast cancer is not considered further in this thesis.

Figure 2

Breast Cancer Deaths Worldwide in 2020 (14)



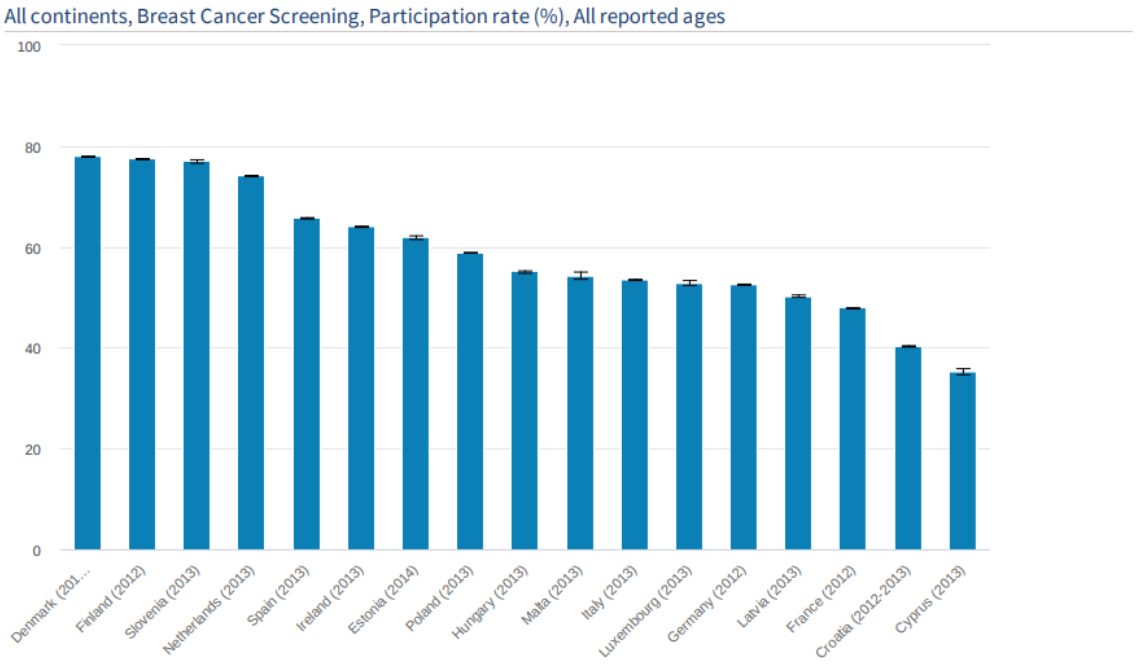
The factors found to decrease the risk of breast cancer include late age at menarche, early age at menopause, parity, early age at first birth, and breastfeeding (6). Established risk factors for developing breast cancer are family history of breast cancer, personal history of proliferative benign breast disease, dense breasts on mammogram, radiation exposure, alcohol consumption, low physical activity, being thin before menopause, postmenopausal obesity, recent use of postmenopausal hormone therapy, inherited mutations in breast cancer predisposition genes, and use of oral contraceptives (6). The rising incidence rates observed in many HICs during the past five decades -- and in LMICs more recently -- can be attributed partly to the changing prevalence and distribution of several reproductive and hormonal factors, such as lower parity, earlier ages at menarche, and later ages at first birth (6).

Breast cancer screening programs aim to detect breast cancer at an early stage when treatment is more likely to succeed. The observed improvements in breast cancer mortality are most likely due to a combination of detection of early-stage disease through screening and improved treatment (6). Breast cancer screening using mammography is generally offered to women between 50 and 69 years of age every 1 to 3 years (6). A mammogram is formed by recording the two-dimensional pattern of X-rays transmitted through the volume of the breast onto an image receptor (8). Breast cancer is detected radiographically on the basis of four major signs: a mass density with specific shape and border characteristics, microcalcifications, architectural distortions, and asymmetries between the radiological appearance of the left and right breast (8). These signs are often very subtle, and for them to be detected accurately and when a cancer is at the smallest detectable size, the technical image quality of the mammograms must be excellent (8). In practice, less than one third of the breast cancers detected by mammography screening would also be detectable by clinical examination (8). Women with abnormal findings on a screening mammogram must be referred for further assessment. Triple assessment (comprising clinical examination, imaging, and tissue sampling) is an approach that is cost-effective, easy to perform, and time-saving, but is only achievable in high-resource settings with excellent diagnostic imaging facilities and pathology services (8). In low-resource settings, a stepwise approach according to level of resources and health system capacity is recommended, shifting the focus from breast self-examination to clinical breast examination, and from hospital-based mammography screening to population-based programs (6).

Breast cancer screening programs are available and have been established for a long time in many HICs (8). In Canada, breast cancer screening is delivered mostly through organized programs, with a 70% participation rate among the target population (8). In the USA, screening is mostly opportunistic (8). In Europe, participation rates in organized programs vary from just under 20% in Poland to nearly 90% in specific regions of Spain, with an average across Europe of about 50% (8) (Figure 3). It is unknown how many women are screened opportunistically (8). Although Japan was the first country to introduce a national screening program with clinical breast examination in 1987, and later also included mammography, organized screening remains insufficient in Japan (8). The overall organization and availability of breast cancer screening programs influences which citizens will attend screening. For example, affluent women are generally more likely to participate in breast cancer screening, whereas ethnic minority status women, particularly immigrants, are likely to decrease the overall participation in breast cancer screening programs (8).

Figure 3

Breast Cancer Screening Participation Rates (15)



Data source: CanScreen5
Map production: IARC
World Health Organization

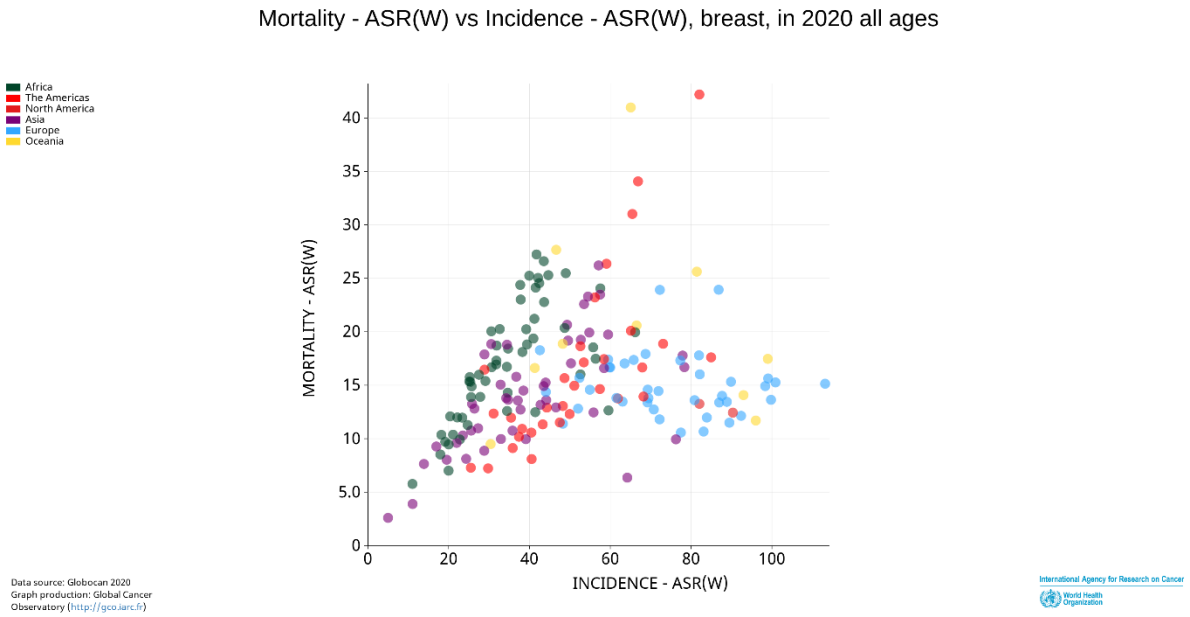
The balance of potential benefits against potential harm in breast cancer screening has been regularly debated over the past decades, especially regarding questions about overdiagnoses and mortality reduction being caused by screening or by better treatment (8). A thorough discussion of these questions is outside the scope of this thesis, but ethical consideration about how educational interventions provide balanced information on screening is discussed in section 5.4 Ethical considerations. The International Agency for Research on Cancer (IARC) and other international institutions have considered the benefits of mammographic screening to outweigh the harm, and mammographic screening is thus recommended as a secondary preventive intervention (8).

1.2.1 Inequalities in breast cancer screening

Significant disparities exist in breast cancer awareness, detection, treatment, and survival -- between HICs and LMICs, between urban and rural populations, and between different ethnicities within countries (5). Lack of breast cancer awareness, poor availability of and access to public health services, and low participation in mammography screening programs all lead to delays in diagnosis and treatment, which are responsible for the late-stage diagnoses and poor outcomes (5). Substantial regional variations in breast cancer mortality exist (14) (see Figure 4). In HICs such as Australia, the Republic of Korea, and the USA, an average of 9 out of 10 women diagnosed with breast cancer survive the disease, while in parts of Africa and India, the proportion is closer to 1 in 2 (16). In Australia, Canada, and the USA, the mortality of breast cancer has declined by 20% from 2002 to 2012 (6). In Europe, the survival rates have increased, but vary as much as 20%, with eastern Europe having lower survival rates than the rest of the continent (16). More than half of all breast cancer cases are now diagnosed in LMICs, where a greater proportion of cases are diagnosed at later stages, which is linked to poorer survival (5-6). Among the regions with the highest breast cancer mortality rates worldwide are the Pacific Islands (Fiji), the Caribbean (the Bahamas), sub-Saharan Africa (Nigeria), and southern Asia (Pakistan) (14).

Figure 4

Mortality Versus Incidence of Breast Cancer in Different Continents (14)



Racial differences in breast cancer incidence and mortality are evident, and it has become increasingly clear that differences in the distribution of both individual risk factors and societal and contextual factors, as well as tumor biology, all contribute to this variation (5-6). For example, African American women had a lower age-adjusted incidence rate for breast cancer than non-Hispanic White women (123/100,000 vs. 128/100,000, respectively), but higher age-adjusted mortality (31/100,000 vs. 22/100,000) (6). This finding reflects substantially different survival rates (90% vs. 77% at 5 years and 84% vs. 68% at 10 years, respectively) (8). Moreover, African American women had a higher prevalence of triple-negative breast cancers, for which outcomes are poorer, and this is a likely contributor to the higher mortality rates (6). Nevertheless, even among the subset of women diagnosed with similar early-stage disease, mortality rates were higher for African American women, indicating that other factors, such as differences in patterns of care, contribute as well (6). In Europe, immigrant women have been found to be more often diagnosed with late-stage breast cancer than other women (17-18). In Norway, the outcome after a breast cancer diagnosis was significantly worse for women from Pakistan, Sri Lanka, and Somalia than for ethnic Norwegian women (17).

Ethnic background itself is not an independent predictor of attendance in mammography screening, but differences in participation have been found between ethnic groups (8).

A systematic review and meta-analysis of mammography screening attendance (covering 42,000,000 observations of opportunities for screening attendance in 10 countries across three continents) showed that immigrant and minority women, however defined, attended mammographic screening less often than other women (19). Overall, immigrant and minority women had lower attendance rates than the rest of the population, with an odds ratio of 0.64 (19). Immigrants had lower attendance rates than other women in Australia, Canada, Denmark, the Netherlands, Sweden, Switzerland, and the USA (64% vs. 81%) (19). In general, non-Western immigrants appeared to have lower screening attendance than other immigrants (19). The included papers reported lower attendance rates for minority women than for non-minority women (43% vs. 53%) (19). In England, South Asian women had lower attendance rates than other women. In Scotland, women with backgrounds from India, Pakistan, Africa, and other South Asian countries had the lowest attendance rates (19). In the USA, several papers reported lower attendance among ethnic minority women than among non-Hispanic Whites (19).

Barriers reported among ethnic minority women that are specifically related to breast cancer screening and that act in addition to the barriers mentioned for cancer screening in general are often bodily related. A meta-synthesis of 21 studies that included 1,000 women found that women, especially in Islamic and developing countries, mentioned embarrassment as a reason for not attending mammographic screening and did so more frequently when the examiner was male (20). In discussions about why male examiners were undesirable, several Pakistani women in Norway explained that they were uncomfortable undressing in front of, or being touched by, men at the screening center (21). "*It's a bit like, women who never see men they don't already know. And then seeing a man, especially of another race -- that would be a crisis. It's just a no-go*" (21). In some cases, this was linked to previous, self-experienced, and upsetting incidents with male examiners (21). A qualitative study of 55 low-income urban Black women in the USA found that some women thought that bruises from domestic violence could later turn into lumps and cancer, and therefore screen-positive results of screening could disclose an abusive home situation (22). "*Sometimes I think like in black women, most black women are be abused and kicked and beaten in the chest and sometimes a bruise can cause cancer... You can hit a person too hard and they never go about seeing about it or reporting it or nothing*" (22). For some women, only a husband should touch a women's breast, and, therefore, a husband's permission would be required to attend screening (23). Some women feared social consequences of potentially losing a breast to a screen-

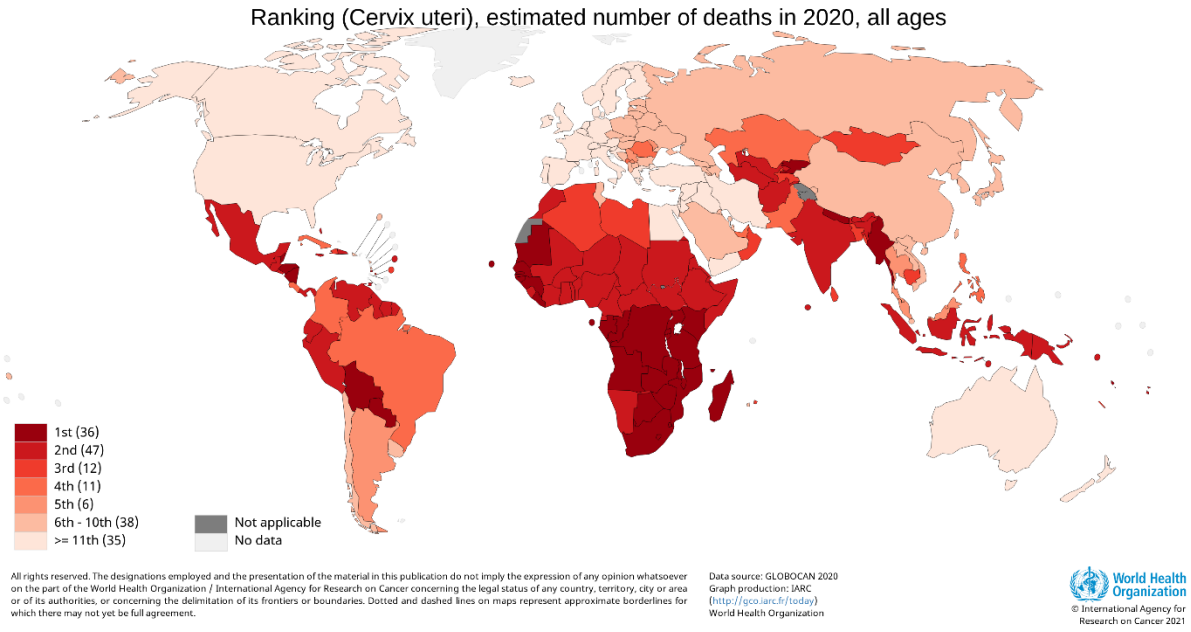
positive result (8). A systematic review of factors contributing to late presentation of breast cancer among African women found that the most important drivers were the following: negative symptom interpretation (unserious, absence of pain, and ignorance), fear (related to cancer, surgery, embarrassment, divorce, and death), belief in alternative medicine (local and foreign therapies), social relations and networks (social influence and social control), lack of trust and confidence in orthodox medicine, and access to healthcare (physical access and economic access) (24).

1.3 Cervical cancer screening

Cervical cancer is cancer of the cervix -- the lower, narrow end of the uterus that forms a canal between the uterus and vagina (2). Cervical cancer is a leading cause of mortality among women worldwide (6). In 2020, an estimated 604,000 women were diagnosed with cervical cancer worldwide, and about 341,000 women died from the disease (24). Cervical cancer is the leading cause of cancer death in 36 countries, most of these countries being located in sub-Saharan Africa, Melanesia, South America, and South-Eastern Asia (14) (Figure 5).

Figure 5

Cervical Cancer Deaths Worldwide in 2020 (14)



Human papillomavirus (HPV) transmits through sexual intercourse and is estimated to cause all cases of cervical cancer -- notably HPV types 16, 18, 31, and 45 (6). Known co-factors associated with disease progression include infection with HIV and other immunosuppressive conditions, smoking, multiparity, and long-term use of oral contraceptives (6). To prevent cervical cancer, women can be screened using various tests to identify those who have or are at risk of cervical pre-cancer (25). Cervical intraepithelial neoplasia (CIN) is characterized by cellular changes in the transformation zone of the cervix (25). CIN1 lesions -- also referred to as low-grade squamous intraepithelial lesions -- are morphological correlates of HPV infections (25). CIN2/3 lesions -- also referred to as high-grade squamous intraepithelial lesions -- are correlates of cervical pre-cancers that, if left untreated, may progress into cervical cancer (25).

Organized cervical cancer screening is available and established in many HICs (15). Screening with treatment of pre-cancerous lesions is among the few cancer-related "best buys" or "very cost-effective strategies" according to WHO's *Global Action Plan for the Prevention and Control of Noncommunicable Diseases* (26). The traditional method used in cervical cancer screening has been cytology, offered every 1 to 3 years to women from between 20 and 30 years to women between 60 and 70 years of age (6). The test is known as the Papanicolaou test, or Pap smear, or smear test, and is used to gently scrape cells from the cervix to examine for abnormal growth (25). When cytology results are positive, the diagnosis is confirmed by colposcopy, and appropriate treatment is informed by biopsy of suspicious lesions for histological diagnosis (25). In countries with effective cytology-based cervical cancer screening and treatment programs, the mortality from cervical cancer has been reduced fivefold over the past 50 years (25). However, the cytology-based screening approach has proven less effective in developing countries, mainly because of requirements for laboratory infrastructure, equipment, and logistic challenges associated with the screening process, in addition to the test sensitivity being less than 50% (27). Since 2021, the WHO recommends HPV detection as the gold standard for cervical cancer screening (25).

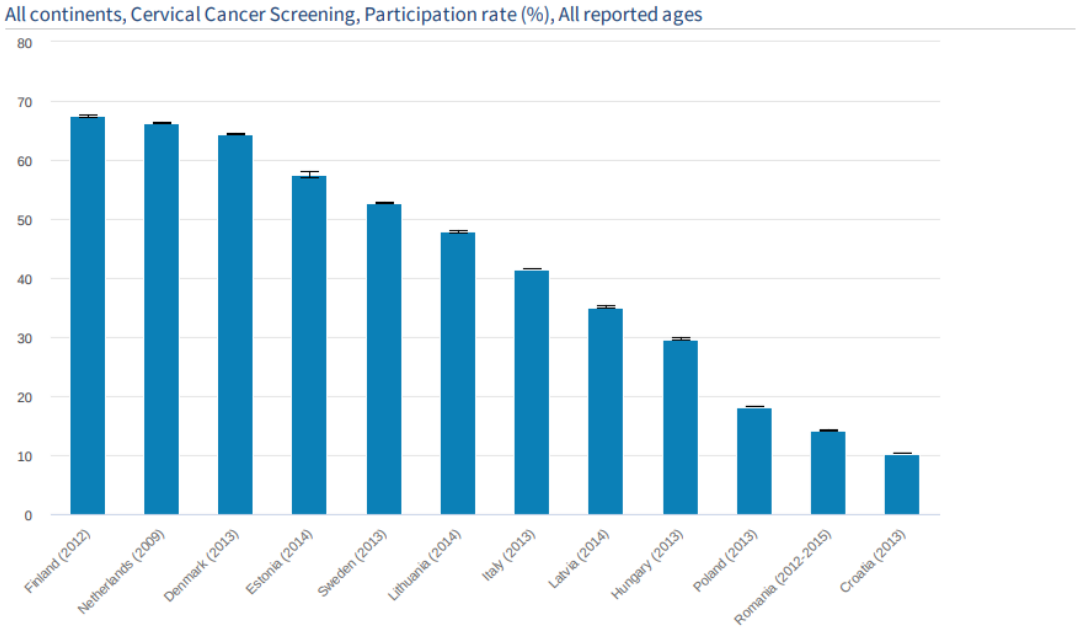
The WHO has recommended visual inspection after application of acetic acid (VIA) as the most feasible and affordable alternative to cytology screening (27). VIA involves naked-eye examination of the uterine cervix with appropriate illumination after application of freshly prepared 3 to 5% acetic acid solution (27). VIA is widely used as a screening test in LMICs, often in a "screen and treat" approach where screen-positive women are offered immediate

treatment (27). Such an approach has been demonstrated to reduce the number of clinic visits by women, improve compliance with treatment, and make the program efficient (27). VIA can generally be performed by health providers after a short period of training (27). The interpretation of the test is based on the detection of a well-defined dense acetowhite area on the transformation zone of the cervix appearing one minute after the application of acetic acid solution (27). Due to the subjective nature of the test, success of the screening program depends on the high quality training of provider (27).

Screening coverage of 70% is one of the main pillars in the WHO's global strategy to eliminate cervical cancer as a public health concern during this century (25). Most European countries have a population-based cervical cancer screening program offering cytology tests free of charge (15). The screening participation in Europe ranges from 10% in Croatia to 67% in Finland (15) (see Figure 6). In many Latin American and Caribbean countries, where cervical cancer screening programs have been instituted in most regions since the beginning of the 1970s, the screening coverage remains low and the mortality remains high (10). In India, which accounts for about one fifth of the global burden of cervical cancer, screening rates are as low as 6% in several states (6).

Figure 6

Cervical Cancer Screening Participation Rates (15)



1.3.1 Inequalities in cervical cancer screening

In HICs where screening programs have been successfully implemented, cervical cancer rates have decreased up to 65% over the past 40 years (28). But given the relatively high costs and the requirement of an adequate healthcare infrastructure, mass screening programs have not been implemented in many LMICs (29-30). The estimated percentage of women who are accessed by at least one screening test in their lifetime is still very low in LMICs (32). Consequently, the incidence rate and mortality trends for cervical cancer ranges greatly between regions and countries, where the large majority of cervical cancers diagnosed worldwide occur in Africa, Latin America and the Caribbean, or Asia (14;30) (see Figure 7 and 8). In many countries in Africa and South-East Asia, the incidence and mortality rates of cervical cancer are about 10 times those in North America, Australia, and New Zealand (6). For example, the cervical cancer mortality rate is 12 times higher in Bolivia than in Canada (21/100,000 women vs. 1.7/100,000 women, respectively) (10). Although many LMICs have introduced VIA-based screening programs, these services are generally restricted to small scale pilots, and even in countries with longstanding screening programs, coverage is often low (at around 10% to 20% of adult women in the poorest countries) resulting in socioeconomic, geographical, cultural, and educational disparities in screening rates (31).

Figure 7

Mortality versus Incidence of Cervical Cancer in Different Continents (14)

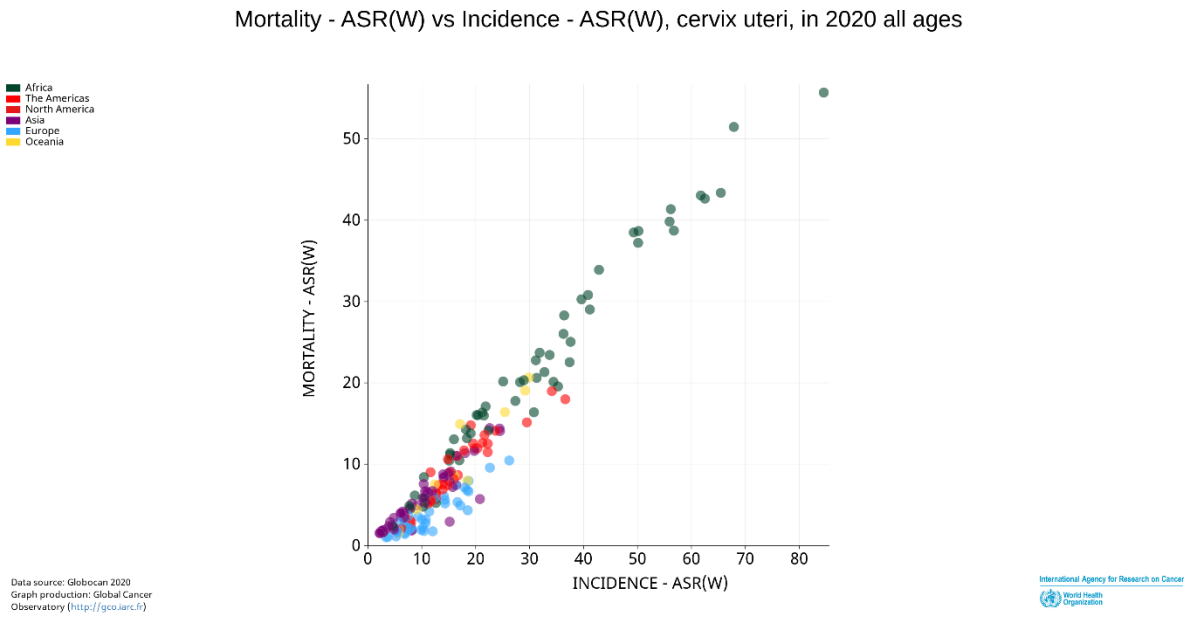
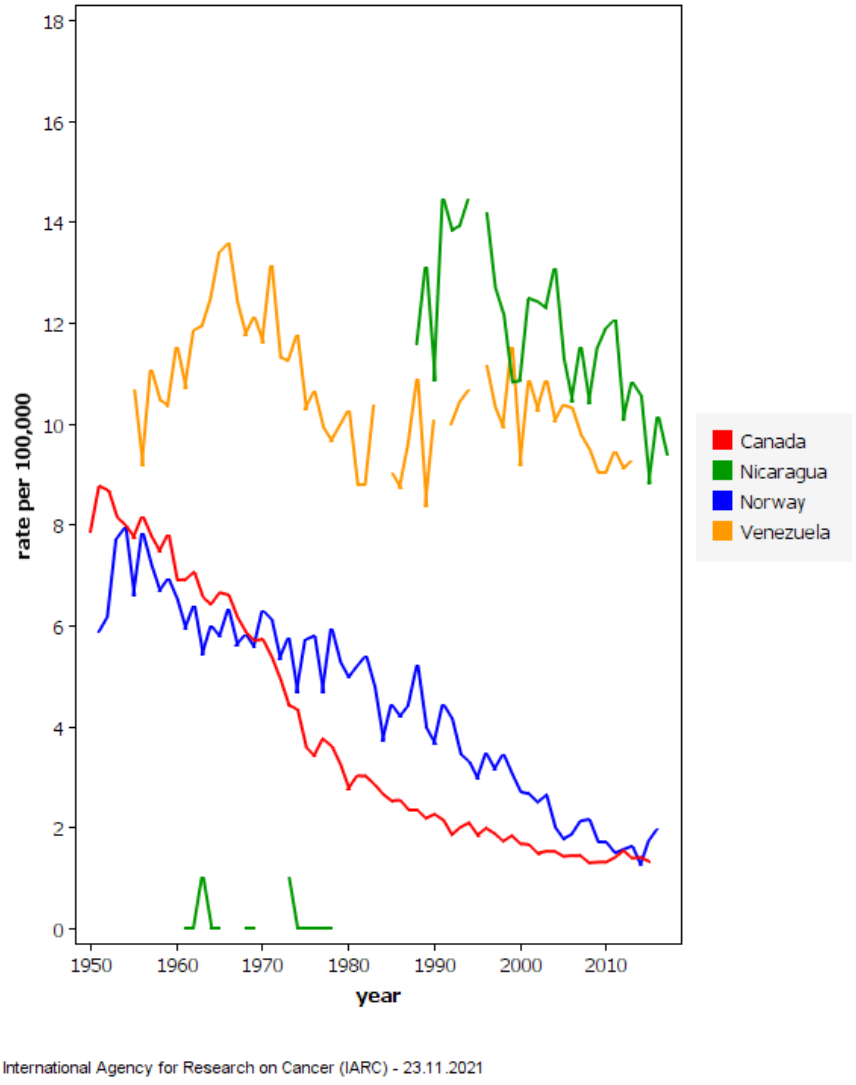


Figure 8

Cervical Cancer Mortality Trends in Four Countries (14)

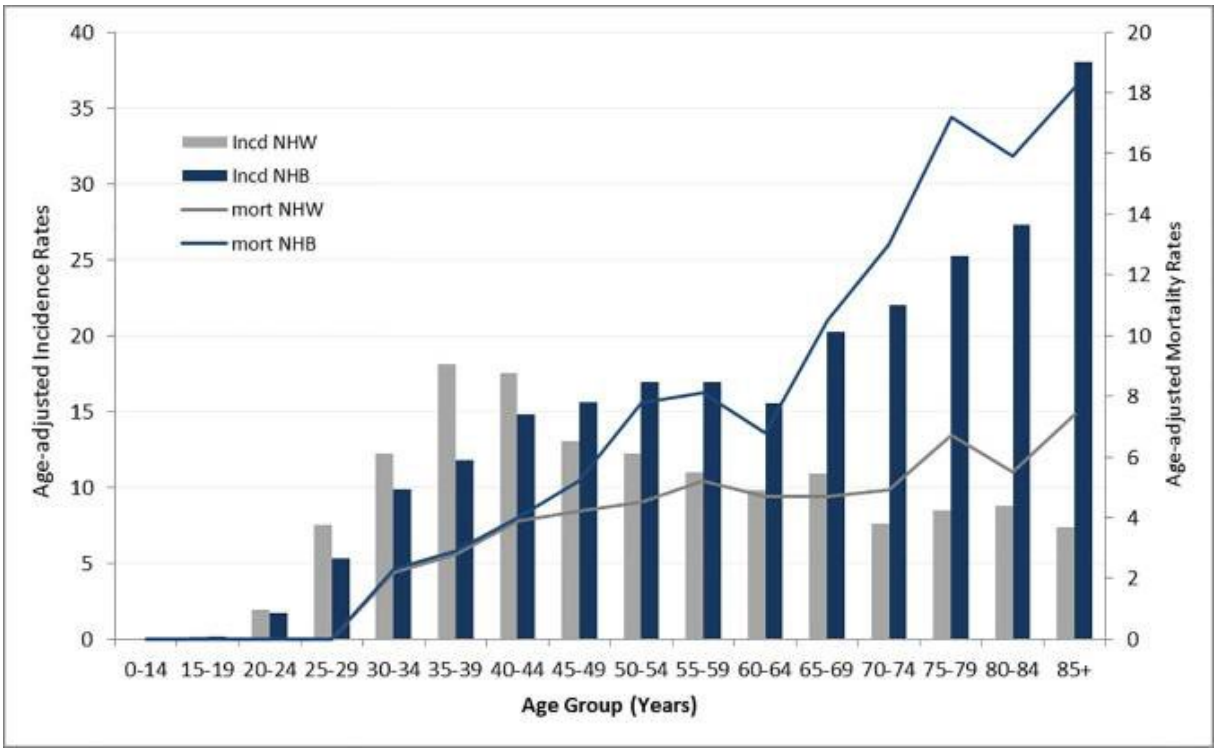


Racial disparities in cervical cancer outcomes are well recognized and related to unequal access to and participation in prevention, screening, and treatment services. In Europe, migrants from non-Western countries were more likely to develop cervical cancer, compared with the general population of their industrialized host country (33). In the USA, Black women had higher cervical cancer incidence rates than Non-Hispanic Whites (10.4/100,000 vs. 7.8/100,000) and the highest mortality rate (4.3/100,000) than any other racial or ethnic groups, where the disparities became even greater after 40 years of age (34) (see Figure 9). Of Hispanic women presenting with severe stages of cervical cancer, 20% had never had a Pap test, compared to 3% of women presenting at a similar disease stage (35). A systematic review and meta-analysis of cervical cancer in Indigenous women in Australia, New Zealand, Canada, and the USA found that Indigenous women had a higher risk of cervical cancer

morbidity and mortality but no increased risk of early-stage disease (36). These findings suggest that structural, social, or individual barriers to screening, rather than baseline risk factors, are influencing poor health outcomes (36).

Figure 9

Trends in Racial Disparities in Cervical Cancer Incidence and Mortality Rates in the USA (34)



For screening participation, many ethnic minority women and immigrant women have shown low attendance at cervical cancer screening in Europe, Canada, the USA, and Australia (37-44). Estimated cervical cancer screening rates across 57 diverse countries showed that 94% of eligible women in developed countries had taken a pelvic exam in their lifetime, whereas in developing countries this proportion was 45% (35). In Norway, registry data showed that immigrants were 1.7 times more likely to be non-adherent in the cervical cancer screening program compared with the majority population (43). African and Eastern European women had the lowest participation rate in the Norwegian cervical cancer screening program (40). In the USA, 81% of eligible women had taken a cytological screening within the last 3 years, while these rates were significantly lower among Asian and Hispanic women (35).

Ethnic minority women can face barriers to cervical cancer screening, in addition to the barriers mentioned for cancer screening in general. Lack of knowledge and misunderstandings related to cervical cancer have been reported as substantial barriers among many ethnic minority women (45-49). For example, many women did not recognize or understand the terms *cervical screening* or *smear test* (46). African immigrants in Australia did not know about cervical cancer prior to coming to Australia (47). In many cultures, living in monogamous relationships with a single sexual partner during a lifetime is considered an ideal or an obligation. Thus, some women did not perceive themselves as being at risk of cervical cancer: "*I don't think I need the Pap smear test as I have only one man, my husband, in my life. Thus, I am not at risk for cervical cancer*" (45). Moreover, some women feared the consequences of a potentially screen-positive result or the screening procedure itself, fearing, for example, that a Pap test could threaten their virginity (48). A systematic review of barriers to cervical cancer screening among immigrants and ethnic minorities showed that commonly held beliefs across several cultural groups emerged (48), as, for instance, the following alternative understanding of cancer epidemiology: "*I know, a friend of a friend was sexually abused and is currently dying of colon and cervical cancer, and she never dealt with the sexual abuse, and I think the body experiences emotions… you stuff emotions into the body, and I think, I think that is one level of cause of cancer*" (46).

The fact that cervical screening is carried out through a vaginal test poses a challenge for many women, in general, and for ethnic minority women, in particular. Women who have experienced female circumcision, which is a common cultural practice in several communities, found it challenging exposing their genitals for fear of stigmatization by healthcare providers (47). By some women, the vaginal area was considered a sacred area that should not be seen or touched by another, apart from the sexual partner (47). Some women feared talking openly about cervical screening because other society members might see them as not being virgins or as being sexually promiscuous (47). Some women experienced vulnerable feelings associated with the cervical screening procedure: "*When I lie down on the table and open my legs, I know it's only an instrument, but I feel like I am being raped*" (45). Moreover, physical pain could be present: "*I have been to an English-speaking doctor for a Pap test, and the speculum she used was much bigger than the one the Chinese doctor used. I believe White women and Chinese women are a bit different*" (45).

1.4 Educational interventions

The World Cancer Report states that targeted health interventions are potentially powerful ways of reducing cancer inequalities (6). Educational interventions are considered a key approach to increase cancer screening participation and access. An umbrella review of the influence of health systems on breast and cervical cancer screening showed that educational interventions that focus on overcoming capacity and intention barriers are among the facilitators with the most supporting evidence (9). The educational interventions can be directed at eligible individuals or to healthcare providers. To obtain an effective approach, the interventions should be comprehensive, appropriately timed, use varied teaching methods, have sufficient dosage, be administered by well-trained staff, provide opportunities for positive relationships, be socioculturally relevant, be theory-driven, and include outcome evaluation (6).

1.4.1 Proportionate universalism

The notion that "the 'hardest to reach' are often the ones we need to reach most" has contributed to discussions about how to deliver health interventions to disadvantaged populations to ensure health equity (50). This discussion started with Rose in 1985, where, in his article titled *Sick Individuals and Sick Populations*, he distinguished between population-based interventions that target an entire population and interventions that target high-risk groups (5). Rose stated that population-based interventions were likely to lead to larger improvements in health, because they shifted the risk distribution of the entire population to a lower risk (5). More recently, Rose's framework has been challenged from a social inequality perspective, suggesting a replacement of a high-risk-group approach by a vulnerable-group approach -- where a vulnerable group is defined as a group that is at higher risk because of shared socioeconomic conditions (5). From this perspective, a population-based intervention strategy may lead to a widening in health inequalities, because these interventions may affect people with different socioeconomic status in different ways and may have a stronger effect among the groups with highest status (5). This phenomenon is referred to as *the inverse prevention law* (5).

To be fully effective in improving the health of a population without increasing social inequalities in health, prevention policies should therefore combine a population strategy with

a vulnerable-group approach -- an approach that is called *proportionate universalism* (5). This type of intervention targets the entire population, but the scale and the intensity of the intervention are proportionate to the level of disadvantage (5). A review that compared several interventions implemented to improve participation in breast cancer and cervical cancer screening in the most disadvantaged groups found that local interventions in disadvantaged populations were the most effective for increasing participation in cancer screening (5). The review showed that a combination of a population-based and vulnerable-group approach may be the best strategy to improve participation in breast cancer and cervical cancer screening among all women (5-6).

In practice, proportionate universalism combines a degree of "selectivism" within a universal framework (50). Here, *selectivism* refers to the targeting or tailoring of services, policies, or programs for defined groups (50). For programs targeting a disadvantaged group, there must be a degree of selectivism, because although universalism is regarded as a necessity of equality, it does little to promote redistribution and ignores existing inequalities (50). The framework of specific interventions must be grounded in the position that different standards need to be applied to different groups to ensure that needs and structural disadvantages are adequately dealt with (50). Specific health programs for minority populations are examples of positive selectivism where targeted approaches (that sit alongside universal services) are needed to meet highly specific needs.

1.4.2 Educational interventions for ethnic minority women

Studies from different cultural contexts indicate that greater knowledge about cancer does not automatically increase screening participation rates (8). Hence, a broader educational and behavioral approach than exclusively providing information is required. *Tailored educational intervention* can be defined as the use of communication that is specific to an individual or a group to improve health or change behavior (2). It contains specific and organized information for a purpose, presented within a context that provides meaning and relevance, and can lead to increased understanding (51). The term *culturally sensitive* has been widely employed to describe initiatives which have been tailored to increase their appropriateness for minority ethnic communities (52). However, the understanding of the factors needed is still developing -- within a wider context of competing theory-based strategies for changing health behavior. There is some consensus on the importance of addressing deep-rooted influences on

health behavior, including cultural influences and structural factors (52). In tailored educational interventions for ethnic minority women, the following five principles can guide the planning and evaluation:

Principle 1: Use community resources to increase intervention accessibility
Community resources can publicize the intervention to the target population and increase its accessibility. Examples of community resources are the use of ethnic-specific media and networks, local community leaders, and community events (52).

Principle 2: Identify and address barriers to participation and access
Low income, being uninsured, and living in rural versus urban areas are all factors associated with lower levels of participation. To address such barriers, interventions can include providing transport or keeping costs of participation low (52). These measures take account of the disadvantaged socioeconomic position of many target groups. Interventions may need to take account of gender as well as ethnicity, as, for example, offering childcare during the screening appointment and using female health providers to perform screening tests.

Principle 3: Develop communication strategies which address language use and differential information requirements
Target groups may have differential access to information in their daily life (52). One of the main issues in providing educational interventions for ethnic minority women is overcoming language barriers through, for example, bilingual educators. If educational sessions are provided in native languages, participants will be able to discuss concerns with health educators and each other (52). Such education can be given one-to-one or in groups, through written information or oral presentations. Additionally, the information must be adapted to the target group and be provided in an easy-to-understand way.

Principle 4: Identify and work with cultural or religious values that either motivate or inhibit behavioral change
Interventions to ethnic minority women should always consider the culture-specific context as a framework for maintaining the multidimensional nature of health behavior change (23). Humans are a product of their social and cultural context, cultural beliefs, life experiences, and socioeconomic factors. The aim of cancer screening is to contribute to bettering lives, but failure to understand women's cultural context can result in ineffective health-promoting

strategies (23). However, cultural barriers vary widely -- both between groups and between individuals -- underlining the importance of sensitive and appropriate educational approaches when addressing identified cultural or religious barriers.

Principle 5: Accommodate degrees of cultural affiliation in the planning and evaluation of targeted interventions

A target population is heterogeneous in most characteristics, such as income, education, history, language, country of origin, immigration history, and language. Therefore, the large (and expected) variation within and between ethnic groups can influence the behavioral intervention. An educational intervention should take account of varying degrees of cultural identification and acculturation among a target population (52).

2 Objective

One of the most important aspects of cancer screening from a health system perspective is the substantial inequality in screening access and participation -- between continents, countries, and social groups of society. Women's opportunities to participate in breast and cervical screenings are not equally distributed. In this PhD project, we aimed to explore educational interventions on breast and cervical cancer screening. Most HICs offer breast and cervical cancer screening services, but ethnic minority women have low participation rates and are defined as a disadvantaged group requiring special attention. Although tailored educational interventions are considered a key approach to increasing the screening participation of these women, the effectiveness of these interventions remains unknown. In most LMICs, cervical cancer screening services are offered, but these services are only available for certain women. Educational interventions hold a key position in enhancing cervical cancer screening access and participation in LMICs because the screening programs depend on high quality training of health providers. However, it remains unknown to what extent health providers are trained and how well the training guidelines are adhered to.

The objectives of this PhD project were to

1) determine the effectiveness of culturally tailored educational interventions on screening attendance at mammography and the Pap tests among ethnic minority women;
2) explore whether women's screening histories impact screening attendance after tailored education;
3) and examine essential training components in cervical cancer screening programs implemented in low-resource settings.

Reducing inequalities in health is one of the main public health challenges of our times (5). According to the World Cancer Report (2020) will achieving relatively high screening coverage and participation rates reduce health inequality (6). In breast and cervical cancer control, only strategies proven to be effective and successful should be proposed to a population (8). This means that interventions must be critically evaluated to help inform and prioritize evidence-based and resource-appropriate strategies and policy making (32). This thesis is positioned as health policy and system research (HPSR) (53). In HPSR projects, the focus is on promoting quality, coverage, efficiency, and equity of health systems to increase

health outcomes (53). They can address specific diseases or services that raise specific challenges for the health system. Moreover, they seek to unpack the behavior, reactions, and interconnectedness of health systems and the people within those systems (53). The way HPSR conceptualizes and analyzes these interactions helps illuminate not only what works, but for whom, and under what circumstances (53). HPSR projects can have a wide array of research methods and disciplines, but among the most used approaches are research on interventions that have been tried out as solutions to an identified health system problem (53). In these cases, HPSR can produce reliable and rigorous evidence about whether interventions have improved a specific problem as well as assess how an intervention could be further improved.

3 Methods

This PhD project is composed of three systematic reviews, including two meta-analyses and a narrative synthesis. Study I was a systematic review on the effectiveness of culturally tailored educational interventions on screening attendance at mammography and Pap tests among ethnic minority women. Study II was a systematic review on women's screening histories and their impact on screening attendance after tailored education. Study III was a systematic review on essential training components in cervical cancer screening programs implemented in low-resource settings.

Systematic review and meta-analysis are complex and strict methodologies composed of multiple tasks, where many small choices can determine the results and the conclusions. Meantime, articles have a strict and standardized format. According to the publication *Doing and Reporting Meta-Analyses* (54), an article is not written to teach a reader how to undertake a meta-analysis and should not explain common decisions or procedures nor explain to the reader the difficulty of the meta-analytic methodology. Therefore, this PhD thesis will provide information, explanations, and my own reflections on all stages of the systematic review to provide transparency and reproducibility.

In all three systematic reviews, we followed the *Cochrane Handbook for Systematic Reviews of Interventions* (55) and the *Centre for Review and Dissemination's Guidelines for Undertaking Reviews in Healthcare* (56). These handbooks are among the most recognized and preferred guidelines for undertaking systematic reviews and meta-analysis in healthcare. Additionally, I used the textbooks *Research in Medical and Biological Science* (57), *Introduction to Meta-Analysis* (58), and *Systematic Reviews in Educational Research* (59). The systematic reviews were conducted and reported in line with the PRISMA statement (*Preferred Reporting Items for Systematic reviews and Meta-analysis*) (60-61).

3.1 Review team

Guidelines recommend that at least two reviewers are involved in a review process in order to minimize bias and errors implemented at different stages of the review (56). The review team members will manage and conduct the review and should have a range of skills, such as expertise in systematic review methods, information retrieval, the relevant clinical area, and

statistics where appropriate (56). Additionally, it is recommended that reviewers seek advice from other clinical or methodological experts (56).

In Study I and II, the review team consisted of my supervisors and me. The review team members had extensive knowledge of educational intervention, cancer screening, systematic reviews, and statistics. The review team members contributed actively to discussions on research questions, eligibility criteria, and limitations. Moreover, they played key roles in the assessment of risk of bias, data extraction, and interpretation of findings. The statistical analyses were conducted by my co-supervisor and me, about which more details are provided in Section 3.7.1 Statistical data analyses.

Study III was conducted during my research stay at the Early Detection, Prevention, and Infections Branch at International Agency for Research on Cancer (IARC). The review team was composed of members from IARC, Newcastle University, and the Center for Global Health Inequalities Research (CHAIN) at the Norwegian University for Science and Technology (NTNU), with final inputs from the Pan American Health Organization (PAHO). The review team members' extensive and diverse knowledge about cancer screening, systematic reviews, and health inequality research had a high impact on the quality of the work. The systematic review process -- from idea to publication -- was mainly led by me as the first reviewer in collaboration with my research assistant at IARC and the rest of the review team members.

3.2 Eligibility criteria

The objective of systematic reviews is to synthesize results across primary studies. Therefore, the eligibility criteria used in the reviews had to be operationalized definitions or concepts (56). Defining the eligibility criteria is a vital part of a review process, as it can influence the findings and conclusions. The inclusion criteria should capture all studies of interest and be practical to apply (56). If the criteria are too narrowly defined, there is a risk of missing potentially relevant studies, and the generalizability of the results might be reduced (56). On the other hand, if the criteria are too broad, the review might contain information which is hard to compare and synthesize (56). Due to the diversity of research questions, there can be no gold standard on how precise the criteria should be.

In Study I and II, we chose strictly defined criteria compared to previous meta-analyses on the research topic (62-63). The population of interest was ethnic minority women, but I found it challenging to locate definitions of ethnic minority women that were operationalized, hands-on, and politically correct. Empirical studies use inconsistent and wide variations in defining immigrants, migrants, and ethnic or racial populations (64). In Study I and II, we aimed to explore the effectiveness of educational interventions on screening participation. We found studies from Europe, the USA, Canada, Australia, and New Zealand showing low screening participation among ethnic minority women. In Study I, we chose to operationalize these countries as *Western countries* – a terminology that can be challenged from several positions. First, the terminology implies that there exists a "non-Western" category, which can be interpreted as a residual category and creates a false image of a world divided into the West and the rest. Second, the terms *Western countries*, *developed-*, *less developed-*, *least developed-*, and *developing countries*, as well as *HIC* and *LMIC*, are often used for partly overlapping populations (65). While classification schemes are convenient for analysis and communication, they all come with a set of limitations, biases, and cultural overtones (65). With these arguments in mind, I chose to not use the term *Western* in Study II. Moreover, I shifted the main focus from the participants (being ethnic minorities) to the educational intervention (being targeted to ethnic minority women). Although identifying and agreeing upon operationalized definitions was a time-consuming process, I would argue that without these strictly defined eligibility criteria, our extracted data could not have been combined in a meta-analysis due to heterogeneity.

3.3 Search strategy

Search strategies contain all the steps that lead to the actual literature search. This includes establishment of a search query, selection of relevant sources of information, determination of the dates to be covered in the search, the search terms to be used, and the use of different search techniques (66). Scientific bibliographic databases comprise enormous amounts of information, which can present a challenge. A literature search can turn into a search for a needle in a haystack if proper search techniques are not applied (66). In the three systematic reviews, I created the search strategies in collaboration with librarians and carried out all of the searches myself. I followed recommendations from guidelines and textbooks (56-57) and collaborated with librarians at Molde University College (Study I), the Norwegian Institute of Public Health (Study II), and IARC (Study III).

The review questions were divided into Population, Intervention, Comparator, and Outcomes (PICO) elements. Since none of the systematic reviews had defined comparators, C was not included in the PICO tables. For each of the PICO elements used, it is important to consider and critically assess all alternative search terms (56). The search strategies included a broad range of search terms and searching techniques. By truncating search terms, the search became broader; for example, retrieved *migra** records on *migrant*, *migrants*, and *migration*. However, truncation also retrieves irrelevant records, such as on *migraine*, and must therefore be carefully chosen. Thesaurus were used to compensate for variations in spelling and operationalization. Especially for research topics with poor or diffuse terminology, a search can be greatly enhanced if mapped to thesaurus (56). Boolean search operators *OR* and *AND* were used to combine search terms and thesaurus. To broaden the search, related terms were combined with OR (e.g., *immigrant* OR *foreigner*). AND was used to ensure that all relevant concepts within the review questions appeared in each record (56). Due to the wide diversity of review questions, there cannot be an agreed-upon international standard regarding which databases and what number of databases are recommended to use (66). I chose to conduct the searches in recognized databases for health research recommended by the librarians that I collaborated with. The PICO forms and search strategy were adjusted to each database (56). In all three reviews, all the database searches were updated before publication to ensure that no recent papers were missed.

Although I intended to create the perfect search strategies in each of the systematic reviews, I understood that search strategies in general are highly influenced by subjective and qualitative interpretation. The search strategy will, for example, be influenced by how the reviewers understand the review question and the research topic. Moreover, after collaborating with different librarians, I also found that their professional opinions and preferences could influence the search strategy. For example, the PICO form in Study I is substantially different from the PICO forms in Study III. The librarian I collaborated with in Study I recommended a narrow search strategy in an effort to retrieve relevant records and not retrieve irrelevant ones. This search was conducted in five databases but retrieved only 207 records. This is a low number of records compared to other systematic reviews and compared to Study III. In hindsight, I would argue that this search was too narrow, resulting in potentially missing studies. In contrast, I collaborated with librarians in Study III who preferred the opposite strategy -- striving to not miss any relevant articles by accepting a high number of irrelevant records. The PICO forms and search techniques used in Study III looks impressive, in my

opinion, as it contained a high number of keywords and retrieved almost 5,000 records. We spent over three months creating this search strategy, whereby we systematically tested 12 different PICO forms and used key papers on the research topic to test the search. However, during the review process, we changed the objective of our systematic review -- from provider-directed interventions on cancer screening, in general, to VIA training. Hence, we know in retrospect that most of the search terms included in the PICO forms were not required to answer the final review question, which means that most of the 5,000 records we retrieved were irrelevant. I use these examples to illustrate how difficult (or impossible) it is to create perfect search strategies, as well as to illustrate why a reader should be careful in judging the quality of a search strategy only on the extensivity of the PICO form and the high number of retrieved records.

3.4 Selection of studies

The aim of a study selection is to ensure that all relevant studies are included in a review. Since the decision to include or exclude a study can be affected by opinions and interpretations, the selection process must be explicit and objective to minimize the risk of errors and bias (56). I have reported the study selection process in flow charts, showing the number of studies and records remaining at each stage, as recommended in PRISMA statements (60-61).

The abstract assessments in Study I and II were undertaken individually by me as the first reviewer. This procedure is in line with guidelines, which underline that abstracts that explicitly do not meet the inclusion criteria can be rejected by one reviewer (56). Although we had created specified and explicit eligibility criteria, there was always a risk of single rater error. Since we intended to combine the included studies in a meta-analysis, the selection process became a vital stage of the systematic review. Poorly chosen articles can give mathematically correct results but be clinically misleading. Therefore, the selection of studies must be well documented to ensure reliability, validity, transparency, and reproducibility. Although it was not required, I chose to document reasons for exclusion and discuss excluded records with my supervisor to ensure that no records were excluded on an inadequate basis. These discussions resulted in further exploration of several studies and provided a deeper understanding of the terms and definitions used in the included studies. My impression is that our discussions on included and excluded records reduced the risk of misunderstandings and

errors and also provided a deeper understanding of the research topic. The full text assessment was performed independently by my supervisor and me, as recommended in guidelines (56). Discrepancies between us were solved by consensus discussion.

The study selection process in Study III was undertaken in Covidence -- a leading software for managing and streamlining systematic reviews. Using this software increased the transparency, reliability, and productivity of the study selection process. The study selection process was undertaken by my research assistant at IARC and me. Members of the review team with extensive experience in conducting systematic reviews recommended that both reviewers would assess 10% of the abstract. If we agreed on most of the decisions (with a Cohen's Kappa coefficient (κ) > 0.7), I would, as the first reviewer, continue the abstract assessment independently. Our κ was 0,86. All the excluded abstracts were automatically categorized in Covidence and available to the review team. The full text assessment was conducted by both reviewers, with discrepancies between us being resolved by internal discussion or by consulting the project leader at IARC who had the final say in a decision.

3.5 Risk of bias

All primary studies included in a meta-analysis should be formally assessed for risk of bias (RoB) (67). A bias is a systematic error or deviance from the true variance that has a negative impact on the validity of the results (55). RCTs can have shortcomings in the design, conduction, or analyses -- where bias potentially can have a larger impact on the study result than the intervention itself (67). The RoB should not be confused with study quality. While bias refers to the extent to which the results of a primary study should be believed, the study quality, on the other hand, refers to the extent to which a study adheres to the highest possible standards (68). For educational interventions, blinding of participants and study personnel is difficult (or even impossible), and, therefore, the methodological quality could be of the highest possible standard (for answering the research question), but the RoB may still be high (55).

We used Cochrane Collaboration risk of bias tools to assess included studies. We used the first version of the tool (67) in Study I, and the revised version of the tool (69) in Study II. The RoB assessments were performed separately by my supervisor and me. Since the RoB assessment is a subjective judgment that can be influenced by opinions and interpretation, we

thoroughly discussed the Cochrane RoB guidelines and piloted a RoB assessment, as this can improve the reliability (55). The domains covered in Cochrane Collaboration RoB tools are standardized and designed to cover all randomized trials. The tools are structured into a fixed set of domains of bias, focusing on different aspects of trial design, conduct, and reporting. Within each domain, a series of questions aims to obtain information about aspects of the trial that are relevant to RoB. Because the tools are standardized, the reviewers must reflect upon which domains are the most important in the context of their review (67). In our systematic reviews, we considered the following domains as of particular concern.

3.5.1 Randomization process

When we assessed the included studies in Study I and II, we found that the randomization procedure was often insufficiently described. Additionally, most studies included women regardless of their screening history or included women who had not participated at screening within the past 12 months. In our opinion, there is a substantial difference between women who have taken a mammography screening within the last 12 months and women who have never been screened, especially when the effectiveness of educational interventions to increase screening participation are being explored. We found that all studies used baseline questionnaires to obtain information on the participants' screening histories, but few studies used this information in the randomization process. In some studies, the between-group differences regarding the number of *ever-screened* and *never-screened* participants was substantial. In some studies, this between-group difference in screening history favored the intervention group.

3.5.2 Deviations from the intended interventions

In RCTs on educational interventions, blinding of participants and educators can be difficult (or even impossible), which automatically provides some concerns of RoB. In Study I, we discussed whether this domain should be reported as *not relevant*, as we had seen in some meta-analyses. However, we examined a comprehensive meta-analysis on educational interventions (70) and consulted with experts in systematic reviews at the Norwegian Institute of Public Health. We were advised to assess the domain for bias, because although a bias is not a result of flaws in design or conduction, the lack of blinding can still influence the results.

When we assessed the included studies, we found that many studies had RoB related to deviations from the intended interventions or inconsistent interventions. Some studies used lay health workers to schedule the screening test for *some* participants in the intervention group (71-73) or offered free mammograms to *some* of the participants (74). In our opinion, these services were important additional exposures that could be prognostic for the outcome, as a potential effectiveness found in these studies could not be related exclusively to the educational program. Examples of inconsistent interventions included extensive variations in duration and contents of the educational intervention within the same study.

We found that several studies reported substantial contamination between intervention and control groups (75-78). In one study (75), only a handful of the participants in the intervention group had actually participated at the educational intervention, while more than 20% of the participants in the control group knew about, or even participated in, the educational intervention. In another study (78), 33% of the participants in the control group reported that a health educator had visited them at home to talk about Pap testing during the trial, and 8% said they had been attending a meeting where Pap testing was discussed. Although such contamination can lead to an overall increase in screening participation, it presents a substantial RoB for the studies' effect estimates.

3.5.3 Measurement of the outcome

All studies used self-reported data, which can result in RoB in the outcome measurement (69). Only one study (78) validated the self-reported data with data from medical records and this study found that the medical reports only confirmed the self-reported Pap test among 58% of the participants in the intervention group and 54% of the control group. Such over-reporting has also been found previously by other studies (79-81).

We assessed that providing substantial financial incentives for participants and educators create a high RoB in measurement of the outcome. In one study (76), the educational session ended with a strong recommendation from the health educator to get screened before participants received money. Lay health workers in three studies (71-73) received $1,500 each to educate women they had enrolled in the study themselves. In the last educational group session, the educators re-emphasized screening benefits before, one month later, they called participants to remind them of screening and offered to help with scheduling appointments.

In our opinion, the intervention effect in these studies could be biased because the participants in the intervention group may have felt obligated to take a screening test or to provide a socially desirable answer on their screening status at the self-reported outcome measurement. Additionally, we assessed that some studies had a RoB due to their too short timeframe for the outcome measurement. For example, one study (71) measured the participants' screening attendance three months after the intervention was provided, although the predicted waiting time to receive a screening appointment was more than three months in that county.

3.5.4 Selection of the reported result

We assessed many studies to have RoB in selective reporting of data, especially concerning *never-screened* and *ever-screened* participants. For example, one study (75) reported that 95% of the participants were ever-screened at baseline. The results of this study were reported as an increase of ever-screened -- meaning the change of screening status among the 5% who were never-screened at baseline. We found that in several studies (71-73;75;78), the significant positive results and the study conclusions were caused entirely by the substantial between-group differences of ever-screened and never-screened. For example, one study (73) reported that participants ever-screened increased from 89.6% to 91.8% (+2.2 percentage points) in the control group, and from 84.1% to 91.6% (+7.5 percentage points) in the intervention group. Notably, more participants took a screening test in the control group than in the intervention group. However, the effect size was reported as significantly greater for the intervention group, because the 7.5 percentage point increase in the intervention group was significantly higher than the 2.2 percentage points in the control group ($p < 0.001$). We assessed such reporting of findings as high RoB. Moreover, our subjective and qualitative assessment of the bias in included studies gave us the idea to explore whether tailored education is more effective for never-screened or ever-screened women.

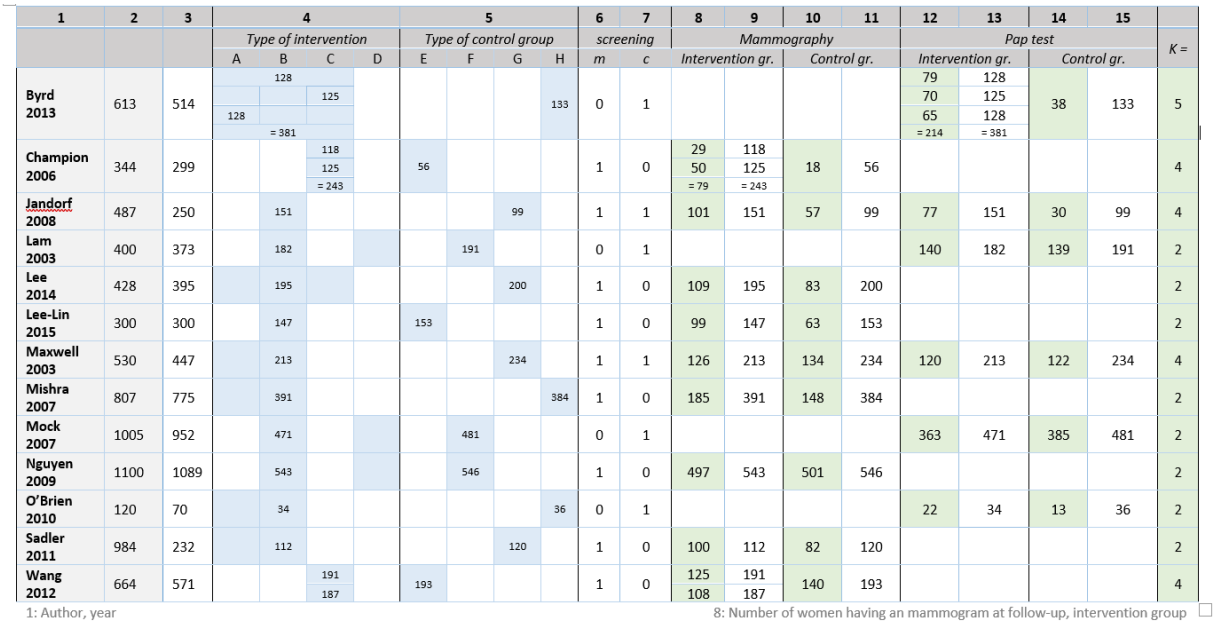
3.6 Data extraction

Data extraction is a process consisting of two connected parts: coding the study characteristics and extracting the findings. The data extraction should be performed separately by at least two reviewers to minimize RoB and errors (56). The main characteristics of the included studies should be presented, preferably in a table (68). For each study, the name and a citation for the source of the study, the study size, follow-up period, and other information relevant for the

research question should be proven to allow the reader to assess the relevance of the included studies (68). Tabulation of study characteristics and findings can aid the examination and comparison of PICO elements across studies, but a table can also facilitate synthesis of the characteristics and grouping of studies for synthesis (55). One of the most difficult parts in the data extraction process is to determine how many and which characteristics should be analyzed (54). It is advisable to extract all information that is likely to be needed and to extract data with both the review question and subgroup analysis in mind (56). I found the data extraction process to be a time-consuming and challenging process due to the large amount (and diversity) of information provided in the primary studies.

In Study I and II, our evidence table was inspired by the publication *Doing and Reporting a Meta-Analysis* (54) and a previous meta-analysis of educational interventions (70). When conducting meta-analyses, it is impossible to find any relationship between an effect size estimate and a specific variable if the information is not coded. Therefore, we extracted information on categories we considered as relevant, such as type of educational intervention (See Figure 10). The RCTs included in the Study I and II reported their outcomes differently (for example participating rates in percent vs. number of women attending screening). Therefore, we had to mathematically convert some estimates to a common format. Ideally, all RCTs would report their outcome in a common format, as this would reduce risks of error when extracting and summarizing data across studies (56). Although the data extraction process should be as unbiased and reliable as possible, the process is prone to human error and subjective decisions can be required (56). I made great effort to reduce the RoB and miscalculations in this process. All data were extracted at separate times, and all datasets were checked multiple times by my co-supervisor and me.

Figure 10
Data Extracted in Study I



1	2	3	4				5				6	7	8	9	10	11	12	13	14	15	
			Type of intervention				Type of control group				screening		Mammography				Pap test				K =
			A	B	C	D	E	F	G	H	m	c	Intervention gr.		Control gr.		Intervention gr.		Control gr.		
Byrd 2013	613	514	128 128 = 381		125					133	0	1					79 70 65 = 214	128 125 128 = 381	38	133	5
Champion 2006	344	299			118 125 = 243		56				1	0	29 50 = 79	118 125 = 243	18	56					4
Jandorf 2008	487	250		151					99		1	1	101	151	57	99	77	151	30	99	4
Lam 2003	400	373		182				191			0	1					140	182	139	191	2
Lee 2014	428	395		195					200		1	0	109	195	83	200					2
Lee-Lin 2015	300	300		147			153				1	0	99	147	63	153					2
Maxwell 2003	530	447		213					234		1	1	126	213	134	234	120	213	122	234	4
Mishra 2007	807	775		391						384	1	0	185	391	148	384					2
Mock 2007	1005	952		471				481			0	1					363	471	385	481	2
Nguyen 2009	1100	1089		543				546			1	0	497	543	501	546					2
O'Brien 2010	120	70		34						36	0	1					22	34	13	36	2
Sadler 2011	984	232		112					120		1	0	100	112	82	120					2
Wang 2012	664	571			191 187		193				1	0	125 108	191 187	140	193					4

1: Author, year
2: Number of participants
3: Number of participants at follow-up
4: Intervention group specified A= written information, B= culturally tailored education, C= video, D=media
5: Control group specified: E= written information, F=media, G=other intervention, H= usual care
6: Measures adherence at mammography (0=no, 1=yes)
7: Measured adherence at Pap test (0=no, 1=yes)
8: Number of women having an mammogram at follow-up, intervention group
9: Number of women in intervention group, mammography
10: Number of women having an mammogram at follow-up, control group
11: Number of women in control group, mammography
12: Number of women having an Pap test at follow-up, intervention group
13: Number of women in intervention group, Pap test
14: Number of women having an Pap test at follow-up, intervention group
15: Number of women in control group, Pap test

In Study III, I created an evidence table and an extraction technique that my supervisor at IARC later referred to as the *rainbow technique*. The overall aim of this technique was for the two reviewers to apply specific colors for specific categories (Figure 11). Since our aim was to synthesize the information qualitatively, I found the data extraction process in Study III to be different compared to the extraction process for the two meta-analyses. For instance, we made great efforts in Study I and II to ensure that we had extracted correct data. In Study III, we focused more on ensuring that we had extracted enough data and how we interpreted the information. For example, under Settings, the first reviewer could under Settings have extracted "*community clinics*", while the second reviewer could have extracted "*we recruited women from rural areas*". The consensus discussion would, in this case, be about understanding the context of the study. I found the consensus discussions in Study III to be very important, but also a time-consuming process where we needed to go through the primary articles many times. However, we found the rainbow technique to be very helpful in this process as it helped us to easily locate a specific sentence in a paper (looking for a specific color), to move from one category to another (discussing a new color), and to discuss several papers at once.

Figure 11

Illustration of Data Extraction Process in Study III

A	B	C	D	E	F	G	H	I	J	K
TITLE	**Author, year**	**Country**	**Setting**	**Screening procedure**	**Providers**	**Training**	**Evaluation of the training program**	**Follow-up**	**Screened**	**VIA+ rate**
Cervical cancer	Ramogola-	Botswana	Program	Reference: WHO 2002.	? (Licensed	A three-day	Discrepancies	March 2009-	2175	253
Cervical cancer prevention program in Jakarta, Indonesia: See and Treat model in developing country.	Nuranna 2012	Indonesia	Community settings in Jakarta, Indonesia, from 2007 until 2010. Women were not screened it they has history of cervical cancer, history of total hysterectomy, or were pregnant women with less than 20 weeks of gestational age by clinical examination.	Reference: WHO 2002.The cervix was assessed as to whether or not there was a presence of gross lesions consistent with possible cancer. Special attention was paid to ensuring that the entire squamo-columnar junction was visualized. The next step was to swab the cervix with 3-5% of acetic acid solution then the cervix was re-examined by an examination light. VIA was said to be positive value if there was a	2216 people (641 general practitioners, 678 midwives, 610 public health cadres and 287 'key person' from the society).	The training consist of five days that include 2 days of basic theory and dry workshop, 1 day of live demonstration and 2 days of working at their own clinic or Public Health Centre. All these examinations were undersupervised . The goal of the	3 months later, a program evaluation to ensure the quality assurance of the test providers.	End of 2007 to 2010:	22989	4.2% (970/22989)

Figure 1. Cervical cancer screen-and-treat workflow.

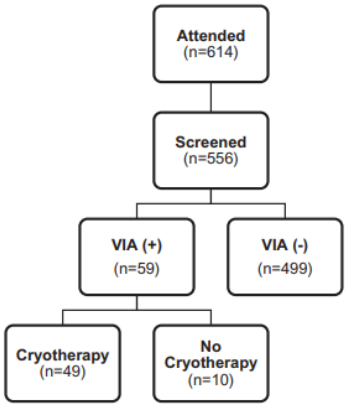


Figure 2. Flowchart of patients attending the screen-and-treat.

Providers who completed the educational component and screen-and-treat requirements received certificates of completion.

Follow-up protocol

Although a single intervention with cryotherapy at age 35 y can drastically reduce a woman's lifetime risk for the development of advanced disease by 25–36%,[6] community sustainability and continued screening are key to the success of screen-and-treat interventions. Providers who received training and certifications of completion were expected to send monthly reports regarding the number of patients screened, VIA-positive findings and treatment outcomes to CCC to ensure continued resource availability to the community. Healthcare workers are also required to keep records of all patients screened and treated in a formatted log book as well as give patients a copy of their results with instructions for follow-up. The two sites were notified that there would be an audit from BMC's Obstetrics and Gynaecology Department as well as an audit by the University of California, Irvine/CCC team annually to ensure supplies are stocked, equipment is functional and trainees are practicing appropriate screening techniques.

Data analysis

Data were analysed using XLSTAT for Windows (Addinsoft, New York, NY, USA). To assess if HPV-positive patients were more likely to be infected with HIV than HPV-negative patients, a χ^2 analysis of the data was completed. Only patients for whom conclusive HPV and HIV results were available were included in the analysis.

Results

During the 5-d training at Buzuruga District Hospital, a total of 614 women attended the screenings and 556 women were screened with VIA, of whom 10.6% (n=59) were VIA positive and 89.4% (n=499) were VIA negative. Of those who were VIA positive, 83.1% (n=49) received cryotherapy while 16.9% (n=10) did not due to suspicion of advanced cancer (n=7), refusal to receive cryotherapy (n=2) or pregnancy (n=1) (Figure 2).

The majority of screened women were sexually active young adults and middle-aged women, with 26.3% 20–29 y of age, 38.5% 30–39 y and 21.6% 40–49 y (Table 1). Furthermore, most of the women were multiparous: 26.8% had 1–2 children, 43.3% had 3–5 children, 12.0% had 6–10 children, 1.6% had ≥11 children and 7.4% were nulliparous. With regard to HIV status, 41.9% (n=233) of individuals were unaware of their status, but of those who were aware, 7.1% (n=23) self-reported being HIV positive and 92.9% (n=300) reported being HIV negative.

3.7 Data synthesis

Synthesis involves the collation, combination, and summary of the findings of individual studies included in the systematic review (56). Synthesis can be done quantitatively, using formal statistical techniques such as meta-analysis, or through a narrative approach (56). As well as drawing results together, synthesis should consider the strength of evidence, explore whether any observed effects are consistent across studies, and investigate possible reasons for any inconsistencies (56).

3.7.1 Statistical data analyses

In Study I and II, we included RCTs. Although RCTs generally can be combined quantitatively, the decision of combing results in a meta-analysis has several important clinical and statistical considerations. Clinical considerations can involve a qualitative assessment of a research question, results of RoB assessment, or other subjective criteria, such as the heterogeneity across included studies (68). Our decision to combine the data material in a meta-analysis was taken after thorough discussions within the review team. Meta-analysis is a complex methodology and guidelines recommend reviewers with limited statistical experience to work with experts in statistical analysis (54). I was involved in all steps of the statistical analysis in Study I and II, with guidance from my co-supervisor. I have contributed to creating the dataset, performing the analyses in Stata, and interpreting the results. As I had limited knowledge on statistics, I used textbooks (58;82) and attended statistical courses to obtain knowledge on statistical analyses.

Effect measure

We analyzed RCTs with binary outcomes (attended screening or not) where the natural effect measures are risk difference (RD) and relative risk (RR) (68). Although both RR and RD are perfectly valid ways of describing effect, there are several important matters related to the choice of effect measure in meta-analyses. For example, RR often suggests more optimistic intervention effects than RD, while RR has greater stability across different risk groups than RD (68). Moreover, RD reflects the baseline risk of individuals, whereas RR does not (68).

In Study I, we initially submitted our paper with RD as the chosen effect estimate. The meta-analyses showed that tailored educational interventions increase screening attendance by

9 percentage points for mammography (RD = 0.09, 95% CI, 0.04 - 0.14, $p < 0.001$; $I^2 = 78.4\%$, $p = 0.003$) and 19 percentage points for Pap test (RD = 0.19, 95% CI, 0.06 - 0.32, $p = 0.003$; $I^2 = 45.9\%$, $p = 0.086$). However, one of the journal's peer reviewers wanted us to use RR as effect estimate, because RR adds more consistency between studies than RD. The new analyses showed that the effectiveness of tailored education was 18% for mammography (RR = 1.18, 95% CI, 1.09 -1.28, $p < 0.001$), with low heterogeneity ($I^2 = 30.0$, $p = 0.237$), and 54% for Pap test (RR = 1.54, 95% CI, 1.14 - 2.09, $p = 0.005$), with substantial heterogeneity ($I^2 = 75.9\%$, $p < 0.001$). This example illustrates the complexity of choosing effect estimates, and how RR can suggest more optimistic results than RD.

Statistical models

Two statistical models can be used for performing a meta-analysis: fixed effect model (FE) and random effects model (RE) (68). The difference between the two models lies in how they treat variability between study results (68). The FE model is recommended if included studies are conducted under similar conditions with similar subjects. The FE model assumes that there exists one true effect and that variations between studies are caused by random variation (chance) (68). RE model rejects the idea of one common study effect and considers each included study to have its own underlying effect (68). The choice between these two models is not obvious and neither model is entirely satisfactory. The random effects model naturally incorporates study heterogeneity, whereas the fixed effects model does not (68). Thus, one common strategy is to use the fixed effects model if the study results are similar, and the random effects model if the study results show apparent inconsistency (68). Whichever model is used, the central idea for meta-analysis is to compute a common effect by assigning a weight to each study (68). Since small studies are more disposed to the role of chance, they must have less influence on the overall effect estimate than larger studies. Therefore, the overall effect is usually determined as the inverse of the study's estimated variance (68). In Study I and II, we chose RE models because the included RCTs were performed in diverse settings with differences in population and intervention. We reported the corresponding results for the fixed model to provide full transparency and give the reader an opportunity to compare the results.

Exploring heterogeneity

Inevitably, studies brought together in a systematic review will differ. Although any kind of variability among studies in a systematic review may be termed *heterogeneity*, it can be

helpful to distinguish between different types of heterogeneity. *Clinical heterogeneity* is variability in the participants, interventions, and outcomes studied (55). *Methodological heterogeneity* is variability in study design, outcome measurement tools, and RoB (55). *Statistical heterogeneity* is variability in the intervention effects being evaluated in the different studies and is a consequence of clinical or methodological diversity, or both, among the studies (55). Statistical heterogeneity is expressed in the observed intervention effects being more different from each other than one would expect due to random error (chance) alone (55).

Is it possible for multiple studies performed by different teams in different places with different methods to all end up with estimating the same underlying parameter? (68) The question is not *if* heterogeneity exists, but to *what degree*. We used I^2 statistic with its *p*-value to assess the heterogeneity. The I^2 statistic describes the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) (55). Thresholds for the interpretation of the I^2 statistic can be misleading since the importance of inconsistency depends on several factors. A rough guide to interpretation of the I^2 in the context of meta-analyses of randomized trials is as follows (55): 0-40% might not be important; 30-60% may represent moderate heterogeneity; 50-90% may represent substantial heterogeneity; 75-100% may represent considerable heterogeneity.

We created L'Abbé plots to visually examine the heterogeneity (68;83). In a L'Abbé plot, each primary study is presented as a circle point, where the size of the circle indicates the size of the trial. The L'Abbé plot has the observed proportion of events for the control group on the x-axis and the observed proportions of events for the intervention group on the y-axis (68). If there is low heterogeneity across studies, the points (studies) will form a straight line, while a strong violation indicates higher heterogeneity (68). Since no information about study precision is included in the data plotted in a L'Abbé plot, it is advisable to use plotting symbols proportional to the precision of the study estimate (83). Visual examination of L'Abbé plots allows inspection of the range of risks among the primary studies, to highlight excessive heterogeneity and to indicate which effect measure may be most consistent across studies (83). For example, in Study I, the points for mammography studies fall along the diagonal line, which suggests that RR could be a better effect estimate than the RD.

When statistical heterogeneity is observed, the reviewers should explore possible factors that may have contributed to differences, since they can be accounted for and taken into consideration when interpreting results and drawing conclusions. One way of exploring heterogeneity is to split studies into less heterogeneous groups and conduct subgroup analyses of particular characteristics (68). In Study I, we intended to conduct subgroup analyses of several characteristics that we had coded for, such as different types of educational intervention. However, there was an insufficient amount of information published in the primary studies to conduct subgroup analyses of these characteristics. Although it may be tempting to conduct post hoc exploratory analyses to revel a higher effect among a specific group, it is not recommended (56). Subgroup analysis should be restricted to a few potentially important characteristics where it is reasonable to suspect that a characteristic will interact with or modify the effect of an intervention (56-57).

Exploring publication bias

Although strict and thorough database searches should ensure that a meta-analysis captures as many relevant studies as possible, they cannot eliminate the risk of the absence of information. *Publication bias* refers to the absence of information caused by either missing studies or selective outcome reporting in published studies (68). Studies that report statistically significant results are more likely to be published, and published sooner, than studies without statistically significant results (68). Publication bias is particularly problematic in RCTs, as it leads to inflated and unreliable results regarding the effect of intervention. Identification and control of publication bias is therefore essential to preserve the validity of a meta-analysis (68).

The main graphical tool used to identify and visualize publication bias due to missing studies is the funnel plot (68;83). The funnel plot has effect estimates on the x-axis and measure of study precision (or study size) on the y-axis (68). All points are the same size, since the size of a study is already described using the vertical axis (83). The scale of the y-axis is reversed, so that studies with low precision are placed at the bottom, and studies with greater precision and many participants are placed at the top of the plot (68). The wide base is a result of small studies with large effect estimate variability. The narrow top is the large studies with small effect estimate variability (68). If there is no (or little) publication bias, the shape of the scatter plot resembles a symmetrical inverted funnel. Presence of large “holes” (most often seen close to the bottom) or asymmetry in the plot indicates publication bias -- although these

holes may have other causes, such as study heterogeneity, reporting bias, and chance (68). Funnel plots with fewer than 10 studies should be avoided or interpreted with great care (83). We also used the Harbord test to examine and interpret funnel plot asymmetry. The Harbord test examines whether the association between estimated intervention effects and a measure of study size is greater than what is expected to occur by chance (84-85).

3.7.2 Narrative synthesis

In Study III, our objective was to examine essential training components in cervical cancer screening programs implemented in low-resource settings. Initially, our aim was to explore quantitative quality indicators to explore the success of each training program. However, the quantitative data and estimates were too diversely reported between studies to link these data to effectiveness, as such reporting could contribute to clinically misleading results and erroneous conclusions. Therefore, we decided to perform a narrative synthesis of quantitative primary studies. This approach is in line with guidelines on systematic reviews, which underline that components of narrative synthesis can be usefully incorporated into a review that is primarily quantitative in focus (56). Narrative synthesis is a more subjective process than meta-analysis. And although narrative syntheses vary widely, they have in common that a simple description of the primary studies is not sufficient for a synthesis (56). The defining characteristic of narrative synthesis is the adoption of a textual approach that provides an analysis of the relationships within and between studies (56).

A general framework for synthesis can be used to guide the process of preparing for a synthesis, undertaking the synthesis, and interpreting and describing the results (55). We chose to use a publication on essential training components in VIA screening (86) to develop a framework. This publication, which reached international consensus among members of the Alliance for Cervical Cancer Prevention (ACCP), is considered a landmark publication within the research field. Informed by this publication and after discussions with screening experts at IARC, we developed a framework to conceptualize essential VIA training components (see Figure 12).

Figure 12

Description of Essential Training Components used as Framework

Essential training components	**Description**
1) Training course delivered over a defined period of time	The length of the training course should depend on the trainees' skill level at baseline and the amount of clinical practice available during training. The training should be long enough to ensure that the VIA screening services are delivered with both competence and confidence. The training should take place in a real clinical setting, if not the actual service-delivery site. A 5- to 10-day duration of training course is generally considered as appropriate for the trainees (clinicians, nurses, and midwives) to obtain adequate knowledge and clinical skills to deliver services competently. In a real health service setting it is challenging for the health professionals to leave their routine jobs for a longer duration to attend such targeted training.
2) Theory-based education	The training course should contain theory-based elements that cover the fundamental purpose, principles, and the specifics of the VIA procedure. There should be an emphasis on anatomy, physiology, and the etiology of cervical cancer at a level that is suitable for the selected trainees and that is highly practical. Understanding how VIA is performed and how to interpret the test by the nature of acetowhite reaction is required.
3) Hands-on competency-based skill acquisition	The training course should include practical hands-on experience that ensures that each trainee can practice the VIA technique on an adequate number of women and, ideally, they should be exposed to both test-positive and test-negative women.
4) Client counselling	Trainees should be trained to counsel women about the VIA screening process. Trainees should also know how to counsel a woman who is VIA-positive or who has cervical cancer, including the risks and benefits of the treatment methods offered. Training in counselling can take many forms, like watching video or real-life demonstrations, practicing in a group or counselling a client as part of the VIA procedure.
5) Visual aids	The training course should contain visual aids to show trainees the spectrum of cervical diseases and normal physiological changes that may be observed. Photographs, digital images, flash cards, and interactive CD-ROMs are valuable supplements to the learning process. Images should be in color and accompanied with VIA diagnosis from an expert for real-time comparison.
6) Competency assessment	At the end of the training course, the trainees should demonstrate performance of all the steps of a procedure correctly and in the right order without prompting from a trainer. The trainee's competency is best assessed with a performance checklist, and a specific score can be required as part of the successful completion of a training course.
7) Quality assurance	The training course should incorporate a quality-assurance module into the general training to allow the trainees to understand the philosophy of quality assurance, its necessity and required components, and how quality assurance will affect their overall performance. The depth of information presented may vary, but the overall value of quality assurance and how to train people in quality assurance are core concepts. Supplying information about quality assurance relates to the way(s) in which records are kept, information is documented, and programs are tracked. Teaching providers being effective supervisors is another required element of quality-assurance training.

We used this framework to answer two research questions:

1. Which essential training components have been described in VIA training programs?
2. How have these training components been carried out in different clinical settings?

To answer the first research question, we performed a dichotomy coding (yes or no) of each training component in each study. Since many authors did not describe their interventions in detail, probably due to word limitations of publications, we contacted all the corresponding authors to obtain more information about their study and training course. Out of 14 corresponding authors contacted, 10 responded. We also corresponded with primary authors on how we interpretated their findings and applied them in our framework. To answer the second research question, we synthesized extracted information on the intervention and provided examples of how the training had been carried out in different settings.

4 Results

The results from each study will be presented individually.

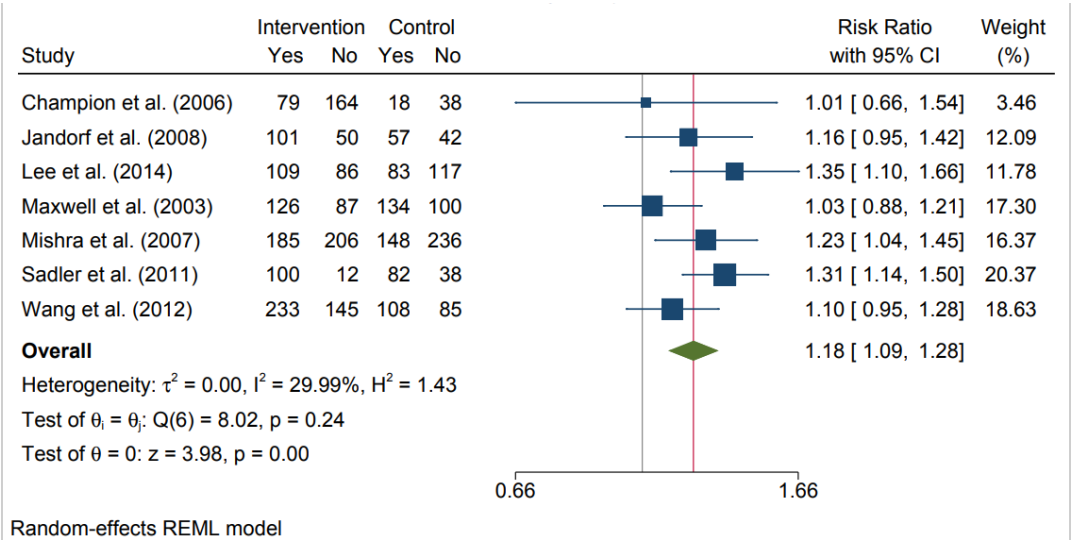
4.1 Article 1: Effectiveness of tailored educational intervention on breast and cervical cancer screening participation among ethnic minority women

The objective of the first article was to determine the effectiveness of culturally tailored educational interventions on screening attendance at mammography and Pap tests among ethnic minority women. Nine RCTs were eligible for inclusion in the systematic review -- 7 studies on mammography attendance (77,87-90) and 4 on Pap test attendance (91-92), where 2 studies measured both mammography and Pap test attendance (76;93).

For mammography screening attendance, the study showed that the overall RR was 1.18 (95% CI, 1.09 -1.28, $p < 0.001$) with low heterogeneity ($I^2 = 30.0$, $p = 0.237$), as shown in the forest plot (Figure 13). The information about heterogeneity contained in the forest plots was confirmed in the L'Abbé plot. Funnel plot asymmetry was explored by the Harbord test, and no statistically significant asymmetry was found ($p = 0.649$).

Figure 13

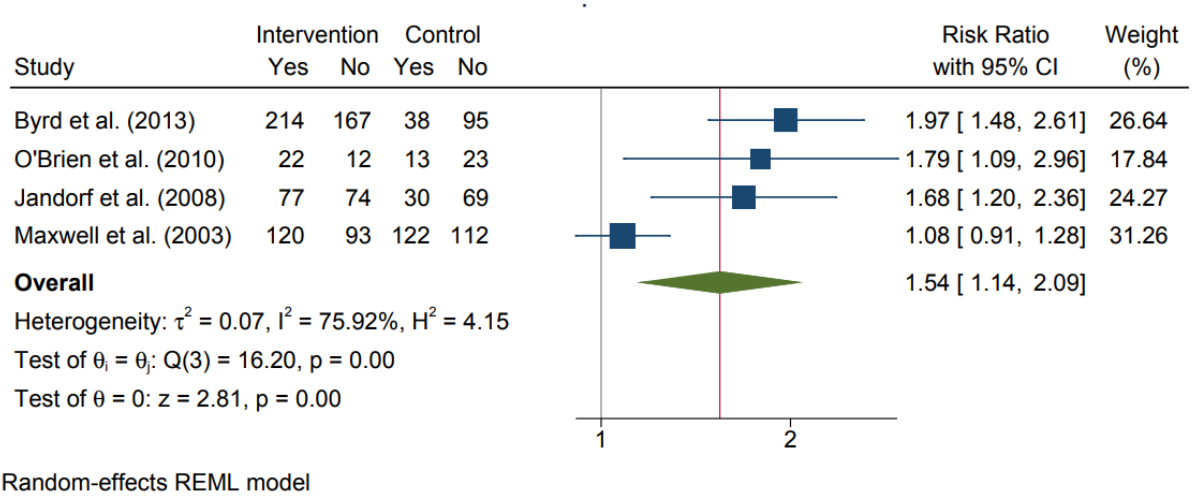
Forest Plot of Mammography Screening Attendance after Tailored Educational Interventions



For Pap test attendance, the RR was 1.54 (95% CI, 1.14-2.09, $p = 0.005$), with substantial heterogeneity ($I^2 = 75.9\%$, $p < 0.001$), as shown in the forest plot (Figure 14). The overall effect estimate must be interpreted within the limitations set by the low number of studies and substantial heterogeneity. The forest and L'Abbé plots confirmed that the effect measure for the Maxwell et al. study (76) differs significantly from the other included studies. When we deleted this study from the meta-analysis, the overall RR was 1.84 (95% CI, 1.50-2.24, $p < 0.001$), with $I^2 = 0.00\%$ ($p < 0.783$). Due to the low number of studies of the Pap test, no funnel plot was made.

Figure 14

Forest Plot of Pap Test Attendance after Tailored Educational Interventions



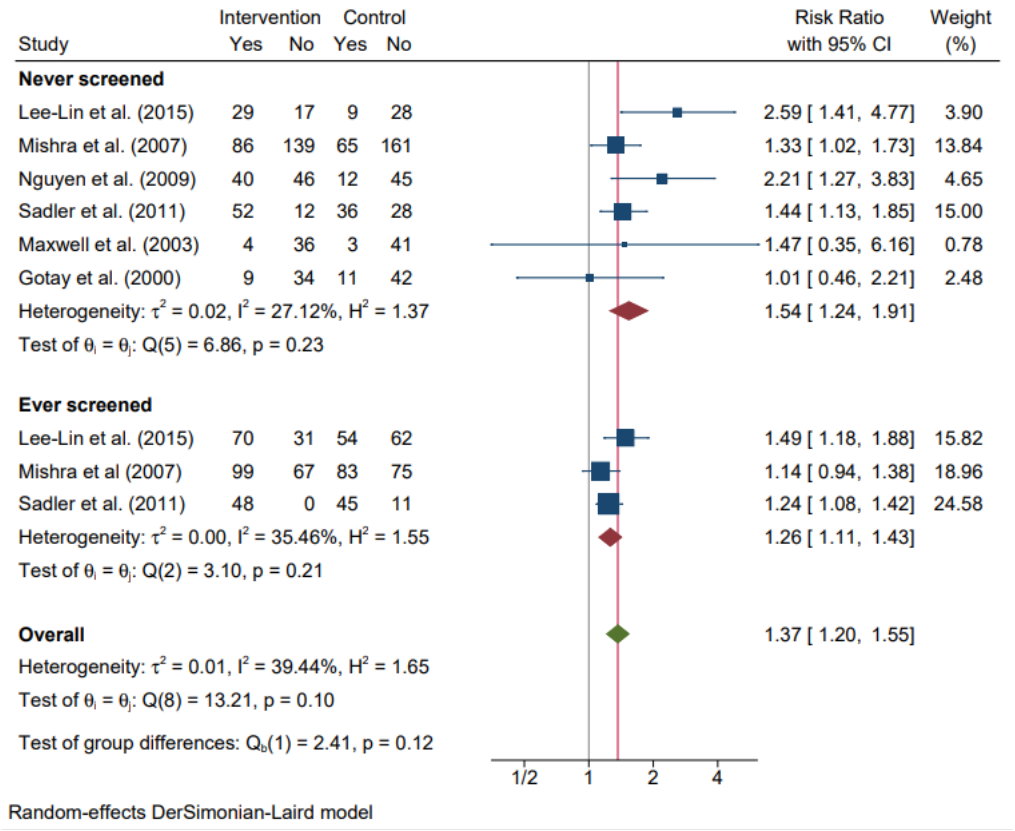
4.2 Article 2: Previous screening history may influence screening participation

The objective of the article was to explore whether women's screening histories impacted screening attendance after tailored education. The review process was carried out with the aim of exploring attendance at both mammography and Pap test. However, the Journal of Medical Care wanted only to publish results on mammography screening attendance. Six RCTs on mammography attendance were eligible for inclusion and included in the meta-analysis (73-77;89). The study showed that the RR for mammography attendance for never-screened women was 1.54 (95% CI, 1.24-1.91, $p < 0.001$), with low heterogeneity ($I^2 = 27.1\%$, $p = 0.231$), as shown in the forest plot (Figure 15). The RR for attendance for ever-screened women was 1.26 (95% CI, 1.11-1.43, $p < 0.001$), with low heterogeneity ($I^2 = 35.5\%$, $p =$

0.213). The overall effect estimates for ever-screened women must be interpreted within the limitations set by the low number of studies and the heterogeneity. The Funnel plot showed no asymmetry, confirmed by the Harbord test (p = 0.867).

Figure 15

Forest Plot of Mammography Screening Attendance among Never-Screened Women and Ever-Screened Women after Tailored Education



4.3 Article 3: Essential training components in cervical cancer screening in LMICs

The objective of our third article was to examine essential training components in cervical cancer screening programs implemented in low-resource settings. In total, 14 unique primary studies were included in this systematic review (94-108), including 2,847 trained health providers and 406,611 screened women. This study showed that VIA training courses were heterogeneous with substantial variability in their objectives, structure, content, duration, and reporting. Figure 16 outlines the reported training components in each of the included studies.

Figure 16

The Reporting of Essential Components for VIA Training Courses

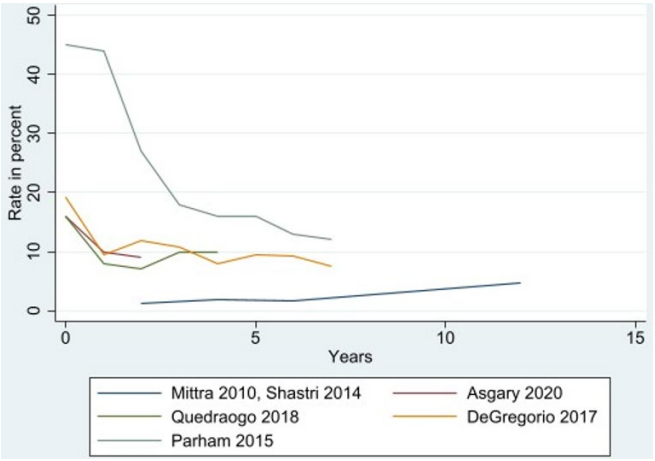
Study ID	*Duration*	*Theoretical education*	*Practical hands-on*	*Client counselling*	*Visual aids*	*Competency assessment*	*Quality assurance*
1	4 weeks	Y*	Y*	Y*	Y*	Y*	Y*
2	5 days	Y	Y			Y	
3	6 days	Y	Y	Y*	Y*	Y*	Y*
4	6 days	Y	Y	Y	Y	Y*	Y
5	5 / 10 days	Y	Y	Y	Y	Y*	Y*
6	3 days	Y	Y	Y*	Y*	Y*	
7	5 days	Y	Y*			Y*	
8	5 days	Y	Y	Y	Y	Y	Y
9	5 days	Y	Y		Y	Y	
10	2 weeks	Y	Y				
11	2 weeks	Y	Y*	Y*	Y	Y	Y*
12	8,5 weeks	Y	Y			Y	Y
13	1 week	Y	Y		Y	Y*	
14	6 days	Y*	Y*		Y*	Y	

* Additional information retrieved through email correspondence with corresponding author.

This study showed that most training courses were held over a period of 5 to 7 days, where theoretical education was combined with skill development, alongside the assessment of competence. It was not always clear how the trainees learned client counselling and quality assessment, or if visual aids were integrated in the training courses. Many programs provided extended training in the providers' clinical settings through additional supervision, feedback, and/or refresher training. Five studies reported serial point estimates of the VIA positivity rate over years and showed that the VIA positivity rates reached the expected level over time (between 5 and 10%) with provided prolonged training after the initial training course (Figure 17). These findings indicate that implemented VIA training programs have been carried out in line with international recommendations (86;109-114), but more importantly, that the training recommendations are feasible to implement in real settings.

Figure 17

VIA Positivity Rates Over Time



5 Discussion

In this Discussion chapter, I will first present our main findings and discuss the validity and reliability of these findings. Second, I will discuss some of the complexity involved in cultural and religious tailoring of educational interventions. Third, I will discuss what kind of knowledge we can gain by applying systematic reviews and meta-analysis to such a complex and intertwined phenomenon. Finally, I will discuss ethical considerations, before providing some thoughts on future research and practice.

5.1 Main findings

The focus on health equality and reducing disparities in disease burden has taken center stage in the past decade (6). Health policy and service research (HPSR) seeks to produce reliable and rigorous evidence about whether interventions have improved a specific problem and to assess how an intervention could be further improved. In breast and cervical cancer control, only strategies proved to be effective and successful should be proposed to a population (8). This means that interventions must be critically evaluated to help inform and prioritize evidence-based and resource-appropriate strategies and policy making (32). By conducting systematic reviews and applying both meta-analysis and narrative synthesis, we have identified, evaluated, and combined findings from relevant primary studies. However, as for any empirical finding, our results must be interpreted within its set of limitations and strengths. In systematic reviews, the validity and reliability of the findings can be threatened by how the review process was conducted and by which and how many primary studies were included (55).

5.1.1 Educational interventions for ethnic minority women

Many ethnic minority women do not attend breast and cervical cancer screening, and their low participation rates have been linked to a variety of complex and intertwined barriers (9;11). Tailored educational interventions for ethnic minority women aim to address deep-rooted influences on health behavior, including cultural influences, structural factors, and barriers (52). In this PhD project, we have summarized evidence on tailored educational interventions and found that they can increase participation among ethnic minority women by 18% for mammography screening and 54% for Pap test screening. These findings are

consistent with other reviews that have found that tailored educational interventions can increase cancer screening attendance and knowledge (9;11;62-63;115-119). Moreover, we have found that tailored education is more effective on ethnic minority women that have never been screened before than on women with previous screening history (54% vs. 26% on mammography attendance). Our findings suggest that women's screening history is an important and ignored variable that affects how effective tailored education is on screening attendance. To the best of our knowledge, our meta-analysis appears to be the first review that validated empirically the importance of women's screening history.

Although these findings indicate that tailored educational interventions can be considered for further implementation, the results must be carefully interpreted. Study I and II had a low number of included studies, especially the meta-analysis on Pap test attendance and on ever-screened women. In my opinion, Study I used a too narrow search strategy that might have resulted in missing studies. On the other hand, the low number of included studies is also related to our strict eligibility criteria, which we applied to increase the validity and reliability of our findings. In two previous meta-analyses on cancer screening interventions to ethnic minority women (62-63), the included primary studies contained samples of up to 60% Caucasian women, where it was impossible to determine whether the general findings were representative for ethnic minority women. In contrast to these previous meta-analyses (62-63), we included exclusively studies with samples containing only ethnic minority women and studies on tailored educational interventions in line with the theoretical framework on how to target interventions to ethnic minority women (52). We excluded studies on multilevel interventions, as effects could not then be attributed to the educational part alone. If we had chosen broader inclusion criteria, we could have included an additional 44 studies in our meta-analysis (see flow diagram of Study I). However, this would, in my opinion, have decreased the validity and reliability of our findings.

A meta-analysis is never better than the primary studies which it consists of (56). The internal validity of primary studies can therefore threaten the validity of the systematic review. Internal validity is the extent to which a study answers its research question and is closely related to RoB (68). The most striking bias across the primary studies is, in my opinion, the inclusion of participants that are up-to-date with their screening tests and how this is not taken into consideration in the statistical analyses and the interpretation of the results. It is well known that bias can occur when a study sample is not representative of the source population

(68). Therefore, it seems like a paradox that researchers who aimed to increase screening among under-screened women included women who had recently been screened. We have questioned why researchers would try to intervene with women who were already following the screening guidelines. This is an important ethical and economic question, but also an important question regarding internal validity. To explore this perspective, we conducted a separate review and found that the effectiveness of tailored intervention was higher among never-screened women than among ever-screened women. Owing to a lack of reported data, we were unable to further explore the effectiveness among ever-screened women, such as separating women who were recently screened versus those who were not compliant with the guidelines. The clinical implication of this finding is that different types of messages or interventions may be required for helping women to schedule and attend their first-time screening appointment (for never-screened women) versus helping them follow guideline-recommended repeated screening (for ever-screened women). The methodological implication is that researchers who aim to increase screening participation among under-screened populations, should not include participants who have recently been screened (or, at a minimum, provide separate analyses) as this can threaten the validity of the results.

The population of interest in Studies I and II was ethnic minority women living in HICs. However, only studies conducted in the USA were eligible for inclusion, which affects the external validity of our results. *External validity* refers to the practical utility of the results (68) and to the extent to which the results can be generalized to other populations and settings (55). For example, if a study enrolls participants who are not representative of the population who most commonly experience a particular clinical condition, the results may have limited generalizability to the wider population, but will not necessarily give a biased estimate of the effect in the highly specific population on which it is based (55). Therefore, the conclusions of a systematic review must be explicit so that the reader can properly assess the external validity (68). We highlighted in our publication that the findings in Study I may not be generalizable to countries other than the USA and that studies are needed to examine whether our findings are similar for ethnic minority women residing in other countries. A recent study with 10,820 Somali and Pakistani immigrant women in Norway showed that a community-based educational intervention targeting these women increased participation in cervical cancer screening (by 3 percentage points) (120). Another study with 10,360 immigrant women in Norway, conducted by the same research group, showed that an educational intervention targeting general practitioners increased participation of immigrant women in

cervical cancer screening (by 2%), especially among those who were not previously screened at baseline (121). These results suggest that immigrant women can benefit from educational interventions, both when the education targets the women themselves and when it targets healthcare providers. Even though the effect sizes were small, the clinical impact of these interventions might be of importance for the individual woman, as immigrant women are otherwise hard to reach (120).

The meta-analysis on Pap test attendance showed substantial statistical heterogeneity (I^2 = 75.9%, p = 0.001). To understand and explain this heterogeneity, we wanted to explore clinical differences (subgroups of ethnic minority groups, types of educational interventions, and socioeconomic factors) and methodological differences (subgroups of self-reported outcome and potential bias). Unfortunately, the primary studies reported insufficient data to statistically explore the statistical heterogeneity through subgroup analyses. We acknowledge that the participants included in our meta-analyses represent a heterogeneous group of women, with variation in age, ethnicity, and socioeconomic status. Moreover, the participants' personal values and beliefs are strongly interwoven with historical, cultural, and social dimensions. These core understandings of what life is all about can influence how each woman understands and responds to an educational intervention. In addition, tailored health interventions are -- by nature -- heterogeneous, as they often need to be composed of packages of components in order to be effective (56). This makes the evaluation of public health interventions complex because the constituent parts may act both independently and inter-dependently (56). It can also be difficult (or impossible) to define and measure the "active ingredient" of a successful multilevel intervention (56). Because of this complexity, traditional criteria for producing systematic reviews have been criticized for being too tightly defined and only partially fulfilling requirements for meta-analysis (56). In our articles, we have highlighted our concerns of clinical and statistical heterogeneity and called for carefulness when readers interpret our results.

Ethnic minority women can benefit from tailored educational interventions and increased participation rates at screening can reduce health inequality (6). However, ethnic minority women depend on stakeholders to act on health inequalities. To illustrate the health service inequality, we can take a closer look at the educational interventions that are already in place in many HICs. Most countries with a screening program have implemented educational approaches to reach the target population for screening, such as personal invitation letters,

social media campaigns, posters, and special awareness campaigns (e.g., the pink ribbon action). Similar actions have not been taken to reach minority women. In many countries, the screening information letter and governmental information on screening is only available in the official languages and targets the general population. To some extent, public information has for decades been created *by* the majority population *for* the majority population -- who in many HICs have better health literacy and higher social economic status than the ethnic minorities. Although implementation of tailored educational interventions alone is not enough to end the ethnic and social inequality affecting screening participation, women must, at a minimum, be provided information that will make them aware of the services available to them. This calls for special actions in providing such targeted educational interventions for ethnic minority women.

From a stakeholder perspective, one of the most important clinical questions arising from our findings is: What types of intervention work best in a particular setting and for a particular population group? Initially, our aim was to explore and compare the effectiveness of different types of educational approaches, such as media approach versus group education. A broad systematic review of immigrants in the USA highlighted that implementation of educational programs could increase participation at and knowledge of mammography screening and Pap test screening (11). Although this review had a much broader scope than our reviews, their findings underline that the most effective form of educational intervention is culturally appropriate interventions in which immigrant women with specific cultural or religious beliefs and practices receive education on how to maintain good breast and cervical health without fear or stigma (11). Although we could not statistically compare the types of education, we identified tailored educational approaches that we considered relevant for further implementation. In line with our results from the forest plot and RoB assessment, we describe below three examples of tailored educational intervention from the included primary studies, which stand out as significantly positive for increasing screening participation.

Tailored education can be provided to women in their local beauty salon by trusted cosmetologists. This educational approach was explored with African American women and increased their attendance at breast cancer screening by 31% (RR 1.31, 95% CI, 1.14-1.50) (89). In this study, the cosmetologists were asked to proactively engage their clients in discussions about breast cancer screening guidelines. The cosmetologists received individual training from an African American ancestral storyteller to enhance their ability to pass along

their health promotion messages (89). Ancestral storytelling is considered an integral element of African culture and a trusted way of spreading information among family and friends. The beauty salons were given a soft plastic breast cancer model to show women how a breast cancer lump felt. The salon also displayed breast cancer brochures and wallposters, all with images of African American women (89). By providing the education in local beauty salons, the tailored approach implied that the educational program was emanating from within the community, rather than as a university-imposed program.

Tailored education can also be provided to couples in interactive group sessions in their own language where information is provided by a male physician. This educational approach was explored with Korean immigrants in the USA and increased their attendance at breast cancer screening by 35% (RR 1.35, 95% CI, 1.10-1.66) (88). In this study, the intervention slogan was “Healthy Family, Healthy Wife” -- emphasizing the importance of a husband’s support in promoting family health by encouraging cancer screening. The intervention was held as a group session, where Korean couples watched a tailored educational video before a discussion of the content with each other and in plenum. The intervention messages were designed around Korean cultural values that had been identified in previous studies (88). To convey the importance of receiving screening and to reduce the women’s feelings of embarrassment regarding talking to male physicians about female cancers, the educational video featured a male Korean American physician. The couples were also given further discussion activities as homework to increase the support provided by Korean American husbands for their wives.

Finally, tailored education can be provided through specially developed educational booklets in women’s own languages, through skill building and behavioral exercises and interactive group discussion sessions. This educational approach was explored with Samoan women in the USA and increased their screening attendance by 23% (RR 1.23, 95% CI, 1.04-1.45) (77). In this study, the educational booklets featured Samoan artwork, scenery, and pictures of Samoans with information especially addressing culture-specific myths and beliefs held by Samoans (77). The health educators were retired Samoan nurses who the women identified as socially similar to them. The group discussions were held in the Samoan language, including familiar terms and phrases, roleplay, and skills-enhancing techniques (77). The discussions addressed identified screening barriers among Samoan women, such as cost, fear of radiation, embarrassment, pain, and navigation.

These examples illustrate how stakeholders and clinicians can tailor educational interventions for ethnic minority women. Although the scientific evidence is generally supportive of education delivered via one-to-one sessions, community interventions, telephone, and small media (9), the World Cancer Report states that the most effective interventions to reduce cancer disparities occur when key institutions and leaders in local settings commit to the implementation of multicomponent interventions that target specific obstacles and barriers (6). The educational interventions above demonstrate the importance of in-depth knowledge of the target population and involvement of the minority communities -- in line with the frameworks on proportionate universalism and culturally sensitive educational interventions for ethnic minority women.

HPSR emphasizes that interventions that are found to be effective can be considered for further implementation in clinical practice (53). However, implementation of new services and targeted approaches are not without costs. Population-based cancer screening programs are extremely resource-demanding services, and it is important to ensure that these services are used as intended and that people benefit optimally and equally (6). For example, if services were used as intended and available for all women in Europe, there could be 4,000 fewer deaths from cervical cancer and 17,000 fewer deaths from breast cancer each year (6). It is important that stakeholders act on assisting the disadvantaged to use screening services. Previous meta-analyses have implied that access-enhancing interventions are the most effective interventions for promoting breast and cervical cancer screening among ethnic minority women, followed by community education (62-63). However, offering educational interventions in clinical practice has a far lower financial cost when compared to increasing the availability of screening equipment. This financial aspect should be taken into consideration when policy makers discuss approaches to increase screening participation among ethnic minority women.

5.1.2 Educational interventions in low-resource settings

Educational interventions hold a key position in enhancing cervical cancer screening access and participation in LMICs since the screening programs depend on high quality training of health providers (27). In this PhD project, we have summarized evidence on VIA training programs for health providers implemented in low-resource settings. We found that the training programs were carried out in line with international recommendations (86;109-114),

but, more importantly, that the training recommendations are feasible to implement in real settings. These findings are optimistic because successful screening programs have shown to reduce cervical cancer incidence and mortality among women in LMICs (6). For example, studies have shown that a single round of screening can reduce cervical cancer mortality in India by 50% for women screened with HPV, and by 35% for women screened by VIA (122-123). It is possible to eventually eliminate cervical cancer, and to achieve a drastic reduction in cervical cancer incidence in successive age-specific cohorts in the foreseeable future, if the currently available prevention and early detection interventions are implemented with high coverage and quality assurance (5). However, many women live beyond access to screening services, and in regions with limited resources and fragile health systems, cancer contributes to the cycle of poverty (6). In all countries, but most pressingly in the poorest, adequate numbers of appropriately skilled health providers at the local level are fundamental to extending coverage and improving the quality of care (124). Investment in training and retaining health providers is vital to the strengthening of healthcare systems (124). Implementation of successful educational programs to health providers is paramount in increasing screening access and participation for women in LMICs.

From a HPSR perspective, an educational intervention proposed to stakeholders must provide some guidance on the educational requirements. The WHO Academy is currently collaborating with IARC to develop a comprehensive learning program for providers of cervical cancer screening and treatment. Such an international standard for educational approaches is needed. Designing an effective training program can be a complex process, and although most of the principles, steps, and interpretations remain similar, the contexts and settings may differ (86). Our initial aim was to explore the effectiveness of each training program in order to provide more robust evidence of what stakeholders should implement in their health systems. Unfortunately, the quality indicators were too diversely reported in the primary studies to link these data to the effectiveness of training programs as doing this could contribute to clinically misleading results and erroneous conclusions. However, our narrative synthesis did produce new knowledge on the body of evidence on VIA training. By providing illustrating examples of how the training components have been carried out in different clinical settings, we hope that our findings can be useful for clinicians and stakeholders who want to implement or scale up a cervical screening program.

Our findings indicate that educational interventions on VIA training should be considered for further implementation in LMICs. However, we acknowledge that our review has limitations. To increase the validity and reliability of our review, we created a search strategy that was comprehensive, critically assessed by experts, and thoroughly tested by the review team. However, this search strategy was initially designed to identify studies on provider-directed interventions on cancer screening participation among disadvantaged populations. When we had finished the initial study selection process, we had 139 primary studies on provider-directed interventions, with 35 studies on VIA training. To decrease the clinical heterogeneity across included studies, the review team decided to move forward on a review on VIA training. Therefore, an essential limitation in our review is that our searches are missing some relevant keywords, such as VIA. However, the searches included relevant keywords related to cervical cancer screening, provider training, and screening participation. We searched manually in reference lists to identify potentially missing studies. Since transparent reporting of review decisions enables readers to assess the reliability of a review for themselves (55), we chose to highlight this limitation in our article.

We performed a narrative synthesis of the extracted data, which is a more subjective process than performing a meta-analysis. It is important that the approaches used are rigorous and transparent to reduce the potential for bias (56). By conducting the study selection process in Covidence, we aimed to increase the reliability and transparency of our review because the software assists the data management process and documents decisions made throughout the review process (55). To synthesize the primary studies, we developed a framework to conceptualize essential VIA training components and applied that framework to the literature. To assess the robustness of our synthesis, we contacted all the primary authors and corresponded with them about how we interpreted and applied their findings in our framework. This technique is adopted from qualitative research and can be used to increase the validity of review findings (56). In my opinion, the correspondence with primary authors influenced the final version of our framework and provided us with useful insights into the possible accuracy and generalizability of our synthesis.

With good training and sustained quality assurance and monitoring, screening of women with VIA followed by appropriate management of screen-positive women can reduce cervical cancer incidence and mortality (27). However, VIA performance varies widely. Studies have shown that the VIA positivity rate in a general population of women aged 30 to 60 years

ranges between 5% and 10% (125). If the test positivity is too low, there is a possibility of missing the disease, while if it is too high, there is a greater possibility of false positives (125). Our findings suggest that the VIA positivity rates can reach an expected level over time when health providers are trained in courses and given prolonged training. However, studies have shown that the VIA positivity rates have high variability between countries[126] and within the same program or setting (127). Although research studies have shown a high sensitivity, around 75%, the sensitivity reported from some real programmatic settings have ranged from 25% to 82% (128). This is essentially due to the subjective nature of the test. The best way to compensate for that is to train the providers rigorously and organize periodic refresher training and mentoring.

In our review, we have shown examples of how the educational interventions can target different health providers, depending on the available workforce in each specific setting. For example, nurses were trained in Botswana because they were familiar with performing pelvic exams and more available than physicians (105), whereas community health workers were trained in Nigeria because nurses and doctors were largely absent in rural communities (101). Studies have shown that a screener's (physician, nurse, or health worker) capacity does not influence the test accuracy of VIA, although it is known that VIA is more accurate when it is performed by screeners who receive regular training (129). This is important given the shortage of physicians in LMICs, especially in rural and remote regions. It would be worthwhile for policy makers to consider training non-physicians to screen women at the community level and to refer them to physicians when appropriate (130). Task shifting in cancer screening is found to improve access, promote program sustainability, and to be cost-effective (96;130). However, regardless of which health providers are being trained, the screening programs' success depends on high quality training, monitoring, and evaluation -- which must be performed continuously at all levels (113).

The paradigm of cervical cancer screening is evolving rapidly (27). The WHO updated their guidelines on cervical cancer screening in July 2021 and is now recommending HPV detection as the gold standard for primary testing for cervical cancer screening (25). Despite these new recommendations, educational interventions to health providers will remain important in LMICs in the future. In countries with enough resources to implement HPV as the primary screening test, the health providers must be trained to visually triage women eligible for cryotherapy based on the women's HPV status (and not on the presence of

acetowhite lesions). Although screening with HPV has many advantages, an important limitation is the low specificity of the test, which means that a high proportion of women with a positive HPV test will not necessarily have cervical pre-cancer or cancer (27). A triage test can be used to reduce the referral for all HPV-positive women for colposcopy and/or treatment. In settings where high-quality cytology is not available due to a lack of human and financial resources, HPV-positive women may be triaged with VIA (27). In settings with a high prevalence of HIV, health providers will perform VIA to triage women (27). Therefore, educational interventions to health providers will continue to hold a key position in enhancing cervical cancer screening access and participation in LMICs.

5.2 Culturally and religiously tailored education

During my PhD mid-evaluation, the first opponent asked me: In your opinion, what is a "false religious belief", or the opposite, a "correct religious belief"? The reason for this question being raised was that in our first article, I had written that barriers to screening participation include "*religious barriers, such as false religious beliefs (fatalism)*" (131). Although I had referred to another systematic review that had used this terminology (20), I felt embarrassed because I had not critically reflected upon the meaning of this term. During and after my mid-evaluation, I discussed the cultural and religious dimension of tailoring an educational program with several colleagues with diverse professional backgrounds. Through these discussions, I tried to get a deeper understanding of what it really means when educational interventions are described as *religiously* or *culturally* tailored? Theoretically, it means that the education has taken into consideration important values, traditions, or beliefs that are represented within a specific group. However, in clinical practice, providing culturally tailored education is not necessarily easy or straight-forward. HPSR seeks to unpack the behavior, reactions, and interconnectedness of health systems and the people within those systems (53). By providing an overview, HPSR can help to illuminate not only what works, but for whom, and under what circumstances. By using fatalism as an illustrating example, I will now discuss some of the complexity that lies within cultural and religious tailoring of educational interventions and provide examples of how values and beliefs, such as fatalism, can be constructively approached.

Fatalistic beliefs about cancer often characterize cancer as a predetermined condition that is unavoidable regardless of personal action (132). Fatalistic attitudes can be expressed as "*We pray to Allah that we don't get the disease*" (49) or "*One was going to die the day they were supposed to die and participating in health prevention would not change this outcome*" (133). This is unquestionably a powerful belief. In research, the concept of fatalism is portrayed as a passive acceptance of life's difficulties and has a negative connotation (132). Fatalism can be expressed and understood as a cultural or religious belief or value. Yet, what is considered as religious and as cultural is not easy to differentiate, as these terms are strongly interwoven: Religion is part of culture and vice versa. Regardless of position, fatalism creates images of God as an opponent to cancer screening, and those with fatalistic beliefs as irrational -- from a medical point of view. To understand how religious fatalism can be constructively approached and integrated in educational interventions on cancer screening, we need to understand how religious fatalism relates to rationality.

Many educational interventions are grounded on the Health Belief Model (HBM). The HBM is based on a rational choice model that assumes adherence to Western biomedical claims is rational (134). In short, the HBM suggests that a person's belief in an illness or disease (e.g., cancer), together with a person's belief in the effectiveness of the recommended health behavior or action (e.g., screening), will predict how a person will adopt a behavior (e.g., attend screening) (135). Though the HBM and social cognitive theories as frameworks have provided useful perspectives on screening attendance and non-attendance, the theoretical model has several limitations. First, the HBM is widely used in Western, White middle-class contexts, but the model is not always feasible for adopting in studies of the preventive health behavior of other populations (134). Second, the HBM proposes fairly linear relations between cause and effect and, as a result, could give rise to rather simplistic ideas about interventions to promote screening attendance (21). The model indicates that if a person merely had (or acquired) the right beliefs, or if obstructive barriers were simply removed, screening attendance would improve (21).

Ever since fatalism was identified as a phenomenon in conflict with making supposedly rational behavioral changes (encouraged by the healthy lifestyle movement), fatalism has presented health education with a serious pedagogic problem (136). The negative perspective regarding fatalism is founded on the idea that an entire cultural structure of fatalism exists which must be either destroyed or modified -- if the goal of healthy-lifestyles-for-all is to be

attained (136). Recently, researchers claimed that interventions must be implemented to *decrease* or *disrupt* fatalism (137). However, we argue that there is a major difference between approaching religious fatalism as "something" that needs to be disrupted than as something that needs to be taken seriously. Educators and stakeholders need to acknowledge how strongly integrated fatalistic views might be in a person's belief system. We risk ignoring people's core values by viewing fatalism exclusively as a barrier. Furthermore, fatalism is by nature not necessarily addressable through brief educational sessions, as culture and religion influence people's lives, values, beliefs, and social networks. Furthermore, one might question how fatalism, when referred to as "false religious beliefs" can be respectfully addressed in educational interventions. When educators embrace terminologies like *false* religious beliefs, they convey an unspoken message to others that theirs is an illegitimate belief. Health educators with a negative view of fatalistic beliefs may end up having disrespectful approaches that could, potentially, result in non-attendance.

Fatalism can become visible when questions about cancer screening are raised because it puts in question what actions people can take to change the outcome of an event. For example, Somali women in the USA expressed their view that accepting the will of God is important and that prevention has no impact if God plans for someone to get sick (133). Healthcare providers who do not share similar religious beliefs can find it hard to understand why some women do not attend cancer screening (133). This can be related to the dissonance between medical knowledge and fatalistic attitudes on screening (47). However, clinicians, educators, and stakeholders must acknowledge that explanatory paradigms that are not necessarily grounded in scientific evidence appear logical and rational to a believer in such a paradigm (134). Regarding educational interventions on cancer screening, such an acknowledgement provides the basis for working with the different rationalities in play and not nourishing a conflict by describing science as rational and religious beliefs as irrational.

To summarize, complexity is inherent in the cultural and religious tailoring of educational interventions. Values and beliefs (whether they are religious or not) are strongly interwoven with historical, cultural, and social dimensions. These core understandings of what life is all about must be taken into consideration and respected when providing educational interventions. Neither the different rationalities in play nor the images of God are necessarily in conflict with attending cancer screening. A study on cultural beliefs among Latinas found that God's presence often complemented rather than obscured the women's own efforts to

participate at cancer screening (132). Another study found that Islamic religious messages can encourage women to get screenings as part of their efforts to stay healthy (138). These findings demonstrate that educational interventions do not have to disrupt religious fatalism in order to increase screening attendance. "*Allah has created these screening tests and it's up to us to use them*" is an illustrating example of an educational approach that neither challenges God's sovereignty (in other words, accepting fatalism) nor abandons insight from natural science. Such approaches are in line with the theoretical framework that emphasizes that interventions to ethnic minority women must work *with* cultural or religious values.

5.3 Scientific position

A question that I have been frequently asked during this PhD project is: What kind of knowledge can you gain by applying meta-analysis to such a complex and intertwined cultural, social, and relational phenomenon? One of the most important aspects of cancer screening from a HPSR perspective is the substantial inequality in screening access and participation -- between continents, countries, and social groups of society. Within this topic, there are many important research questions and several methodological approaches that would have been relevant to address. However, a PhD project is restricted to exploring a precise part of a specific phenomenon. Our overall aim in this project was to provide new knowledge on educational interventions on breast and cervical cancer screening. Researchers are encouraged to systematically explore whether interventions implemented in clinical practice are effective or not. Meta-analyses can provide such answers by applying advanced mathematical methods that consider both statistical and methodological strengths and limitations (56). Moreover, meta-analyses are appropriate for examining tendencies of society, health outcomes, and challenging established truths (56). However, as previously discussed, the meta-analytic approach comes with a set of limitations. When researchers apply statistical methods to human, social, and cultural phenomena, they risk losing sight of the fundamental bases of human life – its meaning, purpose, intention, and consciousness (139). From this perspective, one should rightly be critical about what kind of knowledge researchers gain by applying meta-analysis to cultural and social phenomena. Statistical analyses should not replace knowledge based on people's own experiences but should be considered a valuable supplement. The development of knowledge must be understood as an ongoing process under constant expansion, change, and revision. To contribute to that

process, researchers will need to acknowledge, interpret, and build on each other's work -- regardless of scientific position.

The Norwegian philosopher Arne Næss claimed that mathematics can be used to explore life experiences, but that pure mathematics is without application in itself -- it must be interpreted subjectively for theory to emerge (140). In this PhD project, our subjective and qualitative interpretation of the quantitative estimates in Study I gave us the idea to explore tailored education among never-screened and ever-screened women. In Study II we found that the education was more effective among never-screened women versus ever-screened women (54% vs. 26%). This finding suggests that women's screening history is an important and ignored variable that affects how effective tailored education is on mammography screening attendance. To our knowledge, our meta-analysis is the first review exploring this perspective. One of the strengths of meta-analysis is that it can serve as a tool for critical assessment and contribute to the discovery of new interpretations and perspectives. In our opinion, this new perspective on the importance of screening history emerged because of our subjective interpretation. We did not interpret the numbers exclusively, but also understood the participants as individuals who had a choice to attend screening or not. The Norwegian philosopher Hans Skjervheim argued that the fundamental basis of human existence is that human behavior follows an intention -- it is not causal, but meaningful (141). From this perspective, it becomes clear that women who have recently performed a screening test can act differently than women who have never attended screening -- especially after having attended a tailored educational intervention. This example illustrates how new knowledge can be produced when applying meta-analysis methodology to such a complex phenomenon.

5.4 Ethical considerations

5.4.1 Balanced information on screening

Over the past decades, there have been ongoing debates about the balance of benefits over harm in screening. Although these questions are outside the scope of this thesis, there are important ethical considerations about how educational interventions provide information on screening to women. The overall objective of tailored educational intervention is to provide women information that they are not necessarily accessing through the existing healthcare service. For example, for some minority groups, this can mean receiving the information in

their own language or from persons in their local communities. The objective is that the educational intervention will contain information about all possible outcomes of the screening so that the women can decide whether they want to participate at screening or not. Several terms have been used to describes this process, such as *informed decision-making* and *informed choice* (8).

If autonomy of choice is the leading ethical principle, then women should be provided with balanced evidence-based information to enable them to make informed decisions about their healthcare (8). However, informational materials and educational approaches on screening have been criticized as being pro-screening and biased -- especially information on breast cancer screening (8). The dominant approach has been to emphasize screening benefits to improve women's participation in screening programs. In late modern societies, discourses on women's participation in mammography screening have been characterized by morality, responsibility, and obligation to participate in available medical examinations (8). Text analyses of information material have shown that women are often not being informed about the potential harms of screening, such as the likelihood of having a false-positive result, about overdiagnosis and overtreatment, or about the possibility of receiving a non-cancerous diagnosis (8). About half of the women in a British study had never heard of overdiagnosis before being confronted with the term during a survey (8). Moreover, women have been found to be significantly more willing to participate at screening if the benefit was expressed as relative risk reduction, rather than either absolute risk reduction or all-cause mortality (8). These results demonstrate that women's choice (or willingness) to participate in screening is influenced by how information is framed (8). From an ethical point of view, this calls for cautiousness when information material is planned and implemented.

Tailored educational interventions for ethnic minority women stand in a special position regarding informed choice. The theoretical framework suggests five principles for tailoring, including working with cultural or religious values that can motivate behavioral change. Many tailored educational interventions use respected community role models to spread or provide the information. Although such approaches can be effective in increasing screening attendance, some argue that such tailoring of the educational interventions influences women's informed choice. The tailoring can provide an underlying message of a particular choice being "more ethical" than another choice (8). The information is therefore no longer balanced. This standpoint raises questions about who should decide what the most ethical

choice of action (participating at screening or not) is, and, moreover, which information should be provided to women and under what circumstances.

5.4.2 Ethical considerations in systematic reviews

Ethical considerations in systematic reviews are not typically discussed explicitly (142). As an illustration, *ethics* is not listed as a term in the index of the second edition of the handbook *An Introduction to Systematic Reviews* (142). Unlike primary researchers, systematic reviewers do not collect deeply personal, sensitive, or confidential information from participants. Systematic reviewers use publicly accessible documents as evidence and are seldom required to seek an institutional ethics approval before commencing a systematic review (142). Nevertheless, in the past four decades, systematic reviews have evolved to become more methodologically inclusive and play a powerful role in influencing policy, practice, further research, and public perception (142). Hence, ethical issues associated with what and how systematic reviews are produced and used have serious implications. As with any other research approaches, systematic reviews can have disadvantages, as well as benefits.

Ethical considerations in systematic review and meta-analysis are closely related to how reviewers choose to combine, present, and interpret their results. Although RCTs are considered the best study design for evaluating the effect of an intervention, the studies can be implemented or reported in such a way that the findings are likely to be seriously biased and therefore of little value in decision making. For example, studies with large sample sizes are more likely to attract research funding, be submitted for publishing, and get published in journals with a high impact factor (142). Research reporting significantly positive effects of an intervention is more likely to be submitted for publishing by primary researchers and be accepted for publishing by journal editors (142). Paradoxically, published studies with significant results can reflect the empirical evidence, while unpublished studies without significant results can reflect the true effect of an intervention. As a result, the effectiveness of educational interventions can get overemphasized in published literature. To maximize an ethical impact of review findings, the reviewers must communicate the insights gained through the review and ensure audience-appropriate transparency (142). In this PhD project, the review teams had thorough discussions about how to summarize findings from the primary studies. In Study I and II, we found it appropriate to combine the results in a meta-analysis, while in Study III, we considered it more appropriate to conduct a narrative

synthesis. In our publications, we have presented our findings and discussed the validity and reliability of these findings to accommodate our ethical responsibility as systematic reviews.

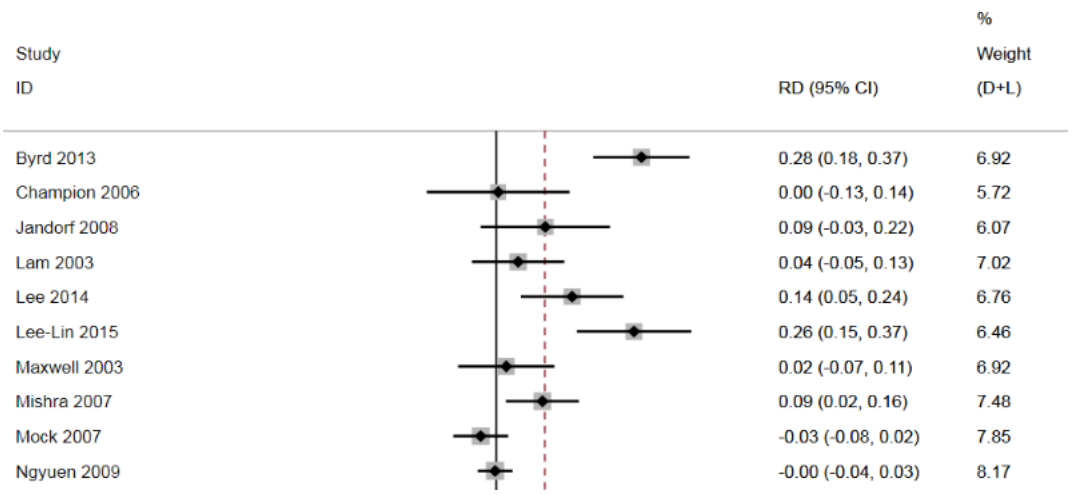
Reviewers can uncover suspected misconduct in the published literature (55). Misconduct includes fabrication or falsification of data or results, plagiarism, and research that does not adhere to ethical norms (55). Reviewers need to be aware of scientific misconduct because the inclusion of fraudulent material could undermine the reliability of a review's findings (55). Also, reviewers extracting estimates for meta-analyses can uncover reporting bias. In this PhD project, we found examples of reporting bias and selective reporting of results. Previously in this thesis, I used Nguyen's study (73) as an illustrative example. In Nguyen's study, 1,100 Vietnamese American women were included in an RCT on educational intervention to improve mammography screening participation. The study reported that participants ever-screened increased from 89.6% to 91.8% (+2.2 percentage points) in the control group, and from 84.1% to 91.6% (+7.5 percentage points) in the intervention group (73). Notably, more participants took a screening test in the control group than in the intervention group after the intervention. These results may be difficult to publish. But the risk difference between the groups was significant, with an odds ratio of 3.6 and a *p*-value of less than 0.001. Nguyen and his colleagues reported that the probability of a Vietnamese American woman participating in mammography screening increases by 260% if she receives this educational intervention. Moreover, that it is less than one percent likely that this result occurred by chance. However, we can see that the risk difference is entirely caused by the substantial difference in the number of ever-screened women at baseline (84.1% in the intervention group vs. 89.6% in the control group). In my opinion, this is an example of an unethical mistreatment and reporting of results.

Such publication bias can influence the perception of the truth and become amplified through spin citation. Meta-analyses seek truth by combining and assessing effects and statistical differences in the results. Reviewers of meta-analyses must ethically consider whether to include studies like Nguyen's study in the overall estimate. As we have seen, the results are clearly biased, and some guidelines suggest excluding studies with high risk of bias. However, if Nguyen's results are imputed in a forest plot, the lack of intervention effect can be revealed (Figure 18). The systematic reviewers can therefore consider including Nguyen's study and conduct subgroup analyses to explore how the overall estimates are influenced by

specific bias. In this way, meta-analyses can serve as a powerful tool to explore and detect publication bias.

Figure 18

Illustrative Example of how Nguyen's Results Would be Presented in a Hypothetical Forest Plot



Selective or incorrect reporting of empirical results is unethical in many ways. First and foremost, researchers are obligated to follow ethical research regulations and scientific standards of honesty (143). Thus, scientific work is not only about seeking truth, but also about telling the truth. The international ethical guidelines for health-related research involving humans emphasize researchers' obligation to ensure openness, integrity, and accountability (144). In addition to juridical obligations, researchers have ethical obligations related to the clinical consequences of presenting interventions as effective. When stakeholders are presented research on effective intervention, they may want to implement the intervention in clinical practice. Such implementation can spread hope to target populations and consume limited financial resources. Moreover, other researchers can be convinced that necessary solutions to a health problem have been identified, which can hinder further exploration of other potential effective solutions. A unique aspect of scientific publication is the fact that each researcher and each individual article is dependent on other researchers' work and other articles (143). This collaboration is the strength of science, but also its vulnerability. The meta-analytic methodology is perhaps the most illustrating example of this vulnerability because it literally consists of other researchers' work. Therefore, the quality of

the research literature is completely dependent on both good research ethics and good publishing ethics.

5.4.3 Ethical responsibilities to act on inequality

During this PhD project, some colleagues argued that our research project is unethical because we can mask substantial heterogeneity by analyzing, discussing, and referring to the participants as "ethnic minority women" and "disadvantaged populations". We acknowledge that -- as in the case of any broad grouping of individuals – these women can have more differences from each other than similarities. However, this PhD project is centered on the WHO's definition of the disadvantaged populations and on previous research. Disparities in cancer outcomes are largely linked to socioeconomic status, ethnicity, and race -- cases where the differences can be substantially reduced if interventions are put in place (6). Worldwide, more than 2 million women are diagnosed with breast or cervical cancer every year, but where a woman lives (i.e., in which country, region, or setting in relation to the nearest healthcare services) and how she lives (e.g., poor or otherwise socially disadvantaged) largely determines whether or not she develops one of these cancers, how early she presents to healthcare services, and her access to affordable, good-quality diagnostic and treatment services (32). This pattern is especially striking for cervical cancer, since around 85% of women diagnosed and 87% of women who die from cervical cancer live in LMICs. Proven approaches exist to reduce these gross inequities, yet most women have few opportunities to access these life-saving interventions (32).

Reducing health inequalities is one of the main public health challenges of our times (5). However, it is still not well understood which interventions and strategies are the most effective to achieve this goal. Having knowledge of which interventions and strategies are the most effective implies that the target population and the relevant determinants in which to intervene have been identified, and that the types of inequalities that we aim to decrease have been clearly specified (5). The primary focus of this project has been on tailored educational intervention. For ethnic minority women, the educational interventions require a degree of selectivism because universalism ignores existing inequalities (50). Therefore, we argue that researchers have ethnical responsibilities to address and focus on health inequality -- not ignore it. To quote the WHO's Commission on Social Determinants of Health (124):

> The poor health of the poor, the social gradient in health within countries, and the marked health inequities between countries are caused by the unequal distribution of power, income, goods, and services, globally and nationally, the consequent unfairness in the immediate, visible circumstances of people's lives ... and their chances of leading a flourishing life. This unequal distribution of health-damaging experiences is not in any sense a natural phenomenon but is the result of a toxic combination of poor social policies and programs, unfair economic arrangements, and bad politics. (p.1)

The fact is that where a woman lives and her socioeconomic, ethnocultural, or migration status can mean the difference between life and death from breast and cervical cancer (32). The burden that arises from breast or cervical cancer is a preventable tragedy for millions of women and their families every year (32). From a HPSR perspective, interventions that have been found to be effective in reducing health inequality should be considered for further implementation in clinical practice. I am not claiming that the results from this PhD project can be a game changer for implementation of educational interventions. However, we found that tailored educational interventions can increase screening participation among ethnic minority women -- especially among women who have never participated in screening before. Moreover, we found that VIA training programs can be implemented in line with international recommendations in real settings. These results can be used to guide stakeholders to act on this health inequality problem.

Stakeholders hold enormous power regarding which health problems need to be acted on or not. Cancer control has received significantly less attention compared with other public health issues from governments in many LMICs despite a significant and increasing disease burden (5). The striking inequalities in cancer burden and outcomes between HICs and LMICs are exemplified by the fact that, although 60% of the estimated 14 million new cases and 75% of the estimated 8.8 million cancer deaths per year occur in LMICs, only 5% of global spending on cancer is directed at these countries and most LMICs spend less than 2% of their gross domestic product on health (5). While most women who develop breast or cervical cancer in a HIC will survive, the opposite is true for women in most LMICs (32). For healthcare systems to improve, stakeholders need to invest in and spread new knowledge about what works. The main principles of action include measuring the problem, evaluating action, expanding the knowledge base, developing a trained workforce, and raising public awareness (5;124). But

evidence is only one part of what swings policy decisions – political will and institutional capacity are important too.

Women worldwide are depending on stakeholders to act on health inequalities. Diseases that mainly affect women present particular challenges in terms of achieving health equality, although there is overwhelming evidence suggesting that investments in women's health provides substantial economic returns (32). But where do women's cancers fit in the global health agenda? In HICs, there is notable advocacy, media attention, and funding for research and treatment of cancer, but in many resource-poor settings, breast, cervical, and other gynecological cancers are effectively neglected diseases (32). That these diseases cause substantial disability, premature death, disruption of family life, and loss to the national economy, thus exacerbating the cycle of poverty, has largely been ignored by the global health and development community (32). Many of the structural problems faced by deprived women are generated at a national or even higher level and may not be solved by local solutions (5). If systematic differences in health for different groups of people are avoidable by reasonable action, their existence is, quite simply, unfair (124) and action towards reduction of health inequities -- between and within countries -- is therefore an ethical obligation.

5.5 Further research and practice

In the past years, there has been increased focus on implementation science research, which is the scientific study of methods that facilitate the uptake of evidence-based practice and research into regular use by practitioners and policy makers (6). Ethnic minority women depend on stakeholders to act and implement services that can ensure that the women, at a minimum, are provided information that will make them aware of the screening services available to them. Our findings indicate that tailored educational interventions can increase the women's participation at breast and cervical cancer screening. Future research would need to focus on how tailored educational interventions can be systematically and successfully implemented into healthcare services. For example: How can national cancer registries provide balanced and tailored information on screening to ethnic minority women? An essential challenge for such national services is that tailored educational approaches both call for some standardization (universal framework) and tailoring (selectivism). Future research may want to explore this balance, because although one size of educational intervention may

not fit all target populations, some guidance on the minimum standardized requirements will be very helpful for stakeholders and clinicians. In addition to the characteristics of the educational intervention, the capacity of the public health infrastructure and the health delivery system to implement and sustain a new strategy is fundamental to the success of the intervention. Future research may want to explore whether specific components of multilevel educational interventions are particularly beneficial -- for example education combined with navigation or education combined with self-collection tests -- and how these strategies can be implemented in line with the capacity and infrastructure of the healthcare system. By applying the principles of implementation science, tailored educational interventions for ethnic minority women can move from research to practice.

The scientific evidence for reducing inequalities in cancer globally calls for an expansion of both research focus and investments in prevention (5). Future research and practice on educational interventions may want to consider how educational interventions can include information both on the importance of screening and primary prevention. For example, the WHO's goal on eliminating cervical cancer depends on a high coverage of both HPV vaccination of adolescent girls and screening of adult women. The integration of HPV vaccine programs with HPV-based testing in screening programs is an attractive approach which has the potential to reduce the burden of cervical cancer, particularly in LMICs (30). Improving both primary and secondary prevention of breast and cervical cancer must remain a key priority for women's health globally for decades to come (31). Educational interventions on breast cancer control in LMICs must continue to focus on increasing the community awareness of risk reduction and promote breast cancer early diagnosis and treatment, in line with the international recommendations of essential interventions for cancer control in LMICs (32). Moreover, as countries are gradually shifting towards HPV-based screening, future practice needs to ensure that educational interventions target both the community and the health providers -- to address the rationale of the shift to ensure there is not a reduction in screening acceptability using HPV testing (31).

6 Conclusions

By conducting systematic reviews and applying both meta-analysis and narrative synthesis, we have identified, evaluated, and combined findings from relevant primary studies. We found that tailored educational interventions increased participation among ethnic minority women by 18% for mammography screening and 54% for Pap test screening. Moreover, we found that tailored education was more effective on ethnic minority women that have never been screened before than on women with previous screening history (54% vs. 26% on mammography attendance). Finally, we found that the training programs on cervical cancer screening in LMICs were carried out in line with international recommendations, but, more importantly, that the training recommendations are feasible to implement in real settings. These results must be interpreted within its set of limitations and strengths.

The results of this PhD thesis contribute to a better understanding of educational interventions on cancer breast and cervical cancer screening. Our results, combined with findings from other studies, suggest that tailored educational interventions can be considered for further implementation in clinical practice. Defining evidence-based interventions is a necessary first step in the implementation of effective strategies in a healthcare system. Evidence-based healthcare can provide access to core and higher-quality information on what works, resulting in a higher likelihood of successful programs being implemented, more efficient use of resources, and reduced health inequality. Further knowledge is needed about how tailored educational interventions can be systematically and successfully implemented into healthcare services. By applying the principles of implementation science, tailored educational interventions can move from research to practice.

7 References

1. World Health Organization. Cancer [Internet]. [Cited 2021 November 01]. Available from: https://www.who.int/news-room/fact-sheets/detail/cancer
2. National Cancer Institute. NCI dictionaries [Internet]. [Cited 2021 November 29]. Available from: https://www.cancer.gov/publications/dictionaries
3. International Agency for Research on Cancer. Glossary and definitions [Internet]. [Cited 2021 August 26]. Available from: https://canscreen5.iarc.fr/?page=help
4. The World Bank. World bank open data [Internet]. [Cited 2021 November 29]. Available from: https://data.worldbank.org/
5. Vaccarella S, Lortet-Tieulent J, Saracci R, Conway DI, Straif K, Wild CP, editors. Reducing social inequalities in cancer: evidence and priorities for research. IARC scientific publication no. 168. Lyon: International Agency for Research on Cancer; 2019.
6. Wild C, Weiderpass E, Stewart B, editors. World cancer report: cancer research for cancer prevention. Lyon: International Agency for Research on Cancer; 2020.
7. Cochrane Methods Equity. PROGRESS-Plus [Internet]. [Cited 2021 November 15]. Available from: https://methods.cochrane.org/equity/projects/evidence-equity/progress-plus
8. International Agency for Research on Cancer. Breast cancer screening. Volume 15. IARC handbooks of cancer prevention. Lyon: International Agency for Research on Cancer; 2016.
9. Priaulx J, Turnbull E, Heijnsdijk E, Csanádi M, Senore C, de Koning HJ, et al. The influence of health systems on breast, cervical and colorectal cancer screening: an overview of systematic reviews using health systems and implementation research frameworks. J Health Serv Res Policy. 2020;25(1):49-58.
10. Pan American Health Organization. Plan of action for cervical cancer prevention and control 2018-2030. Washington, DC: Pan American Health Organization; 2018.
11. Adunlin G, Cyrus JW, Asare M, Sabik LM. Barriers and facilitators to breast and cervical cancer screening among immigrants in the United States. J Immigr Minor Health. 2019;21(3):606-658.
12. Powe BD, Johnson A. Fatalism as a barrier to cancer screening among African-Americans: Philosophical perspectives. J Relig Health. 1995;34(2):119-126.
13. De Los Monteros KE, Gallo LC. The relevance of fatalism in the study of Latinas' cancer screening behavior: A systematic review of the literature. Int J Behav Med. 2011;18(4):310-318.

14. International Agency for Research on Cancer. Cancer today [Internet]. [Cited 2021 November 20]. Available from: Cancer Today (iarc.fr)
15. International Agency for Research on Cancer. CanScreen5 [Internet]. [Cited 2021 November 03]. Available from: https://canscreen5.iarc.fr/
16. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37,513,025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018;391(10125):1023-1075.
17. Latif F, Helgeland J, Bukholm G, Bukholm IR. Ethnicity differences in breast cancer stage at the time of diagnosis in Norway. Scand J Surg. 2015;104(4):248-253.
18. Jack RH, Davies EA, Møller H. Breast cancer incidence, stage, treatment and survival in ethnic groups in South East England. Br J Cancer. 2009;100(3):545-550.
19. Bhargava S, Moen K, Qureshi SA, Hofvind S. Mammographic screening attendance among immigrant and minority women: a systematic review and meta-analysis. Acta Radiol. 2018;59(11):1285–1291.
20. Azami-Aghdash S, Ghojazadeh M, Sheyklo SG, Daemi A, Kolahdouzan K, Mohseni M, et al. Breast cancer screening barriers from the womans perspective: a meta-synthesis. Asian Pac J Cancer Prev. 2015;16(8):3463-3471.
21. Bhargava S, Hofvind S, Moen K. Gender, letters, relatives, and God: mediating actors in mammographic screening among Pakistani women in Norway. Acta Radiol Open. 2019;8(9):2058460119875015.
22. Wardlow H, Curry RH. “Sympathy for my body”: Breast cancer and mammography at two Atlanta clinics. Med Anthropol. 1994;16(1-4):319-340.
23. Rajaram SS, Rashidi A. Minority women and breast cancer screening: the role of cultural explanatory models. Prev Med. 1998;27(5):757-764.
24. Donkor A, Lathlean J, Wiafe S, Vanderpuye V, Fenlon D, Yarney J, et al. Factors contributing to late presentation of breast cancer in Africa: A systematic literature review. Arch Med. 2015;8(2.2):1-10.
25. World Health Organization. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. Geneva: World Health Organization; 2021.
26. World Health Organization. Global action plan for the prevention and control of noncommunicable diseases 2013-2020. Geneva: World Health Organization; 2013.

27. Mittal S, Basu P, Lucas E. Atlas of visual inspection of the cervix with acetic acid for screening, triage, and assessment for treatment [Internet]. International Agency for Research on Cancer. [Cited 2021 October 11]. Available from: https://screening.iarc.fr/atlasvia.php
28. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015;65(2):87-108.
29. Vaccarella S, Lortet-Tieulent J, Plummer M, Franceschi S, Bray F. Worldwide trends in cervical cancer incidence: impact of screening against changes in disease risk factors. Eur J Cancer. 2013;49(15):3262-3273.
30. Vaccarella S, Laversanne M, Ferlay J, Bray F. Cervical cancer in Africa, Latin America and the Caribbean and Asia: regional inequalities and changing trends. Int J Cancer. 2017;141(10):1997-2001.
31. Ogilvie G, Nakisige C, Huh WK, Mehrotra R, Franco EL, Jeronimo J. Optimizing secondary prevention of cervical cancer: recent advances and future challenges. Int J Gynecol Obstet. 2017;138:15-19.
32. Ginsburg O, Bray F, Coleman MP, Vanderpuye V, Eniu A, Kotha SR, et al. The global burden of women's cancers: a grand challenge in global health. Lancet. 2017;389(10071):847-860.
33. Arnold M, Razum O, Coebergh J-W. Cancer risk diversity in non-Western migrants to Europe: an overview of the literature. Eur J Cancer. 2010;46(14):2647-2659.
34. Yoo W, Kim S, Huh WK, Dilley S, Coughlin SS, Partridge EE, et al. Recent trends in racial and regional disparities in cervical cancer incidence and mortality in United States. PloS One. 2017;12(2):e0172548.
35. Musselwhite LW, Oliveira CM, Kwaramba T, de Paula Pantano N, Smith JS, Fregnani JH, et al. Racial/ethnic disparities in cervical cancer screening and outcomes. Acta Cytol. 2016;60(6):518-526.
36. Vasilevska M, Ross SA, Gesink D, Fisman DN. Relative risk of cervical cancer in indigenous women in Australia, Canada, New Zealand, and the United States: a systematic review and meta-analysis. J Public Health Policy. 2012;33(2):148-164.
37. Aminisani N, Armstrong BK, Canfell K. Cervical cancer screening in Middle Eastern and Asian migrants to Australia: a record linkage study. Cancer Epidemiol. 2012;36(6):394-400.
38. Azerkan F, Sparén P, Sandin S, Tillgren P, Faxelid E, Zendehdel K. Cervical screening participation and risk among Swedish-born and immigrant women in Sweden. Int J Cancer. 2012;130(4):937-947.

39. Campari C, Fedato C, Iossa A, Petrelli A, Zorzi M, Anghinoni E, et al. Cervical cancer screening in immigrant women in Italy: a survey on participation, cytology and histology results. Eur J Cancer Prev. 2016;25(4):321-328.
40. Møen KA, Kumar B, Qureshi S, Diaz E. Differences in cervical cancer screening between immigrants and nonimmigrants in Norway: a primary healthcare register-based study. Eur J Cancer Prev. 2017;26(6):521.
41. Rondet C, Lapostolle A, Soler M, Grillo F, Parizot I, Chauvin P. Are immigrants and nationals born to immigrants at higher risk for delayed or no lifetime breast and cervical cancer screening? The results from a population-based survey in Paris metropolitan area in 2010. PLoS One. 2014;9(1):e87046.
42. Brzoska P, Abdul-Rida C. Participation in cancer screening among female migrants and non-migrants in Germany: A cross-sectional study on the role of demographic and socioeconomic factors. Medicine. 2016;95(30).
43. Leinonen MK, Campbell S, Ursin G, Tropé A, Nygård M. Barriers to cervical cancer screening faced by immigrants: a registry-based study of 1.4 million women in Norway. Eur J Public Health. 2017;27(5):873-879.
44. Morrison TB, Flynn PM, Weaver AL, Wieland ML. Cervical cancer screening adherence among Somali immigrants and refugees to the United States. Health Care Women Int. 2013;34(11):980-988.
45. Kwok C, White K, Roydhouse JK. Chinese-Australian women's knowledge, facilitators and barriers related to cervical cancer screening: a qualitative study. J Immigr Minor Health. 2011;13(6):1076.
46. Marlow LA, Waller J, Wardle J. Barriers to cervical cancer screening among ethnic minority women: a qualitative study. J Fam Plann Reprod Health Care. 2015;41(4):248-254.
47. Anaman-Torgbor JA, King J, Correa-Velez I. Barriers and facilitators of cervical cancer screening practices among African immigrant women living in Brisbane, Australia. Eur J Oncol Nurs. 2017;31:22-29.
48. Johnson CE, Mues KE, Mayne SL, Kiblawi AN. Cervical cancer screening among immigrants and ethnic minorities: a systematic review using the Health Belief Model. J Low Genit Tract Dis. 2008;12(3):232-241.
49. Gele AA, Qureshi SA, Kour P, Kumar B, Diaz E. Barriers and facilitators to cervical cancer screening among Pakistani and Somali immigrant women in Oslo: a qualitative study. Int J Womens Health. 2017;9:487-296.

50. Carey G, Crammond B, De Leeuw E. Towards health equity: a framework for the application of proportionate universalism. Int J Equity Health. 2015;14(1):1-8.
51. Business Dictionary. Information [Internet]. [Cited 2019 August 20]. http://www.businessdictionary.com/definition/information.html (Not available).
52. Netto G, Bhopal R, Lederle N, Khatoon J, Jackson A. How can health promotion interventions be adapted for minority ethnic communities? Five principles for guiding the development of behavioural interventions. Health Promot Int 2010;25(2):248-257.
53. World Health Organization. Alliance for health policy and systems research [Internet]. [Cited 2021 November 16]. Available from: https://ahpsr.who.int/
54. Botella J, Gambara H. Doing and reporting a meta-analysis. Int J Clin Health Psychol. 2006;6(2):425-440.
55. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. Cochrane handbook for systematic reviews of interventions, second edition. Hoboken, New Jersey: John Wiley & Sons; 2019.
56. Centre for Reviews and Dissemination. Systematic reviews. CRD guidance for undertaking reviews in health care. York: University of York; 2009.
57. Laake P, Benestad HB, Olson B, editors. Research in medical and biological sciences. from planning and preparation to grant application and publication. Academic Press; 2015.
58. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to meta-analysis. Hoboken, New Jersey: John Wiley & Sons; 2009.
59. Zawacki-Richter O, Kerres M, Bedenlier S, Bond M, Buntins K, editors. Systematic reviews in educational research: methodology, perspectives and application. Wiesbaden: Springer Nature; 2020.
60. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339:b2535.
61. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
62. Han HR, Kim J, Lee JE, Hedlin HK, Song H, Song Y, et al. Interventions that increase use of Pap tests among ethnic minority women: a meta-analysis. Psychooncology. 2011;20(4):341-351.
63. Han HR, Lee JE, Kim J, Hedlin HK, Song H, Kim MT. A meta-analysis of interventions to promote mammography among ethnic minority women. Nurs Res. 2009;58(4):246.

64. Hannigan A, O'Donnell P, O'Keeffe M, MacFarlane A. How do variations in definitions of "migrant" and their application influence the access of migrants to health care services? Copenhagen: World Health Organization; 2016.
65. Khokhar T, Serajuddin U. Should we continue to use the term "developing world"? [Internet]. World Bank Blogs. [Published 2015 November 16; Cited 2021 November 01]. Available from: https://blogs.worldbank.org/opendata/should-we-continue-use-term-developing-world
66. Haraldstad A-MB, Christophersen E. Literature searches and reference management. In: Laake P, Benestad HB, Olsen BR, editors. Research in medical and biological sciences. from planning and preparation to grant application and publication. Academic Press; 2015. p. 125-166.
67. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
68. Fagerland MW. Evidence-based medicine and systematic reviews. In: Laake P, Benestad HB, Olsen BR, editors. Research in medical and biological sciences. From planning and preparation to grant application and publication. Academic Press; 2015. p. 431-461.
69. Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
70. Moreno-Peral P, Conejo-Cerón S, Rubio-Valera M, Fernández A, Navas-Campaña D, Rodríguez-Morejón A, et al. Effectiveness of psychological and/or educational interventions in the prevention of anxiety: a systematic review, meta-analysis, and meta-regression. JAMA Psychiatry. 2017;74(10):1021-1029.
71. Lam TK, McPhee SJ, Mock J, Wong C, Doan HT, Nguyen T, et al. Encouraging Vietnamese-American women to obtain Pap tests through lay health worker outreach and media education. J Gen Intern Med. 2003;18(7):516-524.
72. Mock J, McPhee SJ, Nguyen T, Wong C, Doan H, Lai KQ, et al. Effective lay health worker outreach and media-based education for promoting cervical cancer screening among Vietnamese American women. Am J Public Health. 2007;97(9):1693-1700.
73. Nguyen TT, Le G, Nguyen T, Le K, Lai K, Gildengorin G, et al. Breast cancer screening among Vietnamese Americans: a randomized controlled trial of lay health worker outreach. Am J Prev Med. 20091;37(4):306-313.

74. Lee-Lin F, Nguyen T, Pedhiwala N, Dieckmann N, Menon U. A breast health educational program for Chinese-American women: 3-to 12-month postintervention effect. Am J Health Promot. 2015;29(3):173-181.
75. Gotay CC, Banner RO, Matsunaga DS, Hedlund N, Enos R, Issell BF, et al. Impact of a culturally appropriate intervention on breast and cervical screening among native Hawaiian women. Prev Med. 2000;31(5):529-537.
76. Maxwell AE, Bastani R, Vida P, Warda US. Results of a randomized trial to increase breast and cervical cancer screening among Filipino American women. Prev Med. 2003;37(2):102-109.
77. Mishra Shiraz rB, Cathrine Crespi, Cindy Chang, Pat Luce, Claudia Baquet. Results of a randomized trial to increase mammogram usage among Samoan women. Cancer Epidemiol Biomarkers Prev. 2007;16(12):2594-2604.
78. Taylor VM, Jackson JC, Yasui Y, Kuniyuki A, Acorda E, Marchand A, et al. Evaluation of an outreach intervention to promote cervical cancer screening among Cambodian American women. Cancer Detect Prev. 2002;26(4):320-327.
79. McPhee SJ, Nguyen TT, Shema SJ, Nguyen B, Somkin C, Vo P, et al. Validation of recall of breast and cervical cancer screening by women in an ethnically diverse population. Prev Med. 2002;35(5):463-473.
80. Rauscher GH, Johnson TP, Cho YI, Walk JA. Accuracy of self-reported cancer-screening histories: a meta-analysis. Cancer Epidemiol Biomarkers Prev. 2008;17(4):748-757.
81. Allgood KL, Rauscher GH, Whitman S, Vasquez-Jones G, Shah AM. Validating self-reported mammography use in vulnerable communities: findings and recommendations. Cancer Epidemiol Biomarkers Prev. 2014;23(8):1649-1658.
82. Mehmetoglu M, Jakobsen TG. Applied statistics using Stata: a guide for the social sciences. Sage Publications; 2016.
83. Anzures-Cabrera J, Higgins JP. Graphical displays for meta-analysis: an overview with suggestions for practice. Res Synt Methods. 2010;1(1):66-80.
84. Harbord RM, Egger M, Sterne JA. A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints. Stat Med. 2006;25(20):3443-3457.
85. Sterne JAC, Sutton AJ, Ioannidis JPA, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ. 2011;343:d4002.

86. Blumenthal PD, Lauterbach M, Sellors J, Sankaranarayanan R. Training for cervical cancer prevention programs in low-resource settings: focus on visual inspection with acetic acid and cryotherapy. Int J Gynecol Obstetr. 2005;89:S30-S37.
87. Champion VL, Springston JK, Zollinger TW, Saywell Jr RM, Monahan PO, Zhao Q, et al. Comparison of three interventions to increase mammography screening in low income African American women. Cancer Detect Prev. 2006;30(6):535-544.
88. Lee E, Menon U, Nandy K, Szalacha L, Kviz F, Cho Y, et al. The effect of couples intervention to increase breast cancer screening among Korean Americans. Oncol Nurs Forum. 2014;41(3):185-193.
89. Sadler GR, Ko CM, Wu P, Alisangco J, Castaneda SF, Kelly C. A cluster randomized controlled trial to increase breast cancer screening among African American women: the black cosmetologists promoting health program. J Natl Med Assoc. 2011;103(8):735-745.
90. Wang JH, Shwartz MD, Brown RL, Maxwell AE, Lee MM, Adams IF, et al. Results of a randomized controlled trial testing the efficacy of a culturally-targeted and a generic video on mammography screening among Chinese-American immigrants. Cancer Epidemiol Biomarkers Prev. 2012;21(11):1923-1932.
91. Byrd TL, Wilson KM, Smith JL, Coronado G, Vernon SW, Fernandez-Esquer ME, et al. AMIGAS: a multicity, multicomponent cervical cancer prevention trial among Mexican American women. Cancer. 2013;119(7):1365-1372.
92. O'Brien MJ, Halbert CH, Bixby R, Pimentel S, Shea JA. Community health worker intervention to decrease cervical cancer disparities in Hispanic women. J Gen Intern Med. 2010;25(11):1186-1192.
93. Jandorf L, Bursac Z, Pulley L, Trevino M, Castillo A, Erwin DO. Breast and cervical cancer screening among Latinas attending culturally specific educational programs. Prog Community Health Partnersh. 2008;2(3):195-204.
94. Shastri SS, Mittra I, Mishra GA, Gupta S, Dikshit R, Singh S, et al. Effect of VIA screening by primary health workers: randomized controlled study in Mumbai, India. J Natl Cancer Inst. 2014;106(3):dju009.
95. Nuranna L, Aziz MF, Cornain S, Purwoto G, Purbadi S, Budiningsih S, et al. Cervical cancer prevention program in Jakarta, Indonesia: see and treat model in developing country. J Gynecol Oncol. 2012;23(3):147-152.
96. Martin CE, Tergas AI, Wysong M, Reinsel M, Estep D, Varallo J. Evaluation of a single-visit approach to cervical cancer screening and treatment in Guyana: Feasibility, effectiveness and lessons learned. J Obstet Gynaecol Res. 2014;40(6):1707-1716.

97. Ouedraogo Y, Furlane G, Fruhauf T, Badolo O, Bonkoungou M, Pleah T, et al. Expanding the single-visit approach for cervical cancer prevention: successes and lessons from Burkina Faso. Glob Health Sci Pract. 2018;6(2):288-298.
98. Shiferaw N, Salvador-Davila G, Kassahun K, Brooks MI, Weldegebreal T, Tilahun Y, et al. The single-visit approach as a cervical cancer prevention strategy among women with HIV in Ethiopia: successes and lessons learned. Glob Health Sci Pract. 2016;4(1):87-98.
99. Shikha S, Smita J, Nayanjeet C, Ruchi P, Parul S, Uma M, et al. Experience of a 'Screen and treat'program for secondary prevention of cervical cancer in Uttar Pradesh, India. J Obstet Gynacol Res. 2020;46(2):320-327.
100. Talama GC, Shaw M, Maloya J, Chihana T, Nazimera L, Wroe EB, et al. Improving uptake of cervical cancer screening services for women living with HIV and attending chronic care services in rural Malawi. BMJ Open Qual. 2020;9(3):e000892.
101. Awolude OA, Oyerinde SO, Akinyemi JO. Screen and triage by community extension workers to facilitate screen and treat: task-sharing strategy to achieve universal coverage for cervical cancer screening in Nigeria. J Glob Oncol. 2018;4:1-10.
102. Bernstein M, Hari A, Aggarwal S, Lee D, Farfel A, Patel P, et al. Implementation of a human papillomavirus screen-and-treat model in Mwanza, Tanzania: training local healthcare workers for sustainable impact. Int Health. 2018;10(3):197-201.
103. Parham GP, Mwanahamuntu MH, Kapambwe S, Muwonge R, Bateman AC, Blevins M, et al. Population-level scale-up of cervical cancer prevention services in a low-resource setting: development, implementation, and evaluation of the cervical cancer prevention program in Zambia. PLoS One. 2015;10(4):e0122169.
104. DeGregorio G, Manga S, Kiyang E, Manjuh F, Bradford L, Cholli P, et al. Implementing a fee-for-service cervical cancer screening and treatment program in Cameroon: challenges and opportunities. Oncologist. 2017;22(7):850.
105. Ramogola-Masire D, de Klerk R, Monare B, Ratshaa B, Friedman HM, Zetola NM. Cervical cancer prevention in HIV-infected women using the "see and treat" approach in Botswana. J Acquir Immune Defic Syndr. 2012;59(3).
106. Asgary R, Staderini N, Mthethwa-Hleta S, Lopez Saavedra PA, Garcia Abrego L, Rusch B, et al. Evaluating smartphone strategies for reliability, reproducibility, and quality of VIA for cervical cancer screening in the Shiselweni region of Eswatini: A cohort study. PloS Med. 020;17(11):e1003378.
107. Yeates K, Erwin E, Mtema Z, Magoti F, Nkumbugwa S, Yuma S, et al. Smartphone-enhanced training, QA, monitoring, and evaluation of a platform for secondary prevention of

cervical cancer: Opportunities and challenges to implementation in Tanzania. JCO Glob Oncol. 2020;6:1114-1123.
108. Mittra I, Mishra GA, Singh S, Aranke S, Notani P, Badwe R, et al. A cluster randomized, controlled trial of breast and cervix cancer screening in Mumbai, India: methodology and interim results after three rounds of screening. Int. J. Cancer. 2010;126(4):976-984.
109. JHPIEGO. Cervical cancer prevention. Guidelines for low-resource settings. Guide for trainers. Baltimore, Maryland: Jhpiego; 2007.
110. Alliance for Cervical Cancer Prevention. Planning and implementing cervical cancer prevention and control programs: a manual for managers. Seattle: Alliance for Cervical Cancer Prevention; 2004.
111. International Agency for Research on Cancer. TUTORIAL: a training course in visual inspection with 5% acetic acid (VIA) [Internet]. IARC Learning; 2015. [Cited 2021 November 01]. Available from: https://learning.iarc.fr/edp/courses/tutorial-course-via/
112. World Health Organization. Comprehensive cervical cancer control: a guide to essential practice. Geneva: World Health Organization; 2006.
113. World Health Organization. Comprehensive cervical cancer control: a guide to essential practice - second edition. Geneva: World Health Organization; 2014.
114. Sellors JW, Sankaranarayanan R. Colposcopy and treatment of cervical intraepithelial neoplasia: a beginner's manual. Lyon: International Agency for Research on Cancer; 2003.
115. Chan DN, So WK. A systematic review of randomised controlled trials examining the effectiveness of breast and cervical cancer screening interventions for ethnic minority women. Eur J Oncol Nurs. 2015;19(5):536-553.
116. Duffy SW, Myles JP, Maroni R, Mohammad A. Rapid review of evaluation of interventions to improve participation in cancer screening services. J Med Screen. 2017;24(3):127-145.
117. Lu M, Moritz S, Lorenzetti D, Sykes L, Straus S, Quan H. A systematic review of interventions to increase breast and cervical cancer screening uptake among Asian women. BMC Public Health. 2012;12(1):1-16.
118. Glick SB, Clarke AR, Blanchard A, Whitaker AK. Cervical cancer screening, diagnosis and treatment interventions for racial and ethnic minorities: a systematic review. J Gen Intern Med. 2012;27(8):1016-1032.

119. Luque JS, Logan A, Soulen G, Armeson KE, Garrett DM, Davila CB, et al. Systematic review of mammography screening educational interventions for Hispanic women in the United States. J Cancer Edu. 2019;34(3):412-422.
120. Qureshi SA, Igland J, Møen K, Gele A, Kumar B, Diaz E. Effect of a community-based intervention to increase participation in cervical cancer screening among Pakistani and Somali women in Norway. BMC Public Health. 2021;21(1):1-10.
121. Møen KA, Kumar B, Igland J, Diaz E. Effect of an Intervention in General Practice to Increase the Participation of Immigrants in Cervical Cancer Screening: A Cluster Randomized Clinical Trial. JAMA Netw Open. 2020;3(4):e201903-e.
122. Sankaranarayanan R, Esmy PO, Rajkumar R, Muwonge R, Swaminathan R, Shanthakumari S, et al. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. Lancet. 2007;370(9585):398-406.
123. Sankaranarayanan R, Nene BM, Shastri SS, Jayant K, Muwonge R, Budukh AM, et al. HPV screening for cervical cancer in rural India. N Engl J Med. 2009;360(14):1385-1394.
124. Marmot M, Friel S, Bell R, Houweling TA, Taylor S, Health CoSDo. Closing the gap in a generation: health equity through action on the social determinants of health. Lancet. 2008;372(9650):1661-1669.
125. World Health Organization. WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention. Geneva: World Health Organization; 2013.
126. Arbyn M, Sankaranarayanan R, Muwonge R, Keita N, Dolo A, Mbalawa CG, et al. Pooled analysis of the accuracy of five cervical cancer screening tests assessed in eleven studies in Africa and India. Int J Cancer. 2008;123(1):153-160.
127. Selmouni F, Belakhel L, Sauvaget C, Abousselham L, Lucas E, Muwonge R, et al. Evaluation of the national cervical cancer screening program in Morocco: achievements and challenges. J Med Screen. 2019;26(3):162-168.
128. Bigoni J, Gundar M, Tebeu PM, Bongoe A, Schäfer S, Fokom-Domgue J, et al. Cervical cancer screening in sub-Saharan Africa: A randomized trial of VIA versus cytology for triage of HPV-positive women. Int J Cancer. 2015;137(1):127-134.
129. Sauvaget C, Fayette J-M, Muwonge R, Wesley R, Sankaranarayanan R. Accuracy of visual inspection with acetic acid for cervical cancer screening. Int J Gynecol Obstet. 2011;113(1):14-24.

130. Joshi R, Alim M, Kengne AP, Jan S, Maulik PK, Peiris D, et al. Task shifting for non-communicable disease management in low and middle income countries – a systematic review. PLoS One. 2014;9(8):e103754.
131. Brevik TB, Laake P, Bjørkly S. Effect of culturally tailored education on attendance at mammography and the Papanicolaou test. Health Serv Res. 2020;55(3):457-468.
132. Flórez KR, Aguirre AN, Viladrich A, Céspedes A, De La Cruz AA, Abraído-Lanza AF. Fatalism or destiny? A qualitative study and interpretative framework on Dominican women's breast cancer beliefs. J Immigr Minor Health. 2009;11(4):291-301.
133. Ghebre RG, Sewali B, Osman S, Adawe A, Nguyen HT, Okuyemi KS, et al. Cervical cancer: barriers to screening in the Somali community in Minnesota. J Immigr Minor Health. 2015;17(3):722-728.
134. Straughan PT, Seow A. Fatalism reconceptualized: a concept to predict health screening behavior. Journal of Gender, Culture and Health. 1998;3(2):85-100.
135. Janz NK, Becker MH. The health belief model: A decade later. Health Educ Q. 1984;11(1):1-47.
136. Davison C, Frankel S, Smith GD. The limits of lifestyle: re-assessing 'fatalism' in the popular culture of illness prevention. Sos Sci Med. 1992;34(6):675-685.
137. Keller KG, Toriola AT, Schneider JK. The relationship between cancer fatalism and education. Cancer Causes Control. 2021;32(2):109-118.
138. Islam N, Patel S, Brooks-Griffin Q, Kemp P, Raveis V, Riley L, et al. Understanding barriers and facilitators to breast and cervical cancer screening among Muslim women in New York City: perspectives from key informants. SM J Community Med. 2017;3(1):1022.
139. Thornquist E. Vitenskapsfilosofi og vitenskapsteori - for helsefag. Bergen: Fagbokforlaget; 2010.
140. Næss A, Galtung J. Innføring i logikk og metodelære. 2: Metodelære. Oslo: Universitetsforlaget; 1960.
141. Skjervheim H. Deltakar og tilskodar og andre essays. Oslo: Aschehoug; 1996.
142. Suri H. Ethical considerations of conducting systematic reviews in educational research. In: Zawacki-Richter O, Kerres M, Bedenlier S, Bond M, Buntins K, editors. Systematic reviews in educational research: methodology, perspectives and application. Wiesbaden: Springer Nature; 2020. p. 41-54.
143. Vinther T, Enebakk V, Hølen JC, editors. Vitenskapelig (u)redelighet. Oslo: Cappelen Damm; 2016.

144. Council for International Organizations of Medical Sciences. International ethical guidelines for health-related research involving humans, fourth edition. Geneva: Council for International Organizations of Medical Sciences; 2016.

Article 1

DOI: 10.1111/1475-6773.13271

RESEARCH ARTICLE

HSR Health Services Research

Effect of culturally tailored education on attendance at mammography and the Papanicolaou test

Thea Beate Brevik MSc[1,2] | Petter Laake Dr.philos.[1,3] | Stål Bjørkly Psy.D.[1,4]

[1]Faculty of Health Sciences and Social Care, Molde University College, Molde, Norway

[2]Clinic of Surgery, Møre and Romsdal Hospital Trust, Molde Hospital, Molde, Norway

[3]Oslo Centre for Statistics and Epidemiology, Department of Biostatistics, University of Oslo, Oslo, Norway

[4]Centre for Forensic Research, Oslo University Hospital, Oslo, Norway

Correspondence
Thea Beate Brevik, MSc, Britvegen, 2, 6411, Molde, Norway.

Email: thea-beate@hotmail.com

Funding information
This work was supported by the Møre and Romsdal Hospital Trust.

Abstract

Objectives: To determine the effectiveness of culturally tailored education on attendance at breast and cervical cancer screening among ethnic minority women.

Data Sources: Systematic database searches in Ovid MEDLINE, ProQuest, PubMed, PsycINFO, and Cochrane CENTRAL.

Study Design: Randomized controlled trials (RCTs) of culturally tailored educational interventions to ethnic minority women in Western countries were investigated for a meta-analysis. RCTs that assessed attendance at mammography or the Papanicolaou test (Pap test) were eligible for inclusion.

Data Collection Methods: Study characteristics and results were extracted separately. Independent raters assessed risk of bias by using Cochrane Collaboration's tool.

Principal Findings: Seven RCTs (n = 4246) were included in the meta-analysis of mammography attendance, and four RCTs (n = 1750) were included in the meta-analysis of Pap test attendance. The effect of culturally tailored educational interventions on attendance at mammography was an increase of 18 percent (RR = 1.18, 95% CI, 1.09-1.28, $P < .001$), with low heterogeneity ($I^2 = 30.0$, $P = .237$), and a 54 percent increase at the Pap test (RR = 1.54, 95% CI, 1.14-2.09, $P = .005$), with substantial heterogeneity ($I^2 = 75.9\%$, $P = .001$).

Conclusions: Interpreted within the limitations set by the low number of studies and substantial heterogeneity for the Pap test, findings from the current meta-analyses indicate that culturally tailored educational interventions may increase attendance of ethnic minority women at breast and cervical cancer screenings. There is a need for more studies, in particular RCTs conducted outside the United States, to determine if such findings are similar in other countries.

KEYWORDS

ethnic groups, health education, mammography, meta-analysis, Papanicolaou test

1 | INTRODUCTION

Breast and cervical cancer screening tools can detect cancer at early stages, when treatment is more effective and likely to succeed.[1] Public cancer screening programs using mammography and the Papanicolaou (Pap) test have successfully decreased breast and cervical cancer mortality in Western countries over the past decades.[1] However, ethnic minority women have low

participation rates in breast and cervical cancer screening in the United States, Europe, Canada, and Australia.[2-13] Cancer causes extreme suffering for each woman and her family. In addition, the economic impact of cancer is significant and increasing, with a total annual economic cost of US$1.16 trillion in 2010,[14] and the treatment of breast and cervical cancer is more expensive than the cost of prevention and early detection.[15] Considerable efforts have been invested in reducing breast and cervical cancer incidents and mortality by increasing screening rates. However, disparities in screening rates continue to exist among certain racial and ethnic minority groups.[2-13]

Previous studies have identified several culturally specific barriers to breast and cervical cancer screening among ethnic minority women living in Western countries.[16-25] Low linguistic proficiency, insufficient knowledge about cancer and screening programs, and low health literacy are found to be barriers. The same goes for cultural and religious barriers, such as false religious beliefs (fatalism), confidence in local and conventional curers, women's roles, and sexual issues.[16-25] Educational interventions aim to influence individuals' physical, intellectual, and moral development through training and education.[26] The educational interventions for ethnic minority women must be culture-specific, because women's behaviors and understandings of disease and symptoms are products of their social and cultural contexts, cultural beliefs, life experiences, and socioeconomic factors.[27] Women in similar cultural groups generally share common knowledge, beliefs, and attitudes that fundamentally affect their behaviors.[27]

In the last decades, randomized controlled trials (RCTs) have investigated whether interventions can increase screening participation rates among ethnic minority women. Previous systematic reviews and meta-analyses have explored the effects of different types of interventions to promote breast and cervical cancer screening among minority women.[28-33] Two meta-analyses had several methodological and clinical limitations.[28,29] One such limitation is that the meta-analyses included primary studies with samples of up to 60 percent Caucasian women, without presenting separate results for participants with other ethnic origins. Because the ethnicity of participants lost to follow-up was not reported in the primary studies, it is impossible to determine whether the findings were representative for ethnic minority women. In addition, the meta-analyses failed to report risk-of-bias assessment and forest plots of the findings.[28,29] These flaws invite for a meta-analysis following established procedures in order to avoid spin citation of results that lack empirical research evidence.

It has been claimed that access-enhancing interventions produce the best results for increasing attendance at breast and cervical cancer screening, followed by education, individual counseling, and letters or other reminders.[28,29] In clinical practice, providing education is easier to implement and has far lower financial costs, compared to increasing the availability of mammography equipment worldwide. The two previous meta-analyses investigated strategies to improve breast and cervical cancer screening among ethnic minorities in the United States, but low participation at cancer screening among ethnic minority women is a significant problem in Europe, Canada, and Australia as well.[2-13] Therefore, the scope of the current meta-analysis was to determine whether culturally tailored educational interventions increase attendance at mammography and the Pap tests among ethnic minority women in Western countries.

What this study adds

What is already known on this topic

- Attendance of ethnic minority women for mammography and the Papanicolaou (Pap) test is low in the United States, Europe, Canada, and Australia.
- Culturally tailored educational interventions can use linguistically appropriate methods to increase knowledge about cancer and screening and can address common cultural and religious barriers to screening.

What this study adds

- Culturally tailored education increased attendance at mammography by 18 percent among ethnic minority women.
- For Pap test attendance, an increase of 54 percent was found, but the substantial heterogeneity calls for careful judgment when interpreting the results.

2 | METHODS

Cochrane collaboration guidelines on conducting systematic reviews,[34] Center for Review and Dissemination's guidelines for undertaking reviews in health care,[35] and PRISMA guidelines[36] were followed through the entire review process.

2.1 | Eligibility criteria

Eligibility of randomized controlled trials (RCTs) was based on following inclusion criteria: Participants were women >18 years of Asian, African, Hispanic, or Oceanian (except Australia and New Zealand) origin living in a Western country (defined as Europe, the United States, Canada, Australia, and New Zealand). Educational interventions consisted of verbal teaching (one-on-one or in groups), written material, video or media, or a combination of these interventions and were given by trained lay health workers or health care professionals. Educational intervention was operationalized and defined as a new program, course, curriculum, or pedagogical technique that seeks to reform an older system or practice.[26] Educational interventions were culturally tailored to the targeted group. Outcome of interest was screening attendance at mammography and/or the Pap test at baseline and follow-up, self-reported from the participants or collected from medical records.

Studies were excluded if the educational part had been but one element of a multilevel intervention program or if educational

efforts had been combined with assisted navigation, as effects could not then be attributed to the educational intervention alone.

2.2 | Search strategies

Comprehensive systematic literature searches were conducted in Ovid MEDLINE, ProQuest, PubMed, PsycINFO, and Cochrane CENTRAL. Our search strategy and PICO form included relevant keywords and thesaurus, such as "ethnic group," "immigrant," "women," "education," "teaching," "intervention," "screening," "mammography," and "Papanicolaou test." Experts in database searches critically assessed the search strategy before the searches were conducted in May 2017, with an update in May 2018. The searches included records from inception to present and had no limits regarding languages. References of retrieved articles were also scanned for additional studies of interest. We also systematically examined all articles included in the two previous meta-analyses. Details of the search strategies are available in Appendix S1.

2.3 | Study selection

All titles and abstracts were scrutinized by the first author (TB), and records that obviously did not meet the inclusion criteria were excluded. The causes for exclusion were documented in an evidence table and reviewed by the third author (SB). All excluded records were assessed jointly for a final decision. The remaining records were read in full text and assessed separately by the two reviewers (TB, SB). Any discrepancies between the two reviewers were solved by consensus decision. Articles with insufficient information were excluded. To ensure transparency in the selection of studies, detailed information of excluded studies and cause of exclusion is available.

2.4 | Data extraction

All extracted data from each study were documented in an evidence table inspired by Botella and Gambara.[37] The two reviewers independently coded characteristics, with a 92 percent level of agreement. Because the included studies reported their findings in different ways, the data were converted into a common format. In order to reduce risks of errors, all results were extracted and controlled several times. First, one reviewer (TB) extracted and converted the results two separate times. Then, the two sets of extracted data were compared. Finally, TB and SB studied all extracted data for accuracy and calculated the converted data a third time. Discrepancies were resolved by discussion and recalculation. Researchers from two primary studies were contacted in order to obtain missing or additional data, but none responded.

2.5 | Assessing the risk of bias

The Cochrane Collaboration tool was used to assess the risk of bias.[38] Included studies were assessed independently by the first and third authors, and any disagreement was resolved by discussion. The level of agreement prior to consensus discussions was very good, with an intraclass correlation coefficient (ICC, two-way random-effects model, absolute agreement, single measure reliability) of 0.79 (95% CI, 0.67-0.86).

2.6 | Statistical analysis

The current meta-analysis was conducted in Stata SE release 16. A significance level of $P = .05$ and 95% confidence interval (CI) were used. The effect measure was risk ratio (RR). Risk difference (RD) might be the natural choice in meta-analysis of RCTs with binary outcomes,[39] but ratio-based effect measures have greater stability over different risk groups than difference-based measures.[39] Analyses with both a random-effects and a fixed-effects model were run to test the stability over the models. For this study, the random-effects model was chosen. In such a model, the between-study variation must be estimated. The restricted maximum likelihood estimate (REML) is usually preferred to the simpler DerSimonian-Laird (D + L) pooled estimate.[40] The forest plot presents the effect estimates of the included studies, with the overall effect size, with REML estimation of the between-study variation. For the fixed-effects model, the overall effect was calculated with the Mantel-Haenszel (M-H) pooled estimate.[40]

Statistical heterogeneity was examined using I^2 statistics with its P-value, as recommended for meta-analyses.[41] The I^2 statistic measures the percentage of total variation in study results that is due to heterogeneity. $I^2 < 40$ percent indicates low heterogeneity, values indicate 30-60 percent moderate heterogeneity, and values 50-90 percent may indicate substantial heterogeneity, while I^2 over 75 percent is defined as considerable. We also used L'Abbé plots to analyze heterogeneity of the effect measure.[39]

Publication bias was assessed by visual examination of funnel plots and the Harbord test to examine and interpret asymmetry.[42,43] This test is recommended for meta-analyses of RCTs with binary outcomes. Although the funnel plot and the Harbord test may have undesirable properties in detecting asymmetry, they provide valuable information.[42,43]

3 | RESULTS

3.1 | Search results

The electronic database search identified 207 records (Appendix S2). Scanning references identified 41 studies of interest. Sixty-eight records were duplicates. Of 146 records, five RCTs measured mammography attendance,[44-48] two measured Pap test attendance,[49,50] and two measured both[51,52] (Figure 1).

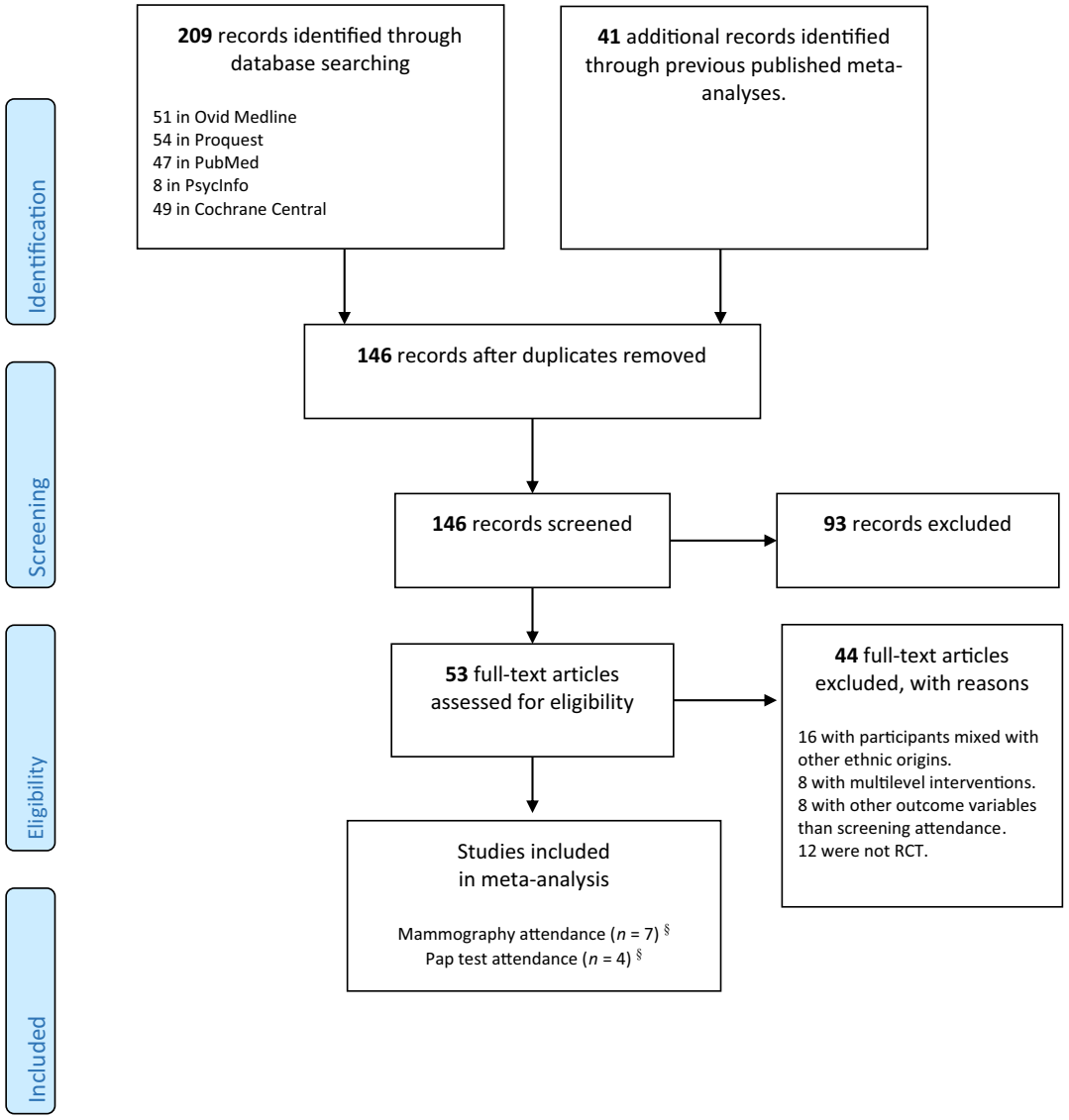


FIGURE 1 Flow diagram. §Two studies measured both mammography and Pap test attendance and were included in both meta-analyses. [Color figure can be viewed at wileyonlinelibrary.com]

3.2 | Characteristic of the included studies

The seven RCTs that measured mammography attendance included 4246 participants. All studies were conducted in the United States and published between 2003 and 2014. Participants were Asian (3), African American (2), Hispanic (1), and Polynesian (1). Sample sizes ranged from 344 to 984. All RCTs used self-reported data. Follow-up ranged from two to 15 months, with four trials conducting follow-up at 6 months. The educational interventions were theory-based, and six RCTs were based on the health belief model alone or in combination with other theories. In five RCTs, the educational interventions consisted of verbal education in groups or one-on-one; three of these RCTs combined verbal education with written information. The education was provided through lay health workers (2), video (2), and professionals (2).

The four RCTs measuring Pap test attendance included 1750 participants with Hispanic (3) and Asian (1) origins. The studies were conducted in the United States and published between 2003 and 2013. Sample sizes ranged from 120 to 613. Outcome was collected through self-reported data, and follow-up ranged from two to 12 months. The educational interventions consisted of verbal education in groups, and two combined verbal education with written information. Lay health workers provided the education in three RCTs. The educational interventions in three RCTs were based on the health belief model alone or in combination with other theories. Characteristics of the included RCTs are described in Table 1.

3.3 | Risk of bias

Among the mammography attendance RCTs, one RCT was assessed to have high risk of bias, two to have moderate risk of bias, and four to have low risk of bias. Among the included RCTs measuring Pap test attendance, one was assessed to have moderate risk of bias and three to have low risk (Table 2).

TABLE 1 Table of characteristics

Author (Year)	N	Sample completed (intervention/control)	Population, ethnicity	Intervention	Cultural tailoring	Educator	Theoretical framework	Control group	Follow-up months
Mammography attendance									
Champion et al (2006)	344	299 (243/56)	African Americans	Three study arms: (a) educational 20-min video; (b) a 40-min interactive computer-assisted instruction program. The targeted videotape was a linear version of the computer program. (c) Control group	The interventions were developed using input from community-based focus groups of African American women who reviewed scripts for sociocultural appropriateness, acceptability, and understandability. The program used African American women (storytellers, media celebrity, physician, and minister) to educate and to demonstrate a mammography procedure	Video	HBM[a], TTM[b], extended parallel process model	Written material	6
Lee et al (2014)	428	395 (195/200)	Korean immigrants in the United States	Educational 30-min DVD, a 10-min group discussion session after video with PowerPoint presentation, and a homework discussion couple activity	The education program used a Korean-language DVD with a Korean American physician to address facts and culture-specific beliefs that prevent Korean American women from receiving screening. The homework discussion activity aimed to increase support provided by Korean American husbands for their wives		HBM[a], Kleinman's model of illness	Diet information	6,15
Mishra Shiraz et al (2007)	809	775 (391/384)	Samoan in the United States	Educational booklets, skill building and behavioral exercises, and interactive group discussion sessions	Educational materials in English and Samoan language, with Samoan artwork, scenery, and pictures of Samoans. Samoan health educators held educational sessions in Samoan language, addressing culture-specific myths and beliefs. Role-play and skill building with cultural and religious considerations	Lay health workers	HBM[a], Freire's empowerment pedagogy	Usual care	8
Sadler et al (2011)	984	232 (112/120)	African Americans	Breast cancer education-session offered in beauty salons. Posters and literature were displayed throughout the salons and cosmetologists used synthetic breast models to show clients how a lump feels.	Cosmetologists were trusted members of the African American society and located in their local community. The cosmetologist received individual training from an African American storyteller, an integral element in African culture. The salon had posters, brochures, and magazines with African American women (eg, black celebrities with cancer)	Trained beauty cosmetologist	HBM[a]	Diabetes education	6

(Continues)

TABLE 1 (Continued)

Author (Year)	N	Sample completed (intervention/control)	Population, ethnicity	Intervention	Cultural tailoring	Educator	Theoretical framework	Control group	Follow-up months
Wang et al (2012)	664	571 (378/193)	Chinese Americans	Three study arms: (a) culturally target video including a Chinese soap opera–style story and recommendations from a Chinese physician; (b) genetic video with a general soap opera story with recommendations from a physician. (c) Control group	The culturally target video in soap opera style had a Chinese breast cancer survivor celebrating her birthday with friends. The female physician was Chinese. The video was in Mandarin, dubbed in Cantonese, with Chinese and English subtitles. The generic video showed multiethnic women discussing cancer at lunch break, with an American physician, talking in English, dubbed in Mandarin and Cantonese with Chinese and English subtitles	Video	HBM[a]	Fact sheet via mail	6
PAP test attendance									
Byrd et al (2013)	613	513 (380/133)	Mexican Americans	Four study arms: (a) the full AMIGA program: video and flip chart with information, including games, activities, and a set of cards; (b) the AMIGA program without the video; (c) the AMIGA program without the flip chart. The 3 interventions included written information. (d) Control group	The intervention was developed by researchers, community members, and lay health workers with Hispanic origins and of similar socioeconomic status as the participants. Bicultural and bilingual lay health workers tested and validated the educational material. Education was given in Spanish or English, and addressed common myths, barriers and beliefs about cervical cancer and screening among Hispanics	Lay health workers	HBM[a], TTM[b], social cognitive theory	Usual care	6
O'Brien et al (2010)	120	70 (34/36)	Hispanics in the United States	Two 3-h workshops, followed by education and pamphlets	Education program designed especially for Hispanic women, addressing common myths and barriers and epidemiology of cervical cancer in Hispanics. Questionnaires, education, and follow-up in Spanish	Lay health workers	HBM[a]	Usual care	6
Mammography and pap test attendance									
Jandorf et al (2008)	487	250 (151/99)	Latinas in the United States	Open health education meetings at local venues (eg, churches, homes, schools), with educational presentations and narrative communication from cancer survivors	The intervention was based on focus group findings with Latina breast cancer survivors, community gatekeepers and local clergy. The education provided specific cultural information and beliefs that resulted in a unique educational program for Latinos	Lay health workers and staff members		Diabetic education program	2

(Continues)

TABLE 1 (Continued)

Author (Year)	N	Sample completed (intervention/control)	Population, ethnicity	Intervention	Cultural tailoring	Educator	Theoretical framework	Control group	Follow-up months
Maxwell et al (2003)	530	447 (213/234)	Filipino Americans	Educational group sessions in 60-90 min and information packages to take home	Several components of the study were based on recommendations of Filipino community partners. Information and questionnaires were given in Tagalog and English. All health educators were born and raised Philippines and fluent in both English and Tagalog. The education was provided by a female Filipino health professional. Traditional Filipino snacks were served	Physicians and nurses	HBM[a], adherence model	Physical activity module	12

[a]The health belief model.
[b]The transtheoretical model.

3.4 | Effectiveness of culturally tailored educational interventions on attendance at mammography

The overall REML risk ratio (RR) for mammography was 1.18 (95% CI, 1.09-1.28, $P < .001$) with low heterogeneity ($I^2 = 30.0$, $P = .237$). The forest plot shows the individual and overall effects with random-effects model (Figure 2). The corresponding results for the fixed-effects model, with the overall M-H estimate, are 1.17 (95% CI, 1.09-1.26, $P < .001$) (results not shown).

We explored the heterogeneity by visual examination of L'Abbé plots (Appendix S3). The information about the heterogeneity contained in the forest plots was confirmed in the L'Abbé plot. Comparing the L'Abbé plot with RD and RR as effect measures, we observed less variability for RR (results not shown). Publication bias was assessed by visual examination of a funnel plot (Figure 3). Funnel plot asymmetry was explored by the Harbord test, and no statistically significant asymmetry was found ($P = .649$). With a small number of studies, it is difficult to identify publication bias.

3.5 | Effectiveness of culturally tailored educational interventions on attendance at the Pap test

RR for the Pap test was 1.54 (95% CI, 1.14-2.09, $P = .005$), with substantial heterogeneity ($I^2 = 75.9\%$, $P < .001$). Figure 2 shows the forest plot with the individual and overall effects with random-effects model. The corresponding results for the fixed model with the overall M-H estimate were 1.45 (95% CI, 1.27-1.65, $P < .001$) (results not shown).

The forest and L'Abbé plots confirmed that the effect measure for the Maxwell et al (2013) study differs significantly from the other included studies. When we deleted this study from the meta-analysis, we found an increased effect of 84 percent, RR = 1.84 (95% CI, 1.50-2.24, $P < .001$), with $I^2 = 0.00\%$, $P < .783$). Because I^2 is calculated from a Cochran's Q value of 0.49, and this is less than the number of studies minus one, I^2 is negative, and therefore converted to zero.[39] Due to the low number of studies of the Pap test, no funnel plot was made.

Both the analyses of mammography and the Pap test included results from Jandorf et al[51] and Maxwell et al[52] There may be dependence between attendance of mammography and the Pap test. Since there was no information about the sample size for those attending both mammography and the Pap test, we were unable to estimate the dependence. We have assumed that the dependence is only minor and have estimated effect sizes and test statistics under standard assumptions of independent samples.

4 | DISCUSSION

The meta-analyses in the current systematic review indicate that culturally tailored educational interventions may increase attendance at mammography and the Pap tests among ethnic minority

TABLE 2 Risk of bias

Author (Year)	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
RCTs measuring mammography attendance						
Champion et al (2006)	1	2	2	0	2	0
Jandorf et al (2008)	0	0	2	0	2	0
Lee et al (2014)	0	1	2	0	1	0
Maxwell et al (2003)	1	1	2	0	0	0
Mishra Shiraz et al (2007)	1	1	2	0	1	0
Sadler et al (2011)	1	1	2	0	1	0
Wang et al (2012)	1	1	2	0	0	0
RCTs measuring Pap test attendance						
Byrd et al (2013)	0	1	2	0	0	0
Jandorf et al (2008)	0	0	2	0	2	0
Maxwell et al (2003)	1	1	2	0	0	0
O'Brien et al (2010)	1	1	2	0	1	0

women. These results are consistent with previous reviews that have found that theory-based and tailored interventions increased screening attendance.[28-30] The aim of early detection is to reduce mortality and other serious consequences of advanced disease.[14] In settings where early detection and basic treatment are available and accessible, the 5-year survival rate for early localized breast cancer exceeds 80 percent.[53] As a result of public screening programs in Western countries, cervical cancer rates have decreased by as much as 65 percent over the past 40 years.[1] Cancer is a major global health problem, responsible for 8.8 million deaths in 2015, and the number of new cancer cases is expected to rise by about 70 percent over the next two decades.[1] The unabated rise of incidence rates among some of the racial and ethnic groups is of particular concern.[54]

Racial and ethnic disparities in breast and cervical cancer incidence and screening attendance are evident in the United States.[54,55] As well, immigrants in Europe, Australia, and Canada have low levels of participation in screening programs.[2-13] At the same time, studies have found that groups of immigrant women, more often than other women, have late-stage cancer when they are diagnosed, a diagnosis associated with a higher rate of mortality,[56,57] and immigrant women have reported cultural, religious, and linguistic barriers to participation at cancer screening programs in their host countries.[16,19,20,23] Currently, the number of migrants worldwide has reached 250 million and grows at a rate greater than the rate of growth of the world's population, and high-income countries host almost two-thirds of all immigrants.[58] Taking into consideration, therefore, the large number of affected women, implementation of effective educational interventions that are relatively inexpensive can potentially reduce disease, illness, and mortality among women worldwide.

Culturally tailored educational interventions in the current study contained theory-based group education, individual counseling, and education provided by local lay health workers or professionals and were combined with linguistic tailored brochures, video, and media campaigns. Culturally relevant strategies, such as relevant graphics, role models, and narrative storytelling from cancer survivors from the target populations, were integrated into the programs. These types of interventions are often referred to as "complex," because the constituent parts may act both independently and interdependently. Thus, defining the "active ingredient" can be less straightforward than in other research topics.[35] Hence, it appears that the most significant clinical issue is to consider what types of intervention work best in a particular setting and for a particular population group. Evaluation of public health interventions is usually complex, as multiple interventions, outcomes, participants, settings, and stakeholders are often necessary components. Success invariably depends on health and on social and economic contexts that have a wide-reaching and sustainable impact on peoples' lives.[35] Because of this complexity, no single evaluation method is likely to be appropriate, and a range of different study designs are used.[35] Indeed, all these differences contribute to the complexity and, thus, heterogeneity at the synthesis stage.[35] In the current systematic review, the intervention effect on mammography attendance had low heterogeneity, whereas the impact of intervention on attendance at the Pap tests generated substantial heterogeneity, mainly due to one study. Subgroup analyses can be used to explore the heterogeneity and aid the evaluation of differential impacts across groups and in assessing inequalities.[35] Unfortunately, the data in the current study did not have sufficient statistical power to analyze differences and

similarities between ethnic minority groups, types of educational interventions, or socioeconomic factors, such as education level, household income, and previous screening history. Thus, careful judgment is needed when interpreting the results.

The results in the current study indicate that education with theory-based instructions, culturally relevant materials, and linguistically appropriate methods may be effective in enhancing cancer screening attendance. Linguistically appropriate approaches have been used for decades as culturally sensitive intervention strategies to enhance participants' understanding.[59] Diverse aspects of culture can be incorporated into an intervention, both superficially, through the use of graphics and features relevant to the target population, and more deeply, through the integration of social and cultural values. Still, culture is a comprehensive social phenomenon that includes knowledge, attitudes, experience, belief, values, and religion for a group of people.[60] As well, culture is not static.[60] Thus, culturally tailored interventions may not necessarily adequately address all aspects of participants' cultural characteristics. Knowing participants' characteristics and preferences is required in order to choose suitable health education materials.[30]

4.1 | Strengths

A broad range of search terms, combined with multiple complementary electronic databases supplemented with hand searches, contributed to a highly sensitive and thorough literature search. The strict and operationalized eligibility criteria, including exclusively RCTs with a study population consisting of only ethnic

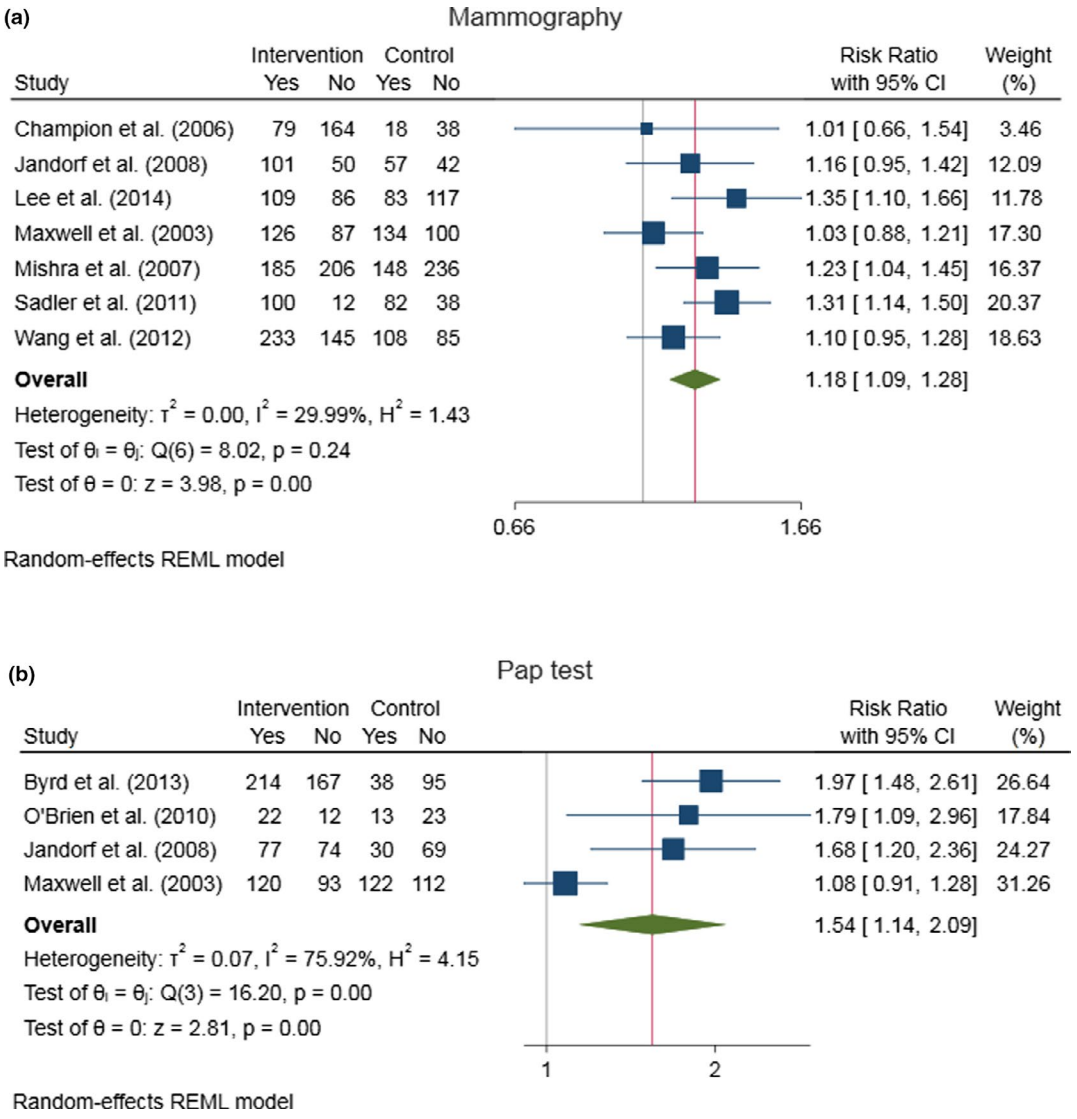


FIGURE 2 Forest plot. The square data markers indicate risk ratios (RRs) from primary studies, with sizes reflecting the statistical weight of the study using random-effects model. The horizontal lines indicate 95% CIs. The diamonds data markers represent the overall RR and 95% CI with random-effects model, with the overall effect estimated by the restricted maximum likelihood estimate (REML). Heterogeneity was estimated using I^2 statistics. The vertical lines through the diamonds show the summary effect estimate, next to the line of no effect (RR = 1) [Color figure can be viewed at wileyonlinelibrary.com]

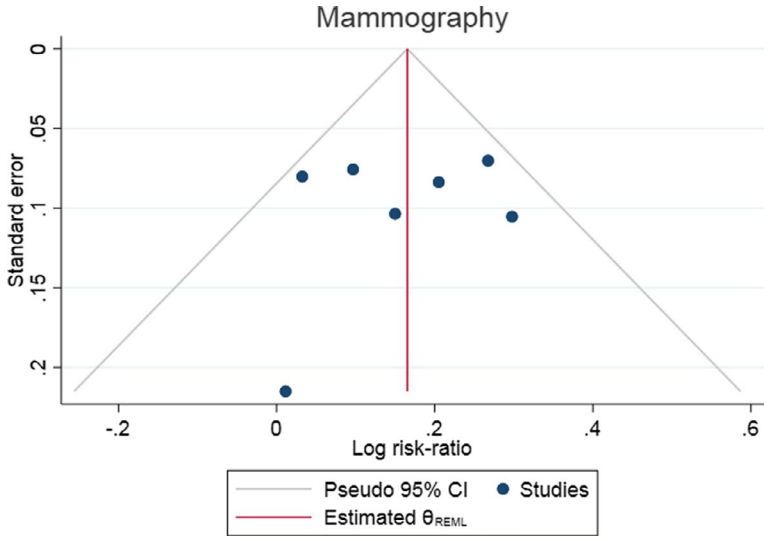


FIGURE 3 Funnel plot. Funnel plots for the meta-analysis of the effects of educational interventions on attendance at mammography. Circles indicate included studies. The effect estimates are on the *x*-axis and standard error estimates on the *y*-axis. The scale of the *y*-axis is reversed, so that studies with low precision are placed at the bottom. Studies with greater precision and large *N* are at the top of the plot. Asymmetry of the plot can indicate publication bias [Color figure can be viewed at wileyonlinelibrary.com]

minority women, allowed us to split the results into two meta-analyses. Independent reviewers performed study selection, data extraction, and risk-of-bias assessment. Only one RCT was assessed as having a high risk of bias. Data were converted into a common format and controlled multiple times to reduce the risk of error. This resulted in high interrater absolute agreement, and in cases of doubt, consensus decisions were used as quality control. In addition, we collaborated with experts in database literature searches, and one of the authors (PL) is an expert in statistical methods for meta-analysis.

4.2 | Limitations

The target of the current meta-analysis was RCTs conducted in Western countries. However, as all the included RCTs were conducted in the United States, the findings may not be generalizable to other Western countries. This is unfortunate, because there are more immigrants in Europe than in the United States,[58] and the low participation rates in preventive screening among immigrant women are also a significant problem in Europe, Canada, and Australia. Hence, future research may want to examine the effectiveness of educational interventions among ethnic minority women outside of the United States.

All RCTs measured outcome by self-reported data. There is always a risk of bias in designs that rely entirely on self-report as a source of information for the outcome variable. Two studies validated some of their self-report data with medical records. Unfortunately, due to the insufficient amount and low quality of the data, it was not possible to synthesize these data. We recommend that future researchers make strong efforts to obtain data from medical records in order to validate their self-reported data.

Although we constructed a structured and accurate search strategy and carried out comprehensive searches in five databases, only seven RCTs met the inclusion criteria for mammography attendance, and four RCTs, for Pap test attendance. Even though there were no restrictions regarding language, only Anglophone trials were identified. There may be RCTs that our search failed to identify.

The current meta-analysis showed substantial heterogeneity for Pap test attendance. Due to the low amount of RCTs and insufficient information published in the primary study reports, we were unable to explore the heterogeneity through subgroup analyses, such as differences and similarities between ethnic minority groups, types of educational interventions, or socioeconomic factors. Thus, we call for careful judgment when interpreting this result.

The current meta-analysis included women of Asian, African, Hispanic, or Oceanian origin. However, ethnic minority women are a heterogeneous group with many differences, and the women in these studies represented diverse ethnic origins. All reviewers are recommended to use operationalized definitions,[35] but a major problem is the inconsistent use and wide variation in the definitions of ethnic minorities and migrants used in empirical studies. For example, there is not even a universally accepted definition for *migrant* at the international level.[61] To research and analyze accurately something like the immigrant phenomenon—or, more specifically, the phenomenon of various ethnic minority women and their relationship to their health care—then clear and consistent terminology needs to be agreed upon for conducting and reporting studies.

5 | CONCLUSION

Interpreted within the limitations set by the low number of studies and substantial heterogeneity for the Pap test studies, findings from the current meta-analyses indicate that culturally tailored educational interventions may increase attendance at breast and cervical cancer screening among ethnic minority women. RCTs conducted outside of the United States are needed to examine whether our findings are similar for ethnic minority women in other Western countries. To inform clinical practice, more research is required to determine which educational approaches and

settings are the most effective for increasing participation in cancer screening.

ACKNOWLEDGMENT

Joint Acknowledgment/Disclosure Statement: Writing of the article was funded by Research and Development Unit, Møre and Romsdal Hospital Trust.

CONFLICT OF INTEREST

The authors have no conflict of interest.

ORCID


Thea Beate Brevik https://orcid.org/0000-0003-2193-6214

REFERENCES

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA: A Cancer J Clin*. 2015;65(2):87–108.
2. Bhargava S, Moen K, Qureshi SA, Hofvind S. Mammographic screening attendance among immigrant and minority women: a systematic review and meta-analysis. *Acta Radiol*. 2018;59(11):1285-1291.
3. Ahmed AT, Welch BT, Brinjikji W, et al. Racial disparities in screening mammography in the United States: a systematic review and meta-analysis. *J Am College Radiol*. 2017;14(2):157-165.
4. Aminisani N, Armstrong BK, Canfell K. Cervical cancer screening in Middle Eastern and Asian migrants to Australia: a record linkage study. *Cancer Epidemiol*. 2012;36(6):394-400.
5. Azerkan F, Sparén P, Sandin S, Tillgren P, Faxelid E, Zendehdel K. Cervical screening participation and risk among Swedish-born and immigrant women in Sweden. *Int J Cancer*. 2012;130(4):937-947.
6. Berens E-M, Stahl L, Yilmaz-Aslan Y, Sauzet O, Spallek J, Razum O. Participation in breast cancer screening among women of Turkish origin in Germany – a register-based study. *BMC Women's Health*. 2014;14(1):24.
7. Bhargava S, Tsuruda K, Moen K, Bukholm I, Hofvind S. Lower attendance rates in immigrant versus non-immigrant women in the Norwegian Breast Cancer Screening Programme. *J Med Screen*. 2017;25(3):155-161.
8. Campari C, Fedato C, Iossa A, et al. Cervical cancer screening in immigrant women in Italy: a survey on participation, cytology and histology results. *Eur J Cancer Prev*. 2016;25(4):321-328.
9. Møen KA, Kumar B, Qureshi S, Diaz E. Differences in cervical cancer screening between immigrants and nonimmigrants in Norway: a primary healthcare register-based study. *Eur J Cancer Prev*. 2017;26(6):521.
10. Woltman KJ, Newbold KB. Immigrant women and cervical cancer screening uptake: a multilevel analysis. *Can J Public Health*. 2007;98(6):470–475.
11. Lofters AK, Moineddin R, Hwang SW, Glazier RH. Low rates of cervical cancer screening among urban immigrants: a population-based study in Ontario, Canada. *Med Care*. 2010;48(7):611–618.
12. Vahabi M, Lofters A, Kumar M, Glazier RH. Breast cancer screening disparities among urban immigrants: a population-based study in Ontario, Canada. *BMC Public Health*. 2015;15(1):679.
13. Vermeer B, Van den Muijsenbergh ME. The attendance of migrant women at the national breast cancer screening in the Netherlands 1997–2008. *Eur J Cancer Prev*. 2010;19(3):195-198.
14. Stewart B, Wild CP. *World Cancer Report 2014*. International Agency for Research on Cancer. Geneva, Switzerland: WHO; 2017.
15. Knaul FM, Arreola-Ornelas H, Atun R, et al. *Investing in Cancer Care and Control*. Boston, MA: Harvard University, Harvard Global Equity Initiative; 2012.
16. Grandahl M, Tydén T, Gottvall M, Westerling R, Oscarsson M. Immigrant women's experiences and views on the prevention of cervical cancer: a qualitative study. *Health Expect*. 2015;18(3):344-354.
17. Rajaram SS, Rashidi A. Minority women and breast cancer screening: the role of cultural explanatory models. *Prev Med*. 1998;27(5):757-764.
18. Johnson CE, Mues KE, Mayne SL, Kiblawi AN. Cervical cancer screening among immigrants and ethnic minorities: a systematic review using the Health Belief Model. *J Low Genit Tract Dis*. 2008;12(3):232-241.
19. Gele AA. Barriers and facilitators to cervical cancer screening among Pakistani and Somali immigrant women in Oslo: a qualitative study. *International Journal of Women's Health*. 2017;9:487-496.
20. Leinonen MK, Campbell S, Ursin G, Tropé A, Nygård M. Barriers to cervical cancer screening faced by immigrants: a registry-based study of 1.4 million women in Norway. *Eur J Pub Health*. 2017;27(5):873-879.
21. Kwok C, White K, Roydhouse JK. Chinese-Australian women's knowledge, facilitators and barriers related to cervical cancer screening: a qualitative study. *J Immigr Minor Health*. 2011;13(6):1076.
22. Møen KA, Terragni L, Kumar B, Diaz E. Cervical cancer screening among immigrant women in Norway- The healthcare providers' perspectives. *Scand J Prim Health Care*. 2018;36(4):415-422.
23. Anaman-Torgbor JA, King J, Correa-Velez I. Barriers and facilitators of cervical cancer screening practices among African immigrant women living in Brisbane, Australia. *Eur J Oncol Nurs*. 2017;31:22-29.
24. Azami-Aghdash S, Ghojazadeh M, Gareh Sheyklo S, et al. Breast cancer screening barriers from the womans perspective: a meta-synthesis. *Asian Pac J Cancer Prev*. 2015;16(8):3463-3471.
25. Marlow LA, Waller J, Wardle J. Barriers to cervical cancer screening among ethnic minority women: a qualitative study. *J Fam Plann Reprod Health Care*. 2015;41:248-254.
26. IGI-Global. *What is Educational Education*; 2018; https://www.igi-global.com/dictionary/educational-intervention/33094. Accessed August 15, 2017.
27. Kleinman A. *The Illness Narratives. Suffering, Healing & the Human Condition*. New York: Basic Bookism; 1988.
28. Han HR, Kim J, Lee JE, et al. Interventions that increase use of Pap tests among ethnic minority women: a meta-analysis. *Psycho-oncology*. 2011;20(4):341-351.
29. Han H-R, Lee J-E, Kim J, Hedlin HK, Song H, Kim MT. A meta-analysis of interventions to promote mammography among ethnic minority women. *Nurs Res*. 2009;58(4):246.
30. Chan DN, So WK. A systematic review of randomised controlled trials examining the effectiveness of breast and cervical cancer screening interventions for ethnic minority women. *Eur J Oncol Nurs*. 2015;19(5):536-553.
31. Corcoran J, Dattalo P, Crowley M. Interventions to increase mammography rates among US Latinas: a systematic review. *J Women's Health*. 2010;19(7):1281-1288.
32. Corcoran J, Dattalo P, Crowley M. Cervical cancer screening interventions for US Latinas: a systematic review. *Health Soc Work*. 2012;37(4):197-205.
33. Masi CM, Blackman DJ, Peek ME. Interventions to enhance breast cancer screening, diagnosis, and treatment among racial and ethnic minority women. *Med Care Res Rev*. 2007;64(5):195S-242S.
34. Higgins JP, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*. Vol. 4. Hoboken: John Wiley & Sons; 2011.
35. Center for Reviews and Dissemination. *Systematic Reviews. CRD Guidance for Undertaking Reviews in Health Care*. University of York. York, UK: York Publishing Services Ltd; 2009.
36. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. 2009;151(4):264-269.

37. Botella J, Gambara H. Doing and reporting a meta-analysis. *Int J Clin Health Psychol*. 2006;6(2):425-440.
38. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
39. Fagerland MW. Evidence-based medicine and systematic reviews. In: Laake P, Benestad HB, Olsen BR, eds. *Research in Medical and Biological Sciences*. Oxford, UK: Elsevier Ltd.; 2015:431-461.
40. Fagerland M, Lydersen S, Laake P. *Statistical Analysis of Contingency Tables*. Boca Raton: Chapman & Hall/CRC; 2017.
41. Guyatt GH, Oxman AD, Kunz R, et al. guidelines: 7. Rating the quality of evidence—inconsistency. *J Clin Epidemiol*. 2011;64(12):1294-1302.
42. Harbord RM, Egger M, Sterne JA. A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints. *Stat Med*. 2006;25(20):3443-3457.
43. Sterne JAC, Sutton AJ, Ioannidis JPA, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ*. 2011;343.
44. Champion VL, Springston JK, Zollinger TW, et al. Comparison of three interventions to increase mammography screening in low income African American women. *Cancer Detect Prev*. 2006;30(6):535-544.
45. Lee E, Menon U, Nandy K, et al. The effect of couples intervention to increase breast cancer screening among Korean Americans. *Oncol Nurs Forum*. 2014;41(3):185-193.
46. Mishra Shiraz RB, Cathrine C, Cindy C, Pat L, Claudia B. Results of a randomized trial to increase mammogram usage among Samoan woman. *Cancer Epidemiol Biomark Preven*. 2007;12:2594-2604.
47. Sadler GR, Ko CM, Wu P, Alisangco J, Castaneda SF, Kelly C. A cluster randomized controlled trial to increase breast cancer screening among African American women: the black cosmetologists promoting health program. *J Natl Med Assoc*. 2011;103(8):735-745.
48. Wang JH, Shwartz MD, Brown RL, et al. Results of a randomized controlled trial testing the efficacy of a culturally-targeted and a generic video on mammography screening among Chinese-American immigrants. *Cancer Epidemiol Biomark Prev*. 2012;21(11):1923-1932.
49. Byrd TL, Wilson KM, Smith JL, et al. AMIGAS: a multicity, multicomponent cervical cancer prevention trial among Mexican American women. *Cancer*. 2013;119(7):1365-1372.
50. O'Brien MJ, Halbert CH, Bixby R, Pimentel S, Shea JA. Community health worker intervention to decrease cervical cancer disparities in Hispanic women. *J Gen Intern Med*. 2010;25(11):1186-1192.
51. Jandorf L, Bursac Z, Pulley L, Trevino M, Castillo A, Erwin DO. Breast and cervical cancer screening among Latinas attending culturally specific educational programs. *Prog Community Health Partnersh: Res Educ Action*. 2008;2(3):195-204.
52. Maxwell AE, Bastani R, Vida P, Warda US. Results of a randomized trial to increase breast and cervical cancer screening among Filipino American women. *Prev Med*. 2003;37(2):102-109.
53. World Health Organization. *WHO Position Paper on Mammography Screening*. Geneva, Switzerland: WHO; 2014.
54. Liu L, Zhang J, Wu AH, Pike MC, Deapen D. Invasive breast cancer incidence trends by detailed race/ethnicity and age. *Int J Cancer*. 2012;130(2):395-404.
55. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):E359-E386.
56. Latif F, Helgeland J, Bukholm G, Bukholm IRK. Ethnicity differences in breast cancer stage at the time of diagnosis in Norway. *Scand J Surg*. 2015;104(4):248-253.
57. Jack R, Davies E, Møller H. Breast cancer incidence, stage, treatment and survival in ethnic groups in South East England. *Br J Cancer*. 2009;100(3):545.
58. United Nations DoEaSA, Population Division. *International Migration Report 2017: Highlights*. New York, NY: United Nations DoEaSA, Population Division; 2017.
59. Resnicow K, Baranowski T, Ahluwalia JS, Braithwaite RL. Cultural sensitivity in public health: defined and demystified. *Ethn Dis*. 1999;9(1):10-21.
60. Samovar LA, Porter RE, McDaniel ER, Roy CS. *Communication Between Cultures*. Toronto, ON: Nelson Education; 2017.
61. Hannigan A, O'Donnell P, O'Keeffe M, MacFarlane A. *How do Variations in Definitions of "Migrant" and Their Application Influence the Access of Migrants to Health Care Services?* Copenhagen: WHO Regional Office for Europe; 2016.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Brevik TB, Laake P, Bjørkly S. Effect of culturally tailored education on attendance at mammography and the Papanicolaou test. *Health Serv Res*. 2020;00:1–12. https://doi.org/10.1111/1475-6773.13271

Article 2

Does Women's Screening History Have Any Impact on Mammography Screening Attendance After Tailored Education?

A Systematic Review and Meta-analysis

Thea B. Brevik, MSc,† Ameli Tropé, MD, PhD,‡ Petter Laake, PhD,*§ and Stål Bjørkly, PsyD*‖*

Background: Many ethnic minority women have low attendance at breast cancer screening.

Objectives: This brief report explores whether women's screening histories impact mammography screening attendance after tailored education.

Research Design: Systematic searches were conducted in 5 databases. Randomized controlled trials of educational interventions tailored to ethnic minority women that measured attendance at mammography screening were eligible for inclusion. Data extraction and risk of bias assessment were performed independently. Data were combined in a meta-analysis by using random effects models. Heterogeneity was estimated by using I^2 statistics.

Results: Six studies with 3521 women were eligible for inclusion. The D+L pooled risk ratio (RR) for mammography attendance for never screened participants was 1.54 (95% confidence interval, 1.24–1.91; $P < 0.001$), with low heterogeneity ($I^2 = 27.1\%$, $P = 0.231$). The D+L pooled risk ratio for attendance for ever screened participants was 1.26 (95% confidence interval, 1.11–1.43; $P < 0.001$), with low heterogeneity ($I^2 = 35.5\%$, $P = 0.213$).

Conclusions: Tailored education increased attendance at mammography by 54% among never screened women and 26% among ever screened women. Although these findings must be interpreted with caution, the findings suggest that women's screening history is an important and ignored variable that affects how effective tailored education is on mammography screening attendance.

From the *Faculty of Health Sciences and Social Care, Molde University College; †Clinic of Surgery, Møre and Romsdal Hospital Trust, Molde Hospital, Molde; ‡Section for Cervical Cancer Screening, Cancer Registry of Norway; §Department of Biostatistics, Oslo Centre for Biostatistics and Epidemiology, University of Oslo; and ‖Centre for Forensic Research, Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway.

The authors declare no conflict of interest.

Correspondence to: Thea B. Brevik, MSc, Faculty of Health Sciences and Social Care, Molde University College, P.O. Box 2110, 6402 Molde, Norway. E-mail: brevikt@fellows.iarc.fr.

Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website, www.lww-medicalcare.com.

ISSN: 0025-7079/21/000-000

Key Words: ethnic groups, minority health, health education, mammography, meta-analysis

(*Med Care* 2021;00: 000–000)

Many ethnic minority women have low attendance at breast cancer screening in Europe, Canada, Australia, and the United States.[1–8] Most breast cancer screening programs offer mammography to women from the ages of 40–50 years to the age of 70–75 years, typically at 2-year intervals.[9] The complex barriers to cancer screening faced by many ethnic minority women reflect socioeconomic disparities and inequitable access to opportunities and resources, such as education, work, and overall standard of living, as well as barriers to cancer detection and information.[10–13] Hence, racial and ethnic health inequities can relate to structural racism.[14] Low linguistic proficiency, low health literacy, lack of knowledge, and some cultural and religious understandings can also prevent screening participation.[12,15–17]

We conducted a systematic review and meta-analysis and found that tailored education to ethnic minority women may increase attendance at mammography and the Papanicolaou test.[18] During the review process, we became aware that many trials included participants and analyzed outcomes regardless of screening history. There is a substantial difference between women who have taken a mammography screening within the last 12 months and women who have never been screened, especially when exploring the effectiveness of providing education to enhance cancer screening. The objective of the current meta-analysis was to analyze women according to their screening history.

METHODS

Cochrane collaboration guidelines on conducting systematic reviews[19] and PRISMA guidelines[20] were followed through the review process. The protocol was registered in PROSPERO (blinded).

Eligibility Criteria

Eligibility of randomized controlled trials was based on the following inclusion criteria:

- Participants: the sample contained only ethnic minority women, defined as a group of people of a particular race or

nationality living in a country where most people are from a different race or nationality.[21] There were no limitations regarding race, nationality, or country.

- Intervention: tailored education to ethnic minority women, defined as the use of communication that is specific for an individual or a group to improve health or change behavior,[22] that contains specific and organized information for a purpose, presented within a context that provides meaning and relevance, and can lead to increased understanding.
- Outcome: mammography screening attendance at baseline and follow-up among participants described as "never screened" or "ever screened." The outcome could be self-reported or collected from medical records.

Literature Search

Systematic database searches were conducted in Ovid Medline, ProQuest, Embase, PsycINFO, and Cochrane CENTRAL, from inception to May 2020. The searches were conducted by 1 of the authors (T.B.B.) and critically assessed by librarians using the evidence-based checklist of peer review of electronic search strategies.[23] PICO forms were used to create a structured search strategy (Supplemental Digital Content 1, http://links.lww.com/MLR/C273). Searches in Epistemonicos identified additional original trials included in relevant systematic reviews and meta-analysis.

Data Selection

The process of study selection was undertaken by 2 authors (T.B.B., A.T.). All records were critically assessed, and only records with irrelevant titles were excluded. Remaining articles were assessed independently in full text, where consensus was obtained through discussions. When full-text articles contained insufficient information, authors were contacted and excluded if data were not retrieved. A table of excluded articles is available upon request.

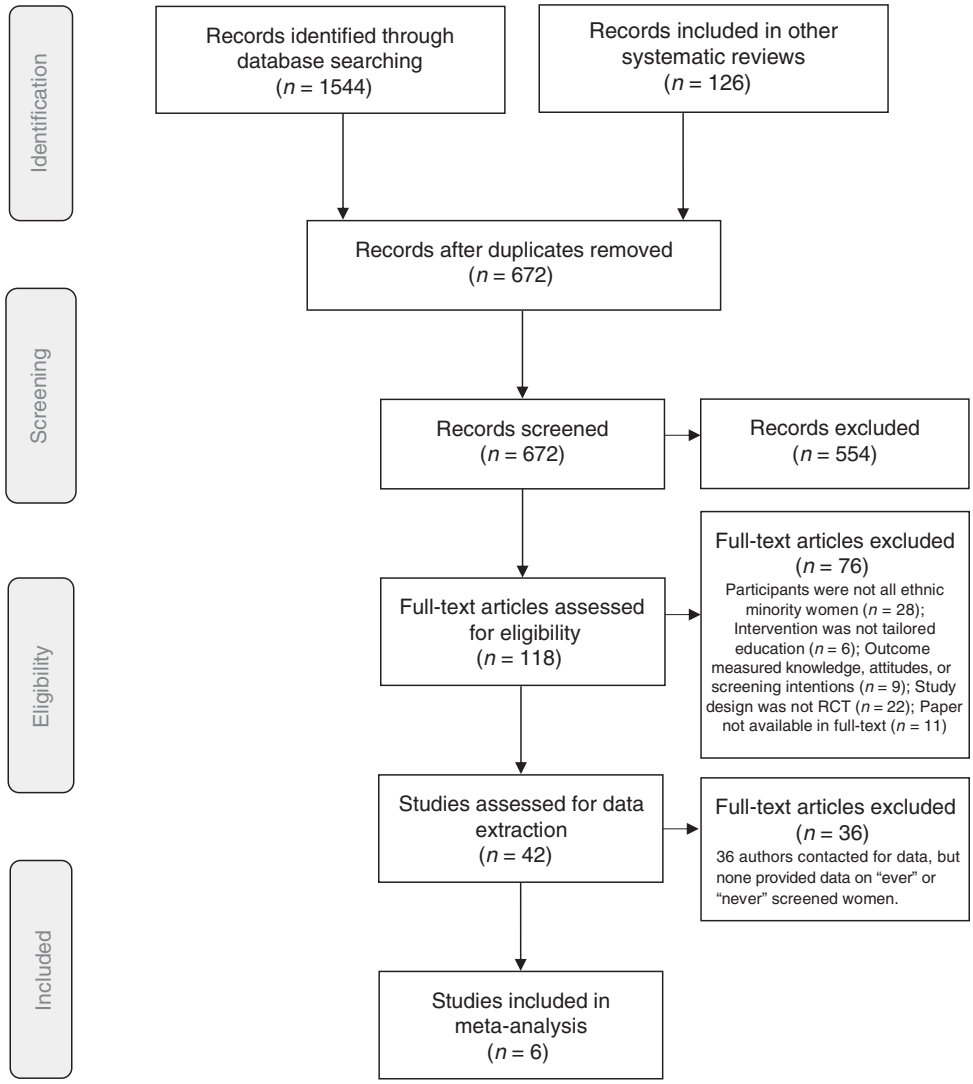


FIGURE 1. Flow diagram of selection of studies included in the meta-analysis. RCT indicates randomized controlled trial.

TABLE 1. Characteristics of the Included Studies

References	Participants Enrolled in the Study/Reported Attendance at Mammography Screening	Inclusion Criteria	Screening History at Baseline	Intervention	Control Group	Follow-up (mo)
Gotay et al[29]	1260/678	Native Hawaiian women, age > 18 y	In the baseline questionnaire, women were asked if they had ever received a mammogram and when they had last done so. Screening history among the participants at baseline: Never screened: 25%. Ever screened: 75% (of these 60% were compliant with screening guidelines)	Group educational program culturally tailored to Hawaiian women, led by female Native Hawaiian lay health workers who focused on traditional Hawaiian interaction and experience sharing among the women. Screening and cancer-related information was provided through group education, audiovisual aids, and written materials in Hawaiian language	Care as usual	4–5
Lee-Lin et al[30]	300/300	Chinese immigrant women (foreign-born), in Oregon (USA). Age > 40 y, with no history of breast cancer and no mammogram within 12 mo	Screening history was assessed with the following questions: Have you had a mammogram in the past 12 mo? Have you had a mammogram any time before the 12 mo? Screening history among the participants at baseline: Never screened: 28%. Ever screened: 72% (those compliant with guidelines were excluded based on inclusion criteria)	Group educational program culturally tailored to Chinese women, led by trained staff, targeted message, and individual counselling sessions that focused on commonly held cultural and health beliefs among Chinese women. Screening and cancer-related information was provided through group education and tailored written materials	Standardized brochure	3, 6, and 12 mo
Maxwell et al[31]	530/447	Filipino women in Los Angeles (USA), age > 40 y	Baseline questionnaire documented breast and cervical cancer screening history (ever had a mammogram, recency of last test). Screening history among the participants at baseline: Never screened: 19%. Ever screened: 81% (48% within the last 12 mo, 21% 1–2 y ago, and 12% over 2 y)	Educational group sessions culturally tailored to Filipino women, led by female Filipino health educators, supplied with tailored information packages to take home. Screening and cancer-related information was provided through group education and brochures in Taglish (local) language	Physical activity module	12
Mishra et al[32]	809/775	Samoan women in California, Samoan (any part) ancestry, age > 42 y, with no mammogram within the past 2 y	Pretest survey included the question "have you ever had a mammogram?" Screening history among the participants at baseline: Never screened: 59%. Ever screened: 41% (those compliant with guidelines were excluded based on inclusion criteria)	Educational group program culturally tailored to Samoan women, led by Samoan health lay workers that focused on team building, interactive group discussions, storytelling, and role play. Screening and cancer-related information were provided through group education and educational booklets in Samoan language	Usual care	8
Nguyen et al[33]	1100/1089	Vietnamese American women in California, age > 40 y	Outcome measures included ever having had a mammogram, and having had a mammogram within the past 12 mo.	Group educational program culturally tailored to Vietnamese women, led by female Vietnamese American lay health	Media campaign and written	2

(*Continued*)

TABLE 1. Characteristics of the Included Studies (*continued*)

References	Participants Enrolled in the Study/Reported Attendance at Mammography Screening	Inclusion Criteria	Screening History at Baseline	Intervention	Control Group	Follow-up (mo)
			Screening history among the participants at baseline: Never screened: 13%. Ever screened: 87% (69% within the last 12 mo)	workers, containing presentations, group discussions, and question answering. Screening and cancer-related information was provided through group education, flipchart, booklets, and culturally tailored media campaign, and tailored written materials in Vietnamese	in-formation	
Sadler et al[34]	984/232	African American women in California, self-identified African American, age > 20 y	Baseline questionnaire covered a self-reported date of the last mammogram. Screening history among the participants at baseline: Never screened: 55%. Ever screened: 45% (compliant with guidelines: not estimable)	Individual customized education, provided by trained cosmetologists at selected beauty salons that used dialog to engage clients to screening. Screening and cancer-related information was provided through conversations, posters, and magazines tailored to African American women that were displayed throughout the salons. Cosmetologists used synthetic breast models to show clients how a lump feels	Diabetes education	6

Data Extraction

Study characteristics were extracted and validated by 2 authors (T.B.B., A.T.). Included studies reported their outcomes in percentages, risk differences, or number of participants, which required data to be converted into a common format. As cell numbers in the 2×2 contingency tables were used as input data in the current meta-analysis, the number of participants was chosen as the common format. All data were independently extracted by 2 authors (T.B.B., P.L.) and converted several times to reduce risk of errors. Discrepancies were resolved by recalculation. The datasets are available upon request.

Risk of Bias Assessment

Assessment of risk of bias (RoB) was performed independently by 2 authors (T.B.B., S.B.) using the Cochrane Collaboration's tool for assessing RoB in randomized trials, version 2,[24] with its guidance documents.[25] The outcome assessed was mammography screening attendance among ever screened and never screened participants.

Statistical Analyses

The analyses were conducted in Stata SE release 16 (P.L.). The meta-analysis used a significance level of $P = 0.05$ and 95% confidence interval (CI). The effect measure was log (RR).[26] Analyses with both a random effects and a fixed effects model were run to test the stability over the models. The random effects model was preferred, with DerSimonian-Laird overall effect estimate.[27] The forest plot presents the effect estimates of the included studies, with the overall effect size, with D+L estimation of the between-study variation. For the fixed effects model, the overall effect was calculated with the Mantel-Haenszel (M-H) pooled estimate.[27]

Statistical heterogeneity was examined using I^2 statistics with its P-value.[26,27] The I^2 statistic measures the percentage of total variation in study results that is due to statistical heterogeneity. An I^2 of 25% can indicate low heterogeneity; 50%, moderate heterogeneity; whereas I^2 over 75%, high heterogeneity.[28] L'Abbé plots were used to analyze heterogeneity of the effect measure.[26] Publication bias was assessed by visual examination of funnel plots and the Harbord test to examine and interpret asymmetry.[26]

RESULTS

Search Results

The literature searches identified 1544 records, where 118 articles were assessed for eligibility in full text. Of the 42 articles that met the inclusion criteria, 36 articles did not report subgroup analyses of participants ever screened and never screened. All corresponding authors were contacted for data, but none provided the results we needed. Six articles were eligible for inclusion and included in the meta-analysis[29–34] (Fig. 1).

Characteristic of the Included Studies

The 6 studies included 3521 women. All studies were conducted in the United States and published between the years 2000 and 2015. Sample sizes ranged from 232 to 1089. All studies used self-reported data. All interventions consisted

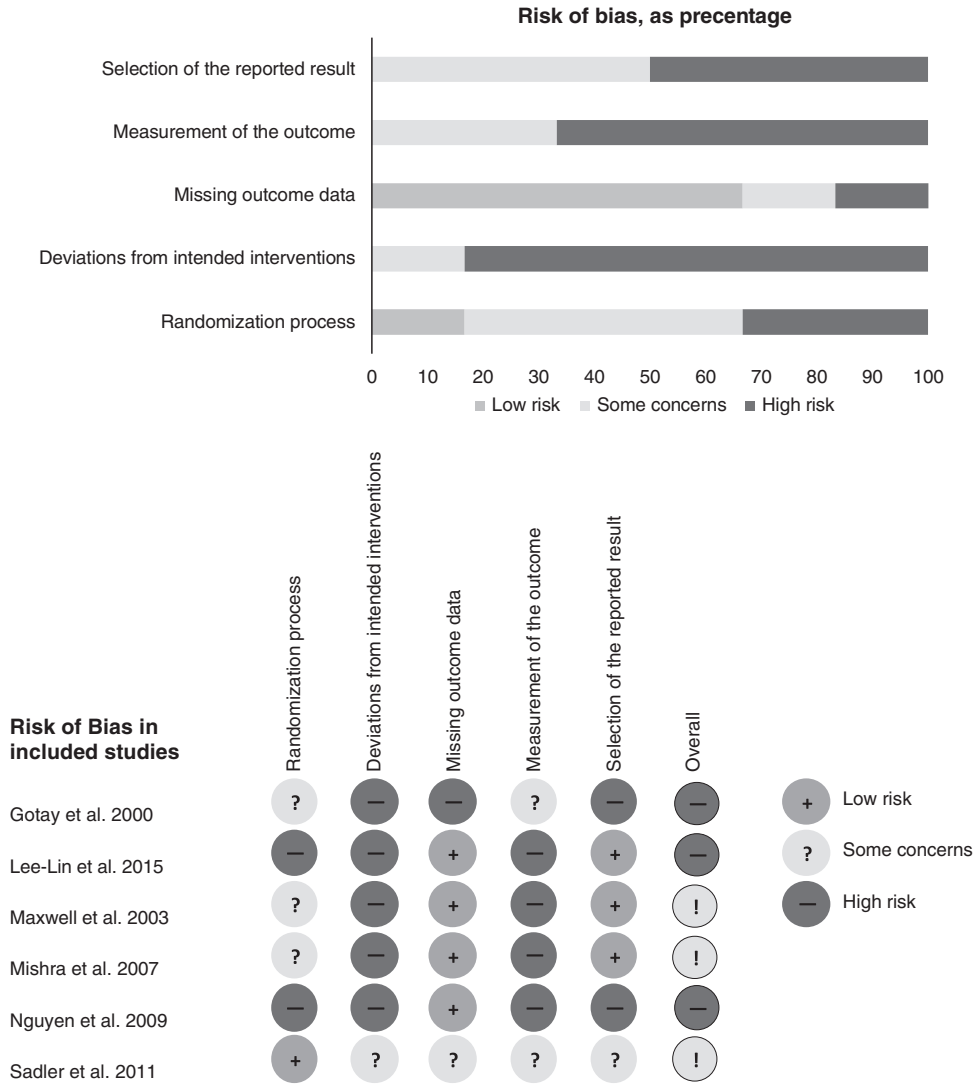


FIGURE 2. Risk of bias in included studies. Summarized results of the risk of bias assessment using the risk of bias 2 tool.

of verbal information provided face-to-face by persons who received standardized training in advance. All interventions combined verbal information with written information, video, or media campaigns targeting ethnic minority women. Examples of cultural strategies used to tailor the interventions were traditional storytelling, blessings, inviting local celebrities, or serving traditional snacks. Study characteristics are described in Table 1.

Risk of Bias

The results of the RoB assessment are presented in Figure 2. There were no disagreements between the 2 authors (T.B.B., S.B.), and, therefore, no statistical measures of agreement before consensus discussions were calculated. The randomization procedure was insufficiently described in most studies. Studies were assessed to have high RoB when the between-group differences could favor the intervention group. All studies relied on self-reported data, and as the participants were not blinded, the outcome could have been influenced by knowledge of received intervention.[25] Studies that offered money to the intervention group before collecting the self-reported data or paid a lay health worker a substantial amount of money to educate, motivate, and collect self-reported data were assessed as high RoB. In several studies, the results for participants ever screened were inadequately reported. Studies that reported significant intervention effects that could have been caused entirely by the large between-group differences of ever screened and never screened at baseline were assessed as high RoB.

Effectiveness of Tailored Education Among Never Screened Women

The D+L pooled RR for mammography attendance for women never screened was 1.54 (95% CI, 1.24–1.91; $P < 0.001$), with low heterogeneity ($I^2 = 27.1\%$, $P = 0.231$). The forest plot shows the individual and overall effects with random effects model (Fig. 3). The pooled RR for the fixed effects model, with M-H estimates, was 1.52 (95% CI,

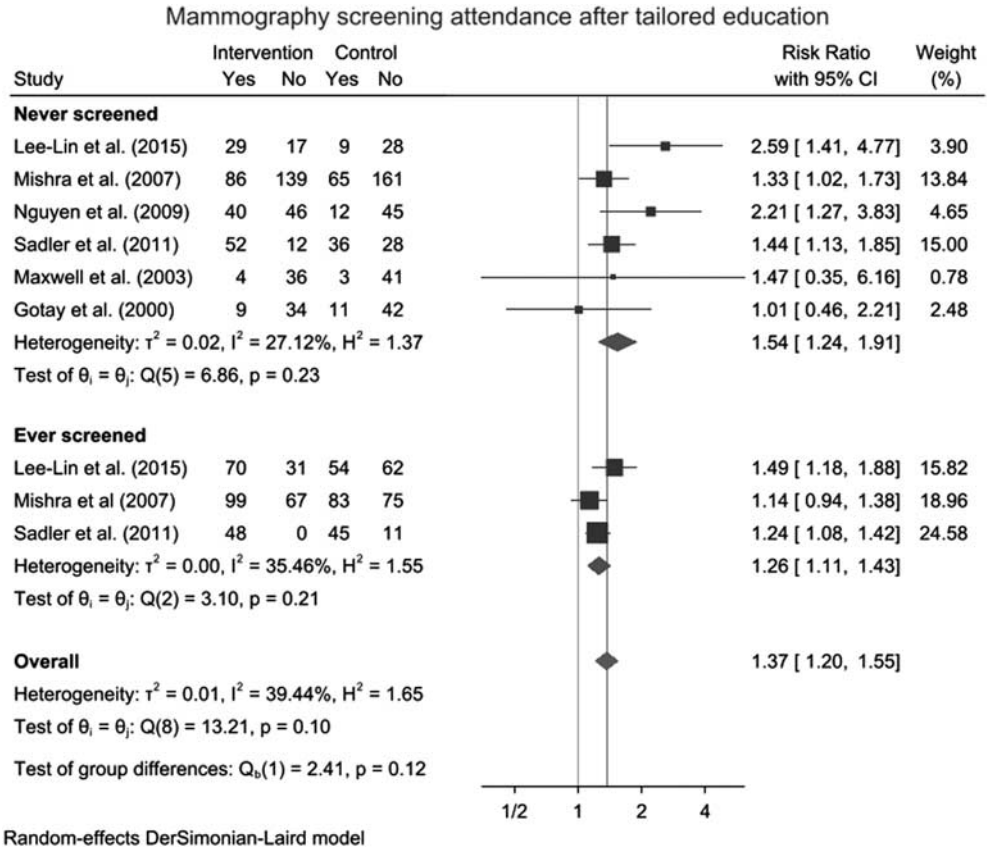


FIGURE 3. Forest plot of mammography screening attendance after tailored education. Forest plots for mammography screening attendance after tailored education for women never screened and women ever screened. Only 3 studies provided outcome data on participants ever screened. CI indicates confidence interval.

1.29–1.80; $P < 0.001$). The heterogeneity was explored by visual examination of L'Abbé plots (Supplemental Digital Content 2, http://links.lww.com/MLR/C274). Publication bias was assessed by visual examination of a funnel plot, showing no asymmetry (Supplemental Digital Content 3, http://links.lww.com/MLR/C275). Asymmetry was also explored by the Harbord test, and no statistically significant asymmetry was found ($P = 0.867$).

Effectiveness of Tailored Education Among Ever Screened Women

Only 3 studies provided outcome data on participants ever screened. The D+L pooled RR for attendance for women ever screened was 1.26 (95% CI, 1.11–1.43; $P < 0.001$), with low heterogeneity ($I^2 = 35.5\%$, $P = 0.213$) (Fig. 3). The corresponding results for the fixed model with the M-H estimate was 1.26 (95% CI, 1.12–1.42; $P < 0.001$).

DISCUSSION

The current meta-analysis shows that tailored education gives statistically increased attendances at mammography of 54% among the women who had never been screened and 26% among ever screened women. Although the increase is more than double among never screened women than among ever screened women, the difference is not statistically significant ($P = 0.10$). Although careful judgment is needed when interpreting these results, due to few included studies and high RoB in several primary studies, the findings suggest that women's screening history is an important characteristic that affects how effective tailored education is on mammography attendance. This meta-analysis appears to be the first review that validated empirically the importance of women's screening history.

The substantial effectiveness of tailored education among never screened women was higher compared with previous meta-analyses and reviews on educational interventions.[18,35,36] This suggests that future research may want to address the never ever screened dichotomy. Different types of messages or interventions may be required for helping women to schedule and attend their first-time screening appointment (for never screened women) versus helping them follow guideline-recommended repeated screening (for ever screened women). Educational programs have extensive variation in time, content, message, setting, and group dynamics. Thus, identifying the most appropriate educational approach and measuring the "active ingredient" is difficult.[37] The World Cancer Report of 2020 states that achieving relatively high participation rates in cancer screening will reduce health inequalities.[38] The findings of this study suggest that tailored education may increase breast cancer attendance, both among never and ever screened women.

It seems like a paradox that researchers aim to increase screening among women with low attendance, while including women who have taken a screening test within the past 12 months and who are compliant with guidelines. We may ask, why intervene with women who are already following the screening guidelines? This is an important ethical and economic question. In addition, when studying the effect of an intervention, there may be questions about risks of bias. Obviously, if a sufficient proportion of participants have recently taken a screening test, the risk of false negatives and false positives becomes high. Owing to a lack of reported data, we were unable to explore the effectiveness among women who were recently screened versus those who were not compliant. Therefore, we recommend research on the elapsed time factor in the ever group. We encourage future research that aims to increase screening among underscreened populations, not to include participants who have recently been screened or, at a minimum, provide separate analyses for these women.

The amount of research on cancer screening is extensive, and there may be studies that our search failed to identify. We identified 42 studies on tailored educational interventions to ethnic minority women on cancer screening, but, unfortunately, only 6 studies provided data on mammography attendance among "never screened" and "ever screened" women. This shows that many studies have been conducted on this topic, but very few have taken screening history into consideration when reporting their findings. We hope that this study can contribute to a shifting focus on the importance of screening history, both when enrolling participants and when reporting results. We encourage researchers to explore the applicability of this study's findings to other ethnic minority groups and to screening for other cancers.

CONCLUSIONS

The current meta-analysis shows that tailored education increased attendance at mammography. Although careful judgment is needed when interpreting these results due to the small number of included studies and high RoB in several primary studies, the findings suggest that women's screening history is an important and ignored variable that affects how effective tailored education is on mammography attendance.

REFERENCES

1. Bhargava S, Tsuruda K, Moen K, et al. Lower attendance rates in immigrant versus non-immigrant women in the Norwegian Breast Cancer Screening Programme. *J Med Screen*. 2017;25:155–161.
2. Bhargava S, Moen K, Qureshi SA, et al. Mammographic screening attendance among immigrant and minority women: a systematic review and meta-analysis. *Acta Radiol*. 2018;59:1285–1291.
3. Ahmed AT, Welch BT, Brinjikji W, et al. Racial disparities in screening mammography in the United States: a systematic review and meta-analysis. *J Am Coll Radiol*. 2017;14:157–165.
4. Rondet C, Lapostolle A, Soler M, et al. Are immigrants and nationals born to immigrants at higher risk for delayed or no lifetime breast and cervical cancer screening? The results from a population-based survey in Paris metropolitan area in 2010. *PLoS One*. 2014;9:e87046.
5. Vahabi M, Lofters A, Kumar M, et al. Breast cancer screening disparities among urban immigrants: a population-based study in Ontario, Canada. *BMC Public Health*. 2015;15:679.
6. Kristiansen M, Thorsted BL, Krasnik A, et al. Participation in mammography screening among migrants and non-migrants in Denmark. *Acta Oncol*. 2012;51:28–36.
7. Brzoska P, Abdul-Rida C. Participation in cancer screening among female migrants and non-migrants in Germany: a cross-sectional study on the role of demographic and socioeconomic factors. *Medicine*. 2016;95:e4242.
8. Norredam M, Nielsen SS, Krasnik A. Migrants' utilization of somatic healthcare services in Europe—a systematic review. *Eur J Public Health*. 2010;20:555–563.
9. Stewart B, Wild CP. *World Cancer Report 2014*. Lyon: International Agency for Research on Cancer, WHO; 2017.
10. Schueler KM, Chu PW, Smith-Bindman R. Factors associated with mammography utilization: a systematic quantitative review of the literature. *J Womens Health (Larchmt)*. 2008;17:1477–1498.
11. Azami-Aghdash S, Ghojazadeh M, Gareh Sheyklo S, et al. Breast cancer screening barriers from the woman's perspective: a meta-synthesis. *Asian Pac J Cancer Prev*. 2015;16:3463–3471.
12. Adunlin G, Cyrus JW, Asare M, et al. Barriers and facilitators to breast and cervical cancer screening among immigrants in the United States. *J Immigr Minor Health*. 2019;21:606–658.
13. American Cancer Society. *Cancer Facts and Figures for African American, 2019–2021*. Atlanta, GA: American Cancer Society; 2019.
14. Bailey ZD, Krieger N, Agénor M, et al. Structural racism and health inequities in the USA: evidence and interventions. *Lancet*. 2017;389:1453–1463.
15. Bhargava S, Hofvind S, Moen K. Gender, letters, relatives, and God: mediating actors in mammographic screening among Pakistani women in Norway. *Acta Radiol Open*. 2019;8:2058460119875015.
16. Wang JH, Mandelblatt JS, Liang W, et al. Knowledge, cultural, and attitudinal barriers to mammography screening among nonadherent immigrant Chinese women: ever versus never screened status. *Cancer*. 2009;115:4828–4838.
17. Miller BC, Bowers JM, Payne JB, et al. Barriers to mammography screening among racial and ethnic minority women. *Social Sci Med*. 2019;239:112494.
18. Brevik TB, Laake P, Bjørkly S, et al. Effect of culturally tailored education on attendance at mammography and the Papanicolaou test. *Health Serv Res*. 2020;55:457–468.
19. Higgins JPTTJ, Chandler J, Cumpston M, et al. *Cochrane Handbook for Systematic Reviews of Interventions Version 60*. Chichester, UK: John Wiley & Sons; 2019.
20. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med*. 2009;151:264–269.
21. Cambridge Dictionary. Ethnic minority. Available at: https://dictionary.cambridge.org/dictionary/english/ethnic-minority. Accessed August 20, 2019.
22. National Cancer Institute. Dictionary of cancer terms. Tailored interventions. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/tailored-intervention. Accessed August 20, 2019.
23. McGowan J, Sampson M, Salzwedel DM, et al. PRESS peer review of electronic search strategies: 2015 guideline statement. *J Clin Epidemiol*. 2016;75:40–46.
24. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
25. Risk of Bias Info. ROB2 tool. Available at: https://www.riskofbias.info/welcome/rob-2-0-tool. Accessed February 2, 2020.
26. Fagerland MW. Evidence-based medicine and systematic reviews. In: Laake P, Benestad HB, Olsen BR, eds. *Research in Medical and Biological Sciences*. Oxford, UK: Elsevier Ltd; 2015:431–461.
27. Fagerland MW, Lydersen S, Laake P. *Statistical Analysis of Contingency Tables*. Boca Raton: Chapman & Hall/CRC; 2017.
28. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557–560.
29. Gotay CC, Banner RO, Matsunaga DS, et al. Impact of a culturally appropriate intervention on breast and cervical screening among native Hawaiian women. *Prev Med*. 2000;31:529–537.
30. Lee-Lin F, Nguyen T, Pedhiwala N, et al. A breast health educational program for Chinese-American women: 3- to 12-month postintervention effect. *Am J Health Promot*. 2015;29:173–181.

31. Maxwell AE, Bastani R, Vida P, et al. Results of a randomized trial to increase breast and cervical cancer screening among Filipino American women. *Prev Med*. 2003;37:102–109.
32. Mishra SI, Bastani R, Crespi CM, et al. Results of a randomized trial to increase mammogram usage among Samoan woman. *Cancer Epidemiol Biomarkers Prev*. 2007;12:2594–2604.
33. Nguyen TT, Le G, Nguyen T, et al. Breast cancer screening among Vietnamese Americans: a randomized controlled trial of lay health worker outreach. *Am J Prev Med*. 2009;37:306–313.
34. Sadler GR, Ko CM, Wu P, et al. A cluster randomized controlled trial to increase breast cancer screening among African American women: the black cosmetologists promoting health program. *J Natl Med Assoc*. 2011;103:735–745.
35. Chan DN, So WK. A systematic review of randomised controlled trials examining the effectiveness of breast and cervical cancer screening interventions for ethnic minority women. *Eur J Oncol Nurs*. 2015;19: 536–553.
36. Han H-R, Lee J-E, Kim J, et al. A meta-analysis of interventions to promote mammography among ethnic minority women. *Nurs Res*. 2009; 58:246.
37. Center for Reviews and Dissemination. *Systematic Reviews CRD Guidance for Undertaking Reviews in Health Care*. York: University of York, York Publishing Services Ltd; 2009.
38. Wild C, Weiderpass E, Stewart B. *World Cancer Report: Cancer Research for Cancer Prevention*. York: International Agency for Research on Cancer; 2020.

Article 3

International Journal of Gynecology and Obstetrics

Training health providers to administer VIA as a screening test for cervical cancer: A systematic review of essential training components.

--Manuscript Draft--

Manuscript Number:	
Article Type:	Review Article
Keywords:	Cervical cancer; Cancer prevention; Screening; VIA; Training; Women's health, Global health, Systematic review
Corresponding Author:	Thea Brevik Molde University College: Hogskolen i Molde Molde, NORWAY
First Author:	Thea Brevik
Order of Authors:	Thea Brevik
	Lara Rodrigues da Matta Calegari
	Isabel Mosquera Metcalfe
	Petter Laake
	Mauricio Maza
	Partha Basu
	Adam Todd
	Andre L Carvalho
Manuscript Region of Origin:	Europe
Abstract:	Background: Cervical cancer screening program using Visual inspection after application of acetic acid (VIA) depends on high-quality training of providers. Objectives: To examine essential training components described in VIA training programs. Search strategy: A systematic review of PubMed, Embase, and Web of Science (from 2006 to 2021) was undertaken. Selection criteria: Studies on VIA screening after training of providers with any level of health education were included. The outcome of interest was the reporting of the VIA training components. Data collection and analysis: We developed a framework to conceptualize seven essential VIA training components and applied that framework to determine how training courses has been carried out in different settings. Two reviewers independently assessed studies and extracted data. Main results: 14 primary studies eligible for inclusion. We found that most training courses lasted 5-7 days, and included theoretical education, practical skill development, and competence assessment. It was unclear how visual aids and training in client counselling and quality assessment were integrated in the courses. Extended on-job training was provided through supervision, feedback, and refresher training. Conclusions: International training recommendations are feasible to implement in real settings. Comprehensive learning programs for providers of cervical cancer screening and treatment are necessary.

The Editor-in-Chief
International Journal of Gynecology & Obstetrics

On-line submission

10 December 2021

Dear Editor,

On behalf of the authors, I am pleased to submit a manuscript entitled '*Training health providers to administer visual inspection after application of acetic acid (VIA) as a screening test for cervical cancer: A systematic review of essential training components'* (3453 words) for consideration of publication.

Cervical cancer screening program using Visual inspection after application of acetic acid (VIA) depends on high-quality training of providers. In WHO's recent updated guideline on cervical cancer screening, HPV DNA detection is recommended as the gold standard for primary testing for cervical cancer screening, rather than VIA or cytology in a 'screen and treat' approach for women in the general population. For women living with HIV, a 'screen, triage and treat' approach is recommended for HPV detection. Despite these recommendations, many countries with limited resources will have to continue with VIA as the primary screening test till they have enough resources to introduce HPV detection tests. In the HPV screen and treat algorithm, health providers will still need similar clinical training to visually triage women eligible for treatment. In some countries, VIA will have a key role as a triage test even after introduction of HPV test, especially in countries with high HIV prevalence. Although VIA can generally be performed by health providers after a short period of training, it has been unknown to what extent the providers of VIA are trained or how far the guidelines on training are adhered to.

In this systematic review, we developed a framework to conceptualize essential VIA training components and have applied that framework to the literature to determine how extensive VIA training has been carried out in different settings. Our review shows that training recommendations given by international institutions are feasible to implement in real settings. I hope the readers of the journal will find this article interesting and learn from the experience of these implemented training programs.

Our review team was composed of eight review members, including members from IARC, Newcastle University, the Center for Global Health Inequalities Research (CHAIN) in Norway, and PAHO. We would therefore kindly ask you to consider our publication with eight authors. All authors contributed to the interpretation of data, to drafting and revising the manuscript, and have provided the final approval of the version to be published. I confirm that neither any of my co-authors nor I have any personal, commercial, political, academic, or financial conflict of interests.

Yours sincerely,

Thea Beate Brevik.

International Journal of Gynecology & Obstetrics
Submission Requirements Form

A completed Submission Requirements Form must be uploaded with your submission. Submitted manuscripts without a completed form will not be considered. Authors should read and adhere to the Author Guidelines when preparing their articles and when completing this form.

If it is found that the statements that have been checked are not a true reflection of the submission, the manuscript may be returned without review.

Instructions: Save the Submission Requirements Form to your computer, check all of the relevant items, and save the file. Upload the saved document along with the other files.

SECTION A: GENERAL

Please complete all boxes in Section A with a check '[x]' or '[n/a]' if not applicable.

[x] The first page of the manuscript contains the names and affiliations of all authors; the name and full contact information of the corresponding author; keywords; synopsis; and word count of the main text.

[x] A breakdown of how each author contributed to the study and write-up has been included in an Author contributions section prior to the references. Please refer to the ICMJE guidelines for authorship.

[x] A conflict of interest statement has been included in the cover letter and before the reference list in the manuscript.

[x] All references and their citations adhere to the format detailed in the Author Guidelines.

[x] All tables and/or figures adhere to the format detailed in the Author Guidelines.

[x] I have read the IJGO policy on plagiarism (see Author Guidelines). I confirm that there are no instances of plagiarism in my manuscript. I understand that IJGO will assess my manuscript using plagiarism detection software.

[n/a] If copyright permission is required to reproduce any material in the article (in print and online), confirmation has been included in the cover letter that such permission has been obtained from the copyright holder; precise reference to the original work has been included at an appropriate location in the manuscript.

[n/a] For papers containing acknowledgments of named individuals, permissions have been cleared.

[n/a] The generic names of all pharmaceutical preparations have been provided.

SECTION B

Please complete only the statements relating to the type of paper you are submitting: (1) Clinical Article/Clinical Trial; (2) Review Article; (3) Brief Communication; or (4) Other.

1. **Clinical Articles**

[ ] A structured abstract not exceeding **200 words** has been submitted. It contains all and only the following headings: **Objective**; **Methods**; **Results**; and **Conclusion**.

[ ] For studies of patients, patient records, or volunteers: the methods include a statement that the research protocol was approved by the relevant Institutional Review Board or Ethics Committee before the study began. The name of the Board/Committee has been provided. The author(s) must agree to provide copies of the appropriate documentation if requested;

OR

[ ] If Institutional Review Board or Ethics Committee approval was not needed/obtained, an explanation is provided in the methods.

If your paper reports on a Clinical Trial, please also complete the following section. Otherwise, please leave blank. All of the below criteria for clinical trials must be fulfilled. Clinical Trial papers with any of the following information missing will be returned without review.

[ ] Participants were prospectively assigned to a health-related intervention, with or without concurrent comparison or control groups.

[ ] Registration was sought **prospectively** from a public clinical trial registry (see Author Guidelines for more information on clinical trial registration).

[ ] Trial registration number, name of registry website, and URL of registration have been listed at the end of the abstract.

[ ] A statement of informed consent has been included in the manuscript.

[ ] The CONSORT statement and checklist have been consulted: http://www.consort-statement.org/consort-2010. A CONSORT flowchart has been submitted as an editable figure in Word/PowerPoint format.

2. Review Articles

[x] Systematic Reviews: An abstract not exceeding **200 words** has been submitted, containing the following headings: **Background**; **Objectives**; **Search strategy**; **Selection criteria**; **Data collection and analysis**; **Main results**; and **Conclusions.**

[ ] Narrative Reviews: An unstructured abstract not exceeding 200 words has been submitted.

[x] Systematic review/meta-analysis. The PRISMA guidelines have been consulted and followed: http://www.prisma-statement.org/.

[ ] Meta-analysis of observational studies. The MOOSE guidelines have been consulted and followed: http://www.consort-statement.org/mod_product/uploads/MOOSE%20Statement%202000.pdf.

3. Brief Communications

[ ] No abstract has been included.

[ ] Case Reports include confirmation that all human participants gave written/verbal informed consent before the study began. The author(s) agree to provide copies of the appropriate documentation if requested.

[ ] For studies of patients, patient records, or volunteers: the methods include a statement that the research protocol was approved by the relevant Institutional Review Board or Ethics Committee before the study began. The name of the Board/Committee is provided. The author(s) must agree to provide copies of the appropriate documentation if requested.

OR

[ ] If Institutional Review Board or Ethics Committee approval was not needed/obtained, an explanation is provided in the methods.

[ ] If informed consent was not needed/obtained, an explanation is provided in the methods.

4. Other types of research

If your paper does not fit any of the categories in Section B, please detail the article type using free text below.

Training health providers to administer visual inspection after application of acetic acid (VIA) as a screening test for cervical cancer: A systematic review of essential training components.

Thea Beate Brevik[1,2], Lara Rodrigues da Matta Calegari[3], Isabel Mosquera Metcalfe[4], Petter Laake[5,1], Mauricio Maza[6], Partha Basu[4], Adam Todd[7,8], Andre L Carvalho[4]

[1] Faculty of Health Sciences and Social Care, Molde University College, Molde, Norway.

[2] Clinic of Surgery, Møre and Romsdal Hospital Trust, Molde Hospital, Molde, Norway.

[3] Mackenzie Evangelical School of Medicine, Curitiba, Paraná, Brazil.

[4] Early Detection, Prevention, and Infections Branch, International Agency for Research on Cancer, Lyon, France.

[5] Oslo Centre for Biostatistics and Epidemiology, Department of Biostatistics, University of Oslo, Oslo, Norway.

[6] Department of Noncommunicable Diseases and Mental Health, Unit of Noncommunicable Diseases, Violence, and Injury Prevention, Pan American Health Organization, Washington, DC, USA.

[7] School of Pharmacy, Newcastle University, Newcastle upon Tyne, United Kingdom.

[8] Centre for Global Health Inequalities Research (CHAIN), Norwegian University of Science and Technology (NTNU), Trondheim, Norway.

Corresponding author
Thea Beate Brevik
Faculty of Health Sciences and Social Care, Molde University College, Molde, Norway.
P.O. Box 2110, 6402 Molde, Norway.
Thea.b.brevik@himolde.no

Keywords: Cervical cancer; Cancer prevention; Screening; VIA; Training; Women's health, Global health, Systematic review

Synopsis: International training recommendations on cervical cancer screening using VIA are feasible to implement in real settings.

Words counts: 3452 words

Type of article: Review Article

Abstract (199 words)

Background: Cervical cancer screening program using Visual inspection after application of acetic acid (VIA) depends on high-quality training of providers.

Objectives: To examine essential training components described in VIA training programs.

Search strategy: A systematic review of PubMed, Embase, and Web of Science (from 2006 to 2021) was undertaken.

Selection criteria: Studies on VIA screening after training of providers with any level of health education were included. The outcome of interest was the reporting of the VIA training components.

Data collection and analysis: We developed a framework to conceptualize seven essential VIA training components and applied that framework to determine how training courses has been carried out in different settings. Two reviewers independently assessed studies and extracted data.

Main results: 14 primary studies eligible for inclusion. We found that most training courses lasted 5-7 days, and included theoretical education, practical skill development, and competence assessment. It was unclear how visual aids and training in client counselling and quality assessment were integrated in the courses. Extended on-job training was provided through supervision, feedback, and refresher training.

Conclusions: International training recommendations are feasible to implement in real settings. Comprehensive learning programs for providers of cervical cancer screening and treatment are necessary.

MAIN TEXT (3452 words)

Introduction

Cervical cancer ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women, with an annual estimated 604,127 cases and 341,831 deaths worldwide[1]. A disproportionate number occur among women living in low-and-middle-income countries (LMICs)[2]. The World Health Organization (WHO) recommended in their guidelines published in 2013 visual inspection after application of acetic acid (VIA) as the most feasible and affordable alternative to cytology screening for the LMICs[3]. VIA involves naked-eye examination of the uterine cervix with appropriate illumination after application of freshly prepared 3–5% acetic acid solution[4]. The test aims to detect precursor lesions as well as early cervical cancers in asymptomatic women[3]. VIA is widely used as a screening test in LMICs, often in a 'screen and treat' approach where screen-positive women are offered immediate treatment[4]. Such an approach has been demonstrated to reduce the number of clinic visits by women, improve compliance with treatment, and make the program efficient[4].

The paradigm of cervical cancer screening is evolving rapidly[4]. WHO updated their guideline on cervical cancer screening in July 2021[5], which recommends Human Papillomavirus (HPV) DNA detection as the gold standard for primary testing for cervical cancer screening, rather than VIA or cytology in a 'screen and treat' approach for women in the general population. For women living with HIV, a 'screen, triage and treat' approach is recommended for HPV detection[5]. Despite these recommendations, many countries with limited resources will have to continue with

VIA as the primary screening test till they have enough resources to introduce HPV detection tests[4]. In the HPV screen and treat algorithm, health providers will still need similar clinical training to visually triage women eligible for treatment. In some countries, VIA will have a key role as a triage test even after introduction of HPV test, especially in countries with high HIV prevalence[4].

VIA can generally be performed by health providers after a short period of training[4]. The interpretation of the test is based on the detection of a well-defined dense acetowhite area on the transformation zone of the cervix appearing one minute after the application of acetic acid solution[4]. Studies have found that the provider's professional background (e.g. physicians, nurses, health workers) does not influence the test accuracy of VIA[6], and that trained non-physicians can perform VIA screening while maintaining high-quality services[3,7]. However, due to subjective nature of the test, success of the screening program depends on the high quality training of providers[4]. Worldwide, there are many training manuals providing guidelines on VIA training[8-14]. However, at present, it is unknown to what extent the providers of VIA are trained or how far the guidelines on training are adhered to. Designing an effective training program can be a complex process, and although most of the principles, steps, and interpretations remain similar, the contexts and settings may differ. In this systematic review, we (1) aimed to examine which essential training components have been described in VIA training programs and (2) provide examples to illustrate how the training components have been carried out in different clinical settings.

Material and methods

The review protocol is registered with Prospero (CRD42021220497) and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[15] (Table S1).

Eligibility criteria

We included studies that reported on an implemented or scaled-up cervical cancer screening program using VIA for all women in all countries. The participants (trainees) could have any background of health education. The outcome of interest was the reporting of the VIA training components. To be included in the systematic review, studies had to be published in English in a peer-reviewed journal. Studies only available as abstracts were excluded from the systematic review.

Literature search

Searches were conducted in PubMed, Embase, and Web of Science; the initial search was undertaken in December 2020 and updated in October 2021 (Table S2). We searched for papers published after 2006 because the framework we used to conceptualize VIA training was based on a landmark publication from 2005 on essential training components in VIA screening with international consensus among members of the Alliance for Cervical Cancer Prevention (ACCP)[8]. PICO forms were used to create a structured and precise search strategy (Table S3). The search strategy and history were critically assessed using the evidence-based checklist of peer review of electronic search strategies (PRESS EBC)[16]. The reference lists of included articles were also hand searched for further relevant articles.

Study selection

The title and abstract and full text assessments were carried out in Covidence by two reviewers (TB and LC). TB reviewed 10% of the titles and abstracts, with checking by LC until the Cohen's Kappa coefficient (κ) was > 0.7. Then TB continued the title and abstract assessment independently. Excluded abstracts were categorized in Covidence and made available to the review team for transparency. The full text assessment was conducted by TB and checked in full by LC. Any discrepancies between the two reviewers were resolved by discussion. If agreement could not be reached, the project leader (AC) was consulted who had the final say in the decision.

Data extraction

Information was extracted for each study using a standardized form, which included the following variables: the contextual settings (country, healthcare setting, and year of VIA implementation), target population eligible for screening, trainees (number and professions), information relating to the training program, and results (timeframe of follow-up, screening participation rates, and VIA positivity (+) rates). Data extraction was carried out by TB and checked in full by LC. Disagreements were resolved by discussion, and if agreement could not be reached, the project leader (AC) had the final say.

Framework to conceptualize VIA training

Informed by the Alliance for Cervical Cancer Prevention (ACCP)[8], and after discussion with screening experts at the International Agency for Research on Cancer (IARC), a framework to conceptualize essential VIA training components was developed (Table 1).

Data synthesis

When synthesizing the reported information on the VIA training, one reviewer (TB) carried out a dichotomy coding (Y/N) for the presence of the seven components in each of the included studies. LC checked the coding, while AC was consulted for consensus on disagreements. Since many authors did not describe their interventions in detail probably due to word limitations of publications, we contacted all the corresponding authors to obtain more information about their training intervention. Out of 14 corresponding authors contacted, ten responded and provided additional information about the VIA training.

Results

Search results

The database searches identified 4867 records: after title and abstract screening, 35 full papers were assessed for eligibility (Figure 1). In total, 14 unique primary studies (representing 15 articles) were included in this systematic review[17-31].

Characteristics of included studies

All included studies reported on implemented VIA screening programs in resource-constrained settings (Table 2). The studies were from nine African countries (Botswana[28], Burkina Faso[20], Cameroon[27], Eswatini[29], Ethiopia[21], Malawi[23], Nigeria[24], Tanzania[25,30], Zambia[26]), Indonesia[18], India[17,22], and Guyana[19]. The cervical cancer screening programs were delivered in community- or hospital-based clinics, with many using existing health facilities, such as HIV clinics. The years the training programs were conducted were between 1998[17] and 2017[23]. Four studies[19,21,23,28] specifically targeted HIV positive

women in their screening approach. In total, the studies included in the final analysis reported to have screened 406,611 women, ranging from 556 women screened in 5 days[25] to 102,942 women screened in 7 years[26]. In the included studies, the total number of VIA trainees was 2847 providers, ranging from 3[29] to 2216[18], although we note two studies[26,28] did not report the number of trainees. The trainees included nurses[19-21,23,24,26-30], midwives[18-21,24,28,29], physicians[18-22,24,30], health workers[17,24,25], and other ranks of health providers[18,19,30].

VIA training courses

The VIA training courses were heterogeneous with substantial variability in their objectives, structure, content, duration, and reporting. In all studies but one[17], VIA was implemented in a screen-and-treat approach, where 5 studies[26-30] integrated digital technologies to enhance performance of VIA, such as using digital imaging[28] or smartphones[30]. Table 3 outlines the reported training components in each of the included studies.

Most training programs were based on international training guidelines, such as the WHO's guide to essential practice in comprehensive cervical cancer control[12,13], and adapted to the specific setting. One study[28], undertaken in Botswana, trained nurses because they were more available than physicians and familiar with performing pelvic exams. Another study[22] trained private practitioners in India, based on the long-standing association of working with doctors in public health programs. A third study[24] trained community health workers in Nigeria because nurses and doctors were largely absent in rural communities.

Training duration

Most of the VIA training courses lasted between 5 and 7 days. In one study[21], for Ethiopian nurses and midwives, the training course lasted for 10 days, while for obstetricians and gynecologists, it was 5 days. Another study[17] implemented a four-week training course for primary health workers in India, which equipped the trainees to perform VIA screening as good as an expert ($\kappa = 0.84$), leading to a statistically significant reduction in cervical cancer mortality[17]. In contrast, one study[18] implemented a standardized 5 day training course for over 2000 trainees in Indonesia: the same training course was provided to doctors as well as community health workers. Three studies[26-28] organized training courses that lasted between 2 and 8 weeks to train the trainees in both VIA screening and new digital technology. Another study[30] included providers who had previously completed a 6-days training course and screened more than 50 women, before organizing a new training program focusing on technical training on smartphone-enhanced VIA.

Theoretical training

All studies reported a theoretical educational component in the training program. In general, however, the included studies reported limited information about the content of the theoretical sessions. The main areas covered were education on: female genital anatomy and cervical cancer pathophysiology; the VIA screening procedure; recognition and interpretation of features on VIA; appropriate treatment and referral of VIA positive women; and, infection prevention. Some of the training courses also included information about specific considerations, such as characteristics of cervical cancer in HIV positive women. One study[20] chose to arrange adaptive educational

sessions that focused on the trainees' weaknesses identified through an initial assessment of baseline knowledge and skills.

Practical hands-on

All the reported training courses included practical hands-on sessions, either classroom-based or clinic-based, although the sessions were conducted in different ways. In one study[18], the trainees went through a one-day live demonstration of VIA, after which they were able to practice on women in a clinic under supervision of appropriately trained professionals. Another study[25] reported that trainees had four days of hands-on training with women called from the community to undergo VIA. A third study[24] reported that trainees were trained in the classroom on techniques related to insertion of a vaginal speculum (with identification of cervix using a pelvic model), visual inspection of the cervix, test sampling, and application of acetic acid (simulated learning).

Client counselling

Overall, the included studies contained limited information regarding how trainees were trained in client counselling. One study[24] reported that the lecture topics included counselling and informed choice, while the classroom-based practical sessions covered post-test counselling of patients. Another study[21] used checklists to validate the trainees' skills in interpersonal communication and counselling. Although the studies reported limited information on the training of client counselling, many of the included studies emphasized that participating women were counselled in the clinical setting about the screening techniques and any side effects that may arise. One study[25] described that healthcare staff explained to the women in

Swahili the risks and benefits of the VIA screening procedure, including the meaning and consequences of a positive test and the availability of treatment. One study[28] highlighted that the technology produced high resolution images that could be used to educate and counsel the women and this was included as a component of the training program.

Visual aids

Some of the studies reported the use of visual aids to support training, such as photographic images[20,24,25], flash cards[21,29], educational videos[21], and PowerPoint presentations[29]. One study[25] reported that several de-identified patient cervical images of VIA-positive and -negative examples were shown to ensure that the trainees could practice categorizing clinical impression. Two studies[20,24] reported using anatomic models for identification of the cervix.

Competency assessment

Several studies reported that the trainees' competence was assessed at the end of the training course. In one study[18], each trainee had to perform VIA on 100 women, out of which the 2-3 VIA positive cases were confirmed by the supervisor. Another study[30] considered the trainees as graduated from the training program based on the number of women screened, the concordance/agreement with reviewers, and the threshold for the number of VIA positive women in their participant history. In one study[28], each trainee had to successfully perform 100 VIA examinations, 100 digital photographs, and 35 cryotherapies.

Quality assurance

Few studies reported on including a quality-assurance module into the general training. One study[24] reported that the educational lectures covered topics on recording, appropriate documentation, and referral systems. Another study[20] let the trained providers collect and monitor the data together with the researchers, which allowed the providers to visualize progress, analyze trends, evaluate themselves, and identify potential bottlenecks in service provision. Furthermore, this approach empowered the trained providers to track progress, identify gaps, and take corrective actions to remedy any shortcomings, thereby reaching more successful outcomes[20].

Continued training in VIA

After the training course, nearly all the VIA training programs made provisions for on-job training at the providers' own clinical settings through supervision, feedback, and refresher training. On-job supervision was provided by allowing the trained providers to work in pairs with experienced gynecologists or nurses who supervised their practice. Regular supportive supervision visits from experts were provided to offer transfer of learning. In one study[26], nurses visited rural facilities every three months for purposes of quality assurance and continued medical education. On-job feedback and mentoring were provided by experts reviewing the cervical images, captured during VIA by the providers, on a regular basis. Such regular meeting with experts offered feedback and education[29], increased understanding[28], and arrival at consensus opinions for treatment options[27]. Regularly organized refresher trainings and workshops were also used to retain or enhance VIA competency.

Needs for additional training or mentorship of the providers were identified through measuring the VIA+ rates as a performance quality indicator for monitoring and evaluation purposes. Studies have shown that the VIA+ in general population of women aged 30–60 years ranges between 5 and 10%[32]. The positivity is a higher in settings with a higher HIV prevalence. If the test positivity is too low, there is a possibility of missing the disease, while if it is too high, there is a higher possibility of false positives[32]. However, it is more important to measure VIA+ serially over time to check if the rate is stable. In one study[29], the VIA+ rate was at 16% after the initial training but increased to 40% after nine months. After a refresher training and continued mentoring were implemented, the positivity rate decreased to an average of 6.3%, which was maintained all along the program[29]. In another study, the proportion of women considered to have inadequate VIA test reduced following additional training of nurses to better expose the endocervical canal[27]. Although all the included studies reported the average VIA+ rate over the length of their screening program, only five studies[17,20,26,27,29] reported serial point estimates of the VIA+ rate over time (Figure 2). These five studies all provided prolonged training after the initial training course and showed that the VIA+ rates reached the expected level over time.

Discussion

In this systematic review, we developed a framework to conceptualize essential VIA training components and have applied that framework to the literature to determine how extensive VIA training has been carried out in different settings. Our study shows that most training courses are held over a period of 5-7 days, where theoretical education is combined with skill development, alongside the assessment

of competence. It is not always clear how the trainees learn client counselling and quality assessment, or if visual aids are integrated in the training courses. Many programs provide extended training in the providers' clinical settings through additional supervision, feedback, and/or refresher training. These findings indicate that implemented VIA training programs have been carried out in line with international recommendations[8-11], but more importantly, that the training recommendations are feasible to implement in real settings. With good training and sustained quality assurance and monitoring, screening of women with VIA followed by appropriate management of screen-positive women can reduce cervical cancer incidence and mortality[4,17,33]. However, VIA performance varies widely, and the VIA+ rates have shown high variability between countries[34] and within the same program or setting[35]. Although research studies have shown a high sensitivity, around 75%, the sensitivity reported from some real programmatic settings have ranged from 25% to 82%[36]. This is essentially due to the subjective nature of the test. The best way to compensate for that is to train the providers rigorously and organizing periodic refresher training and mentoring.

A major pitfall in training is the lack of specific recommendation from international organizations. One size may not fit all, but some training guidance on the minimum requirements (e.g., duration of training, number of cases to be observed, and trainees to trainer ratio) will be very helpful. As the new WHO guidelines[5] refer to the screen and treat approach based on HPV primary screening followed by visual triage for treatment, it is important to have clear standards on how trainings should be conducted. Health providers must be trained to visually triage women eligible for

cryotherapy based on their HPV status and not on the presence of acetowhite lesions. Still, VIA will have a key role as a triage test after introduction of HPV test in some countries. A high proportion of women with a positive HPV test will not necessarily have cervical precancer or cancer, and to reduce the referral for all HPV-positive women for colposcopy and/or treatment, many countries will use VIA to triage HPV-positive women (4). In setting with high prevalence of HIV, health providers will continue to perform VIA to triage women. WHO Academy is collaborating with IARC to develop a comprehensive learning program for providers of cervical cancer screening and treatment.

We found that many of the included studies reported that their training program was adapted to their specific settings, but without explaining which kind of adaptations were done and on what basis. Without a complete published description regarding the details of the training programs, it can be challenging to implement courses that are known to be successful and replicate or build on the research findings[37]. In a systematic review on the context in which cervical cancer screening is delivered in India, the authors mention that many of the included studies did not provide any information on the training[38]. To improve future reporting on training to support cancer screening, we encourage authors to highlight the specific components of the training program, including how the training was delivered, and in what context. There are similar reporting tools in the literature, which could be used to adapted for this purpose; for example, the TIDieR (Template for Intervention Description and Replication) checklist[37] that is used to report interventions in healthcare.

Our review has highlighted a large variability in the organization, structure, content, and delivery of training. However, we have not assessed the quality and impact of training. Monitoring and evaluation of services are required and must be performed continuously at all levels[13]. This requires structured evaluation of the training monitoring the performance of the trainees. Initially, our aim was to explore quality indicators (such as VIA+, treatment, and referral rates), to explore the success of each training program. However, the quality indicators were too diversely reported between studies to link these data to the effectiveness of training programs, as this could contribute to clinical misleading results and erroneous conclusions. We found that most of the included studies only reported the average VIA+ rate by the length of the study programs, while studies reporting point estimates over time showed that the VIA+ rate with prolonged training reached an acceptable level. For future reviewers to be able to explore the effectiveness of VIA training programs, we recommend a more homogeneous reporting of the VIA+ rate and that the positivity rate after training is reported together with measurements over time.

Study limitations

Our search strategy was initially designed to identify studies on provider-directed interventions on cancer screening participation among disadvantaged populations. A limitation in our search is that some relevant keywords are missing, such as “VIA”. However, the search includes relevant keywords related to cervical cancer screening, provider training, and screening participation. We searched manually for additional papers of interest to ensure that relevant studies that potentially could be missing from our database searches were identified.

Author contributions

TB, LC, AT, CB, IM, AC, and PB contributed substantially to the conception and design of the project.

TB and LC were responsible for the literature search, study selection, and extraction of data.

All authors contributed to the interpretation and analysis of data.

All authors contributed to drafting the article and revising it critically for important intellectual content.

All authors have provided the final approval of the version to be published.

Acknowledgements

This publication is supported by a grant awarded by the Norwegian Research Council (project number 288638) to the Center for Global Health Inequalities Research (CHAIN) at the Norwegian University for Science and Technology (NTNU).

Conflicts of interest

The authors declare no conflict of interest.

Disclaimer

Where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy, or views of the International Agency for Research on Cancer /World Health Organization.

References

[1] International Agency for Research on Cancer. Cancer Today, [IARC website]. 2021. https://gco.iarc.fr/today/online-analysis-pie?v=2020&mode=cancer&mode_population=continents&population=900&populations=900&key=total&sex=2&cancer=39&type=0&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&nb_items=7&group_cancer=1&include_nmsc=1&include_nmsc_other=1&half_pie=0&donut=0. Assessed November 22, 2021.

[2] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394-424.

[3] World Health Organization. *WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention*. Geneva: WHO; 2013.

[4] Mittal S, Basu P, Lucas E. Atlas of visual inspection of the cervix with acetic acid for screening, triage, and assessment for treatment [Cancer Screening at IARC website]. 2020. https://screening.iarc.fr/atlasvia.php. Assessed November 08, 2021.

[5] World Health Organization. *WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition*. Geneva: WHO; 2021.

[6] Sauvaget C, Fayette J-M, Muwonge R, Wesley R, Sankaranarayanan R. Accuracy of visual inspection with acetic acid for cervical cancer screening. *Int J Gynecol Obstet*. 2011;113(1):14-24.

[7] World Health Organization. *WHO guidelines: Use of cryotherapy for cervical intraepithelial neoplasia.* Geneva: WHO; 2011.

[8] Blumenthal PD, Lauterbach M, Sellors J, Sankaranarayanan R. Training for cervical cancer prevention programs in low-resource settings: Focus on visual inspection with acetic acid and cryotherapy. *Int J Gynecol Obstet.* 2005;89:S30-S7.

[9] JHPIEGO. *Cervical Cancer Prevention. Guidelines for Low-Resource Settings.* Baltimore: Jhpiego; 2007.

[10] Alliance for Cervical Cancer Prevention. *Planning and implementing cervical cancer prevention and control programs: A manual for managers*. Seattle: ACCP; 2004.

[11] International Agency for Research on Cancer. Tutorial: a training course in visual inspection with 5% acetic acid (VIA). [IARC learning website]. 2015. https://learning.iarc.fr/edp/courses/tutorial-course-via/ Assessed October 10, 2021.

[12] World Health Organization. *Comprehensive cervical cancer control: a guide to essential practice.* Geneva: WHO; 2006.

[13] World Health Organization. *Comprehensive Cervical Cancer Control: A Guide to Essential Practice.* Geneva: WHO; 2014.

[14] Sellors JW, Sankaranarayanan R. *Colposcopy and treatment of cervical intraepithelial neoplasia: A beginner's manual*. Lyon: IARC; 2003.

[15] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Bmj*. 2021;372:n71.

[16] McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. *J Cancer Epidemiol.* 2016;75:40-6.

[17] Shastri SS, Mittra I, Mishra GA, et al. Effect of VIA screening by primary health workers: randomized controlled study in Mumbai, India. *J Natl Cancer Inst.* 2014;106(3):dju009.

[18] Nuranna L, Aziz MF, Cornain S, et al. Cervical cancer prevention program in Jakarta, Indonesia: See and Treat model in developing country. *J Gynecol Oncol*. 2012;23(3):147.

[19] Martin CE, Tergas AI, Wysong M, Reinsel M, Estep D, Varallo J. Evaluation of a single-visit approach to cervical cancer screening and treatment in Guyana: Feasibility, effectiveeness and lessons learned. *J Obstet Gynaecol Res.* 2014;40(6):1707-16.

[20] Ouedraogo Y, Furlane G, Fruhauf T, et al. Expanding the single-visit approach for cervical cancer prevention: successes and lessons from Burkina Faso. *Glob Health Sci Pract.* 2018;6(2):288-98.

[21] Shiferaw N, Salvador-Davila G, Kassahun K et al. The single-visit approach as a cervical cancer prevention strategy among women with HIV in Ethiopia: successes and lessons learned. *Glob Health Sci Pract.* 2016;4(1):87-98.

[22] Shikha S, Smita J, Nayanjeet C, et al. Experience of a 'Screen and treat'program for secondary prevention of cervical cancer in Uttar Pradesh, India. *J Obstet Gynaecol Res.* 2020;46(2):320-7.

[23] Talama GC, Shaw M, Maloya J et al. Improving uptake of cervical cancer screening services for women living with HIV and attending chronic care services in rural Malawi. *BMJ Open Qual.* 2020;9(3):e000892.

[24] Awolude OA, Oyerinde SO, Akinyemi JO. Screen and triage by community extension workers to facilitate screen and treat: task-sharing strategy to achieve universal coverage for cervical cancer screening in Nigeria. *J glob oncol.* 2018;4:1-10.

[25] Bernstein M, Hari A, Aggarwal S, et al. Implementation of a human papillomavirus screen-and-treat model in Mwanza, Tanzania: training local healthcare workers for sustainable impact. *Int Health.* 2018;10(3):197-201.

[26] Parham GP, Mwanahamuntu MH, Kapambwe S, et al. Population-level scale-up of cervical cancer prevention services in a low-resource setting: development, implementation, and evaluation of the cervical cancer prevention program in Zambia. *PloS one*. 2015;10(4):e0122169.

[27] DeGregorio G, Manga S, Kiyang E, et al. Implementing a fee-for-service cervical cancer screening and treatment program in Cameroon: challenges and opportunities. *The oncologist.* 2017;22(7):850.

[28] Ramogola-Masire D, de Klerk R, Monare B, Ratshaa B, Friedman HM, Zetola NM. Cervical cancer prevention in HIV-infected women using the “see and treat” approach in Botswana. *J Acquir Immune Defic Syndr.* 2012;59(3).

[29] Asgary R, Staderini N, Mthethwa-Hleta S, et al. Evaluating smartphone strategies for reliability, reproducibility, and quality of VIA for cervical cancer screening in the Shiselweni region of Eswatini: A cohort study. *PLoS Med*. 2020;17(11):e1003378.

[30] Yeates K, Erwin E, Mtema Z, et al. Smartphone-enhanced training, QA, monitoring, and evaluation of a platform for secondary prevention of cervical cancer: Opportunities and challenges to implementation in Tanzania. *JCO Glob Oncol.* 2020;6:1114-23.

[31] Mittra I, Mishra GA, Singh S, et al. A cluster randomized, controlled trial of breast and cervix cancer screening in Mumbai, India: methodology and interim results after three rounds of screening. *Int. J. Cancer.* 2010;126(4):976-84.

[32] World Health Organization. *Monitoring national cervical cancer prevention and control programmes: quality control and quality assurance for visual inspection with acetic acid (VIA)-based programmes*. Geneva: WHO; 2013.

[33] Sankaranarayanan R, Esmy PO, Rajkumar R, et al. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. *Lancet*. 2007;370(9585):398-406.

[34] Arbyn M, Sankaranarayanan R, Muwonge R, et al. Pooled analysis of the accuracy of five cervical cancer screening tests assessed in eleven studies in Africa and India. *Int J Cancer.* 2008;123(1):153-60.

[35] Selmouni F, Belakhel L, Sauvaget C, et al. Evaluation of the national cervical cancer screening program in Morocco: achievements and challenges. *J Med Screen.* 2019;26(3):162-8.

[36] Bigoni J, Gundar M, Tebeu PM, et al. Cervical cancer screening in sub-Saharan A frica: A randomized trial of VIA versus cytology for triage of HPV-positive women. *Int J Cancer.* 2015;137(1):127-34.

[37] Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *Bmj*. 2014;348.

[38] Adsul P, Manjunath N, Srinivas V, Arun A, Madhivanan P. Implementing community-based cervical cancer screening programs using visual inspection with acetic acid in India: A systematic review. *Cancer epidemiol.* 2017;49:161-74.

Figure legends

Figure 1: Flow diagram

Prisma flow chart of search results and study selection.

Figure 2: VIA positivity rates over time

Five studies reported serial point estimates of the VIA+ rate in percent over years. The five studies all provided prolonged training after the initial training course and showed that the VIA+ rates reached the expected level over time. The VIA+ in general population of women aged 30–60 years normally ranges between 5 and 10%.

Table 1: Description of essential training components

Essential training components	Description
1) Training course delivered over a defined period of time	The length of the training course should depend on the trainees' skill-level at baseline and the amount of clinical practice available during training. The training should be long enough to ensure that the VIA screening services are delivered with both competence and confidence. The training should take place in a real clinical setting, if not the actual service-delivery site. A 5 to 10- day duration of training course is generally considered as appropriate for the trainees (clinicians, nurses, and midwives) to obtain adequate knowledge and clinical skills to deliver services competently. In a real health service setting it is challenging for the health professionals to leave their routine job for a longer duration to attend such targeted training.
2) Theory-based education	The training course should contain theory-based elements, that cover the fundamental purpose, principles, and the specifics of the VIA procedure. There should be an emphasis on anatomy, physiology, and the etiology of cervical cancer at a level that is suitable for the selected trainees and that is highly practical. Understanding how VIA is performed and the interpreting the test by the nature of acetowhite reaction is required.
3) Hands-on competency-based skill acquisition	The training course should include practical hands-on experience that ensures that each trainee can practice the VIA technique on an adequate number of women and, ideally, should be exposed to both test-positive and test-negative women.
4) Client counselling	Trainees should be trained to counsel women about the VIA screening process. Trainees should also know how to counsel a woman who is VIA-positive or who has cervical cancer, including the risks and benefits of the treatment methods offered. Training in counselling can take many forms, like watching video or real-life demonstrations, practicing in a group or counselling a client as part of the VIA procedure.
5) Visual aids	The training course should contain visual aids to show trainees the spectrum of cervical diseases and normal physiological changes that may be observed. Photographs, digital images, flash cards, and interactive CD-ROMs are valuable

	supplements to the learning process. Images should be in color and accompanied with VIA diagnosis from an expert for real-time comparison.
6) Competency assessment	At the end of the training course, the trainees should demonstrate performance of all the steps of a procedure correctly and in the right order without prompting from a trainer. The trainee's competency is best assessed with a performance checklist, and a specific score can be required as part of the successful completion of a training course.
7) Quality assurance	The training course should incorporate a quality-assurance module into the general training to allow the trainees to understand the philosophy of quality assurance, its necessity and required components, and how quality assurance will affect their overall performance. The depth of information presented may vary, but the overall value of quality assurance and how to train people in quality assurance are core concepts. Supplying information about quality assurance relates to the way(s) in which records are kept, information is documented, and programs are tracked. Teaching providers to be effective supervisors is another required element of quality-assurance training.

Table legend

A table illustrating the seven key components of VIA training programs.

Table 2: Characteristics of included studies

Included article	Years of program implemented	Country implemented	Type of screening program	Age-specific inclusion criteria	Number of women screened	Average VIA+ rate over the length of the program	Number of trainees trained	Health education level of the trainees included in the training program
Shastri et al., 2014 (17)	1998-2011	India	Screening approach with referral to treatment.	35-64 years.	63,722	4,6% (2960/ 63,722) over 12 years.	125	Primary health workers: women who had up to 10th grade education, with prior experience of working in community health programs, and good communication skills.
Nuranna et al., 2012 (18)	2007-2010	Indonesia	Screen-and-treat approach.	Unknown.	22,989	4,2% 970/ 22,989) over 3 years.	2216	General practitioners, midwifes, public health cadres, and key people from the society.
Martin et al., 2014 (19)	2009-2012	Guyana	Screen-and-treat approach.	25-49 years.	21,597	13% (2860/ 21,597) over 42 months.	71	Physicians, nurses, midwifes, and medical examiner.

Ouedraogo et al., 2018 (20)	2010-2014	Burkina Faso	Screen-and-treat approach.	25-59 years.	13,999	8,9% over 4 years.	60	Gynecologists, general practitioners, and nurse-midwifes.
Shiferaw et al. 2016 (21)	2010-2014	Ethiopia	Screen-and-treat approach.	30-45 years.	16,527	10% (1656/ 16,527) over 4 years.	77	Nurses, midwifes, and physicians.
Shikha et al., 2020 (22)	2014-2017	India	Screen-and-treat approach.	30-60 years.	100,836	5,4% (5477/ 100,863) over 3 years.	150	Obstetricians, gynecologists, and general practitioners.
Talama et al., 2020 (23)	2017-2018	Malawi	Screen-and-treat approach.	25-49 years.	547	3,9% over 1 year.	6	Nurses.
Awolude, Oyerinde et Akinyemi, 2018 (24)	2016-2017	Nigeria	Screen-and-treat approach.	All women.	950	6,9% (66/ 950) over 1 year.	51	Physicians, nurses, midwifes, and community health workers.
Bernstein et al., 2018 (25)	Unknown	Tanzania	Screen-and-treat approach.	All women.	556	10,6% (59/ 556) over 5 days.	11	Health care workers.
Parham et al., 2015 (26)	2006-2013	Zambia	Digital enhanced screen-and-treat approach.	All women.	102,942	20% (20,319/ 101,867) over 7 years.	Unknown.	Nurses.

DeGregorio et al., 2017 (27)	2007-2014	Cameroon	Digital enhanced screen-and-treat approach.	HIV-positive women >21 years, and HIV-negative women or unknown status >25 years.	44,979	9% (4042/ 44,979) over 8 years.	25	Nurses.
Ramogola-Masire et al., 2012 (28)	2009-2011	Botswana	Digital enhanced screen-and-treat approach.	All women.	2175	11,6-35% (253+506/ 2175) over 2 years.	Unknown.	Nurses and midwifes.
Asgary et al., 2020 (29)	2016-2018	Eswatini	Digital enhanced screen-and-treat approach.	25-49 years.	4247	13,4% (570 /4247) over 1,5 years.	3	Nurses and midwifes.
Yeates et al., 2020 (30)	2016-2017	Tanzania	Digital enhanced screen-and-treat approach.	> 25 years.	10,545	Unknown.	52	Nurses, clinical officers, assistant medical officers, and obstetricians/gynecologists.

Table 3: The reporting of essential components for VIA training courses

Included article [ref]	*Year of implementation*	*Screening program approach*	*Duration of training course*	*Theoretical education*	*Practical hands-on*	*Client counselling*	*Visual aids*	*Competency assessment*	*Quality assurance*
[17] *	1998	Screening	4 weeks	Y*	Y*	Y*	Y*	Y*	Y*
[18]	2007	Screen-and treat (S&T)	5 days	Y	Y			Y	
[19] *	2009	S&T	6 days	Y	Y	Y*	Y*	Y*	Y*
[20] *	2010	S&T	6 days	Y	Y	Y	Y	Y*	Y
[21] *	2010	S&T	5 / 10 days	Y	Y	Y	Y	Y*	Y*
[22] *	2014	S&T	3 days	Y	Y	Y*	Y*	Y*	
[23] *	2017	S&T	5 days	Y	Y*			Y*	
[24]	2016	S&T	5 days	Y	Y	Y	Y	Y	Y
[25]	Unknown	S&T	5 days	Y	Y		Y	Y	
[26]	2006	Digital enhanced S&T	2 weeks	Y	Y				
[27] *	2007	Digital enhanced S&T	2 weeks	Y	Y*	Y*	Y	Y	Y*
[28]	2009	Digital enhanced S&T	8,5 weeks	Y	Y			Y	Y
[29] *	2016	Digital enhanced S&T	1 week	Y	Y		Y	Y*	
[30] *	2016	Digital enhanced S&T	6 days	Y*	Y*		Y*	Y	

* Additional information retrieved through email correspondence with corresponding author.

Figure 1. Flow diagram

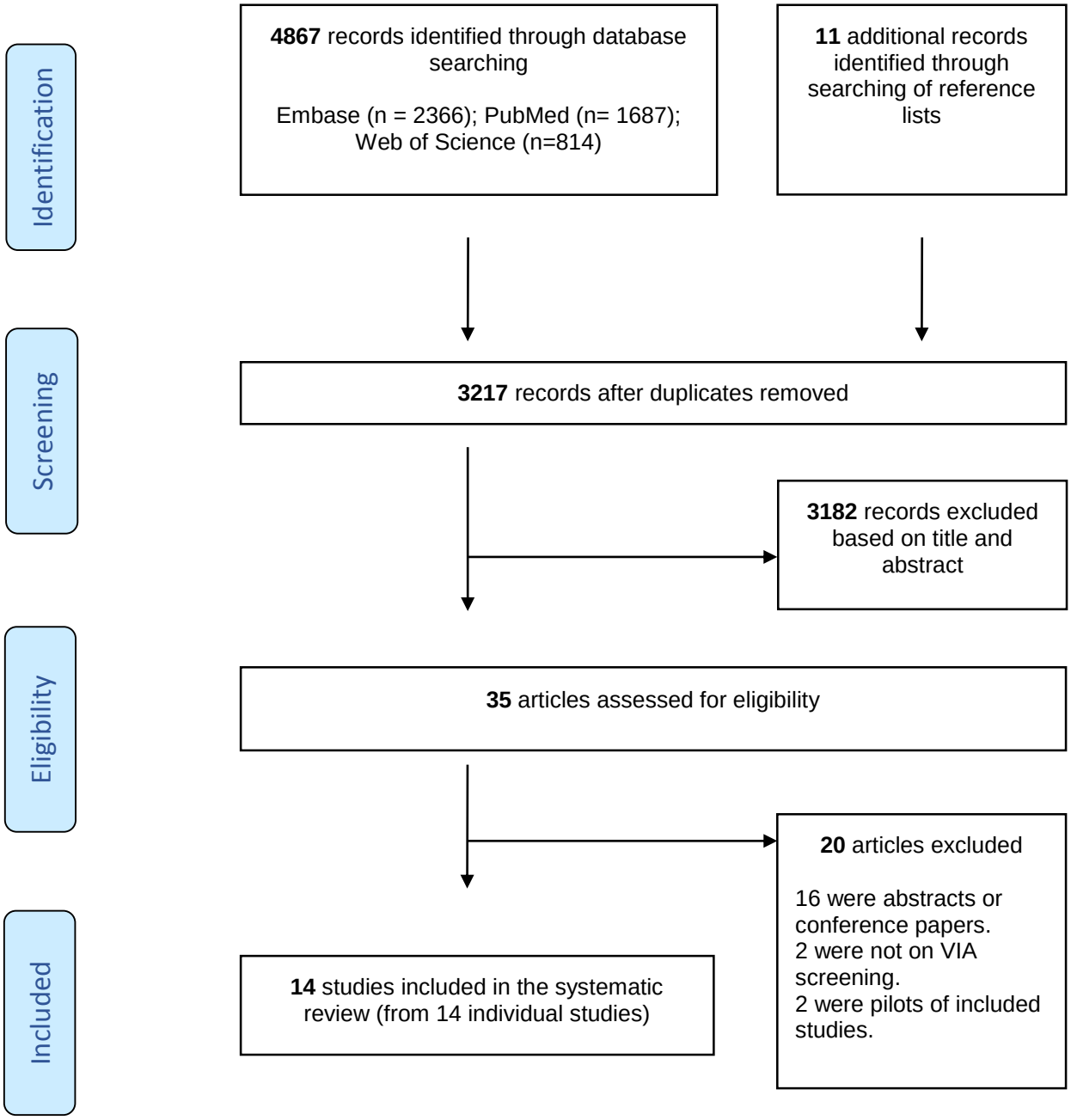


Figure 2: VIA positivity rates over time

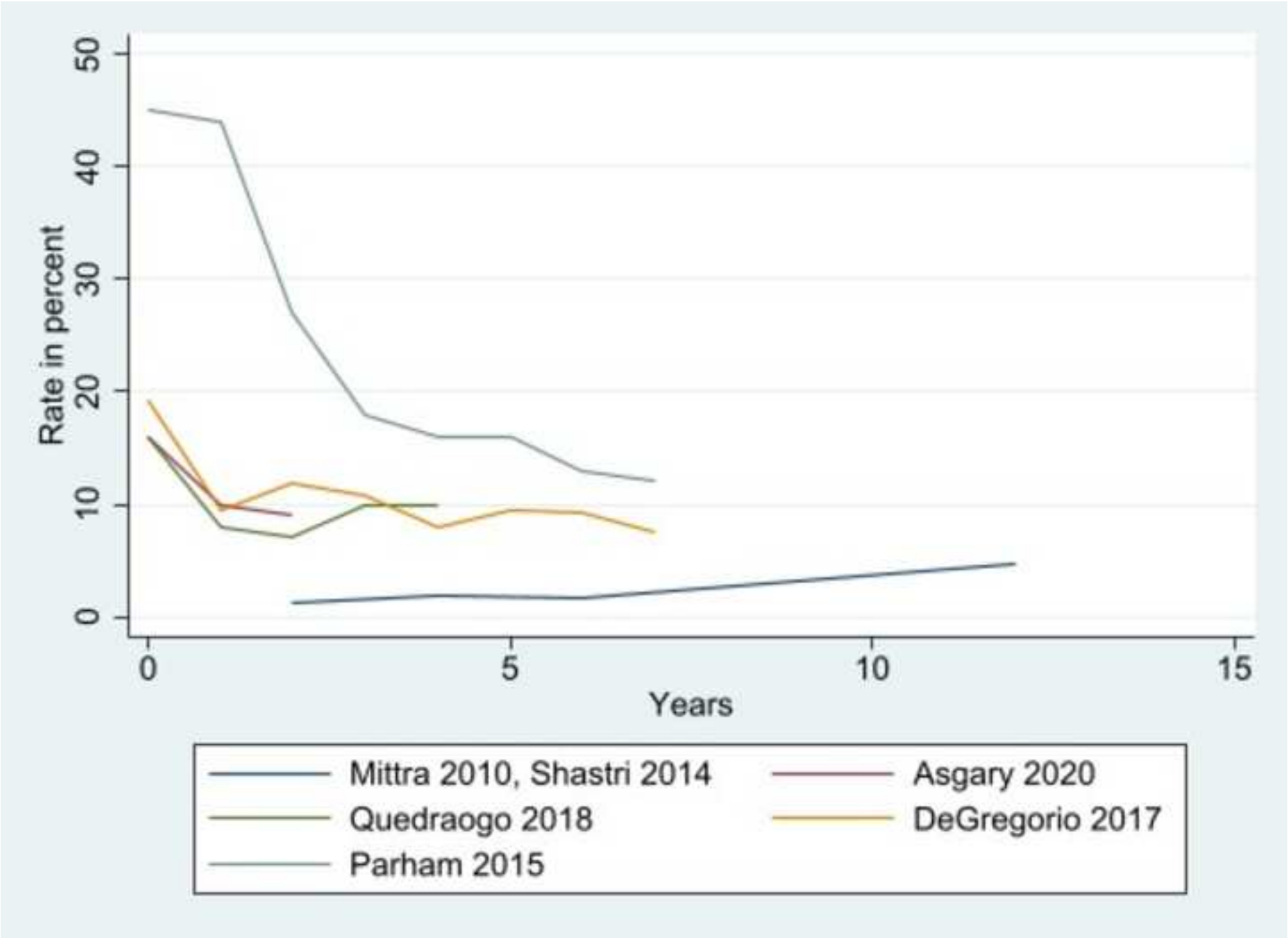
Graph uploaded as a separate file.

Training health providers to administer visual inspection after application of acetic acid (VIA) as a screening test for cervical cancer: A systematic review of essential training components.

Synopsis: International training recommendations on cervical cancer screening using VIA are feasible to implement in real settings.

Figure

Click here to access/download;Figure;Graph2.jpg



ISSN: 2535-2822
ISBN: 978-82-7962-319-9
Trykk: Høgskolen i Molde