



Low-value cancer screening: an evidence- and population-based approach

Study protocol for a PhD thesis

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Student: Frerik Smit, MPH MA

Supervisors: Arnaud Chiolerio, MD PhD & Stéphane Cullati, PhD PD

Background

In the year 2020 in Europe, there were an estimated four million incident cases of cancer and nearly two million cancer-related deaths, where lung, colorectal, and breast cancer represented the three leading causes of cancer mortality accounting for an estimated 770,000 cancer deaths combined [1]. Cancer thereby represents one of most pressing public health challenges that the world faces, particularly given the fact that its burden is expected to keep on rising as a result of our ageing global population [2]. In response to this growing public health concern, cancer screening has been commonly utilised across populations under the premise that such screening can reduce cancer mortality through the detection and treatment of cancers at an early stage in disease progression [3]. These cancer screening efforts have notably been very popular among clinicians and in the wider public [4,5]. However, in an evidence-based public health approach, one of the core tenets that should drive cancer screening decision-making is that its potential benefits need to outweigh its potential harms at a reasonable cost according to existing evidence [6,7]. In turn, cancer screening that does not meet this criterion represents a form of low-value care, which refers to healthcare where existing evidence does not suggest that it brings a meaningful net benefit to patients and population health [8,9].

The highest-quality evidence on cancer screening benefits come from randomised controlled trials [10]. Notably, these trials have shown that the mortality benefits of screening can vary drastically between different cancer and screening types [3]. For instance, a meta-analysis of trials found that mammography screening reduces the relative risk of breast cancer mortality by 20% [11]. In contrast, a meta-analysis of prostate-specific antigen screening for prostate cancer observed a prostate cancer-specific relative mortality reduction of only 4% that was not statistically significant [12]. This evidence thereby shows that the benefits – and therefore also the value – of cancer screening can vary drastically across different screening types.

There is also a wide array of potential harms that cancer screening can lead to. This includes the possibility of false positives – resulting in unnecessary anxiousness and stress – and false negatives – leading people to falsely believe that they are cancer-free [13]. It also includes the potential of serious complications due to the screening test itself and of potential further follow-up testing in the diagnostic confirmation process, such as perforation and major bleeding in the case of colonoscopies [14,15]. Another consequential harm is overdiagnosis, where people who undergo screening are diagnosed with inconsequential cancers that would have never become clinically apparent or symptomatic in their lifetimes in the counterfactual scenario in which they had not undergone screening [3]. While methodological difficulties exist in accurately quantifying rates of overdiagnosis [16], estimates from an independent review indicate that, in the case of mammography screening, there are approximately three women who are overdiagnosed with breast cancer for every breast cancer death prevented from screening [11]. Beyond the potential psychological consequences of a cancer diagnosis on patients and their families [17], such overdiagnosis can also subsequently lead to overtreatment [18]. Looking at the healthcare system as whole, cancer screening also has a considerable cost. For instance, in the United States context it is estimated that the total initial cost of cancer screening (i.e., not counting follow-up costs) on the healthcare system is \$43 billion annually [19]. Correspondingly, any healthcare resources that are allocated to screening also represent an opportunity cost

in terms of the other care – of potentially greater value – that could be provided instead [20]. These potential harms at both an individual- and societal-level thereby emphasise the importance of only utilising cancer screening tests if they bring an overall meaningful net benefit to population health.

Notably, over the years, evidence-based cancer screening guideline recommendations have been developed by independent expert bodies to help guide the general population, patients, clinicians, and policymakers in their decision-making with respect to cancer screening. Of particular significance are the recommendations set forth by the European Commission and the United States Preventive Services Taskforce (USPSTF), which are the culmination of extensive analyses of existing evidence [10,21,22], with the latter being published alongside detailed reports outlining the evidence base and justifications behind their recommendations [15,23–25]. Correspondingly, screening that occurs outside of these guidelines represents screening that is low-value, as existing evidence does not support its use [8].

One key population in which cancer screening is particularly complex is older adults [14,26], namely those above the age of 75 [27,28]. This is because most cancer screening guidelines do not recommend screening after this age (Figures 1 and 2) [21,23–25]. The notable exception to this being screening for colorectal cancer, where certain bodies like the USPSTF recommend that individuals aged 76-85 undergo screening following individualised decision-making [15]. A large proportion of cancer screening among older adults above 75 years of age can therefore be considered low-value [8]. However, it is important to note that there is a general lack of trial evidence on cancer screening's effectiveness within this age group, which is largely driven by individuals above 75 years of age typically being excluded from randomised controlled trials [26]. Obtaining greater clarity regarding cancer screening practices among older adults and its value is therefore critical, and is becoming ever more consequential given the aforementioned rapidly ageing population in which cancer incidence will, in all likelihood, continue to rise [29].

In line with a precision public health approach, there have also been concerted calls for individualised, risk-based approaches to screening [30]. For older adults, this namely includes screening according to life expectancy, with the assertion having been made that older adults whose life expectancy exceeds the lag-time to benefit of screening (i.e., the time period between when screening is undertaken and when a benefit is observed) can still experience a meaningful benefit from being screened [26,31,32]. For the wider population, this also includes screening according to cancer risk, whereby the decision of whether to screen and at what interval frequency is tailored according to people's predicted cancer risk [30,33]. As it stands, these risk-based approaches have yet to be proven effective, but a notable trial of personalised breast cancer screening is currently underway [34].

To date, existing research related to low-value cancer screening and cancer screening in older adults has predominantly been focused on the United States context. This has included a number of studies that have shown that cancer screening is common among people outside of the USPSTF's age recommendations [35–40], as well as among individuals in poor health and/or with limited life expectancy [41–50]. Yet, three notable studies focused on European countries – including Switzerland – have found that over-screening for cervical and breast cancer – from the perspective of screening more

frequently than recommended – is common [51–53]. Further, two studies have found that mammography screening above and below recommendations is common in France [54,55]. This thereby provides reason to believe that low-value cancer screening is likely a frequent phenomenon in Switzerland and across European countries. However, further research is needed to identify and describe the true extent of this form of low-value care within the Swiss and wider European context.

There has also been limited research as to the patterning of cancer screening in older adults who fall above recommended age guidelines. This is partly because most research describing cancer screening utilisation patterns have restricted their study samples to those who fall within recommended age guidelines [52,56–59]. It is therefore not known whether, for example, the differences in cancer screening that have been observed across socioeconomic groups [52,56–59] – in line with the inverse care law [60] – are also present among older adults. Correspondingly, gaining an understanding which groups of the population undergo cancer screening outside of recommendations the most can subsequently help inform efforts aimed at de-implementing this form of low-value care [61,62].

Objectives

This PhD aims to fill these knowledge gaps by describing the frequency of low-value cancer screening in Switzerland and European countries along with its trends and describing the patterning of cancer screening in older adults according to health status and social factors.

Project outlines

Project 1 – Low-value cancer screening in Switzerland

Data:

The four studies that make up Project 1 will utilise data from the Swiss Health Survey, which is a nationwide population-based survey conducted by the Swiss Federal Office of Statistics every five years. The survey aims to provide a cross-sectional overview of the health and health-related behaviours of the population of Switzerland by recruiting a representative sample of the population 15 years of age and above through multistage probability sampling stratified by cantons [63].

Project 1.1A: Cancer screening outside of age recommendations: a population-based study

Aim(s):

1. To describe the frequency of colorectal, breast, cervical, and prostate cancer screening outside of recommended age guidelines in Switzerland.

Methods:

In this study, we will utilise data from the 2022 wave of the Swiss Health Survey, which is the repeated survey's most recently undertaken wave. We will first identify participants who self-reported having undergone screening for breast, cervical, colorectal, and/or prostate cancer specifically for preventive non-symptomatic purposes. Then, for participants who have utilised a screening test, we will calculate their age at screening based on age and self-reported time window of their last respective tests. Participants will subsequently be classified into having been not screened, screened within recommendations, or screened outside of recommendations for each individual screening modality as well as for any cancer screening and any colorectal cancer screening. We will subsequently calculate screening proportions according to recommendations that are weighted using the survey weights provided by the Office of Federal Statistics. The referent evidence-based screening guidelines that will be used are those from the USPSTF published prior to 2022 (Figure 1) [15,23–25], where we will conduct separate analyses according to A, B, and C and A and B graded recommendations [15,23–25].

Project 1.1B: Cancer screening after the age of 75: nationwide population-based trends

Aim(s):

1. To describe trends in prostate, cervical, breast, and colorectal cancer screening after the age of 75 in Switzerland.

Methods:

This study will be limited to the four most recent waves of the Swiss Health Survey (2007, 2012, 2017, 2022) as prior waves have insufficient comparability with respect to their cancer screening variables. For each wave, we will calculate weighted age-standardised proportions of any, prostate, cervical, breast, and colorectal cancer screening specifically for preventive purposes in the past 12 months among older adults above 75 years of age. We will calculate overall proportions, as well as sex- and age-stratified proportions. Subsequently, we will descriptively analyse trends in these proportions over time.

Project 1.2: Cancer screening among older adults above 75 years of age according to health status: a population-based study

Aim(s):

1. To describe cancer screening utilisation among older adults above the age of 75 according to health status in Switzerland.

Methods:

This study will focus on the 2022 Swiss Health Survey. Our primary outcome of interest for this study will be any cancer screening in the past 12 months specifically for

preventive purposes, which will be constructed from self-reported participant information on breast, cervical, colorectal, and prostate cancer screening utilisation. The health status variables of interest will be self-rated health, chronic conditions or long-term health issue, number of morbidities, number of medications, activities of daily living, instrumental activities of daily living, functional limitations, smoking status, and body mass index – all of which are self-reported by participants. We will calculate the weighted proportion of screening according to these health status variables along with weighted prevalence ratios (unadjusted and age- and/or sex-adjusted) using modified Poisson regression models with robust variance estimators. Results stratified by sex will also be calculated, as will results for specific screening types.

Project 1.3: Social distribution of cancer screening among older adults above 75 years of age: a population-based study

Aim(s):

1. To describe cancer screening utilisation among older adults above 75 years of age according to social factors in Switzerland.
2. To describe trends in cancer screening utilisation among older adults within strata of social factors in Switzerland.

Methods:

This study will utilise a similar design to project 1.2 and concordantly focus primarily on the 2022 wave of the Swiss Health Survey. The primary outcome of interest will again be any cancer screening in the past 12 months specifically for preventive purposes, that will also again be constructed through participants' self-reported information on breast, cervical, colorectal, and prostate cancer screening. The predictor variables of interest will be self-reported social factors, namely, education, home ownership, urbanity, nationality, migration background, marital status, type of household, having children, social support, and informal aid received. As was done in project 1.2, we will calculate weighted proportions and weighted prevalence ratios using modified Poisson regression models with robust variance estimators to analyse screening patterns according to social factors, and calculate results stratified by sex and specific screening types. To address our second aim, we will also utilise data from the four most recent waves of the Swiss Health survey as done in project 1.1B. We will subsequently calculate weighted age-stratified proportions of cancer screening in the past 12 months within strata of social variables and descriptively analyse screening differences between social groups over time.

Project 2 – Low-value cancer screening in Europe

Data:

Project 2 will utilise the European Health Interview Survey (EHIS), which aims to provide harmonised nationally representative health survey data of the population 15

years of age and above in individual European Union countries. We will analyse data from the most recent wave of the EHIS (EHIS-3), which has available data on 29 European countries. Data collection for EHIS-3 mainly took place in 2019, with certain countries beginning or ending their data collections in 2018 or 2020 [64,65].

Project title: Cervical cancer screening above age recommendations across 29 European countries: a population-based study

Aim(s):

1. To describe the frequency of cervical cancer screening above recommended age guidelines in Europe.
2. To describe how cervical cancer screening above age recommendations compares to screening within recommendations.

Methods:

For this study, we will use the European Commission's screening recommendations as our referent guidelines, where cervical cancer screening is recommended to women between the ages of 30 and 65 (Figure 2) [21]. Given the lack of granularity of the age variable (EHIS uses a five-year age group anonymisation rule), we are unable to calculate participants' specific age at last screening. As such, we will have our screening outcome be cervical cancer screening within the past 3 years and classify women 70 years of age and above who have screened in the last 3 years as having been screened outside of recommendations. Weighted proportions will be reported individually by European country, with estimates of screening above recommendations among all women above 70 years of age and stratified by five-year age groups. To achieve our second aim, we will calculate and descriptively analyse age-stratified proportions of cervical cancer screening in the past 3 years for all age-strata 20-years of age and above. Further, we will directly compare these proportions between the 60-64- and 70-74-year age-strata to analyse the drop off in screening around the recommended cessation age of 65 years, calculating both relative and absolute reductions in screening. The reason we are comparing the 60-64-year age-strata to the 70-74- instead of the 65-69-year age-strata is because of the age-anonymisation rule, whereby we are unable to classify whether screening among women in the 65-69-year age-strata occurred above or within the recommended age guidelines.

Limitations:

Given that both the Swiss Health Survey and EHIS are the same type of data source, that is, a national health survey, projects 1 and 2 are largely subject to the same limitations. This notably includes information bias given the fact that data is self-reported by participants [66]. For the screening variables, self-reporting is likely to lead to misclassification of screening according to recommendations. This information bias will also apply to health status and social factor variables included in projects 1.2 and 1.3, respectively. For project 2, we also have the added limitation of the five-year age-anonymisation rule utilised by the EHIS, which limits our ability to granularly calculate age at screening. This will lead to an underestimation of screening outside of

recommendations within our sample. Another factor that will also further lead to an underestimation of screening outside of recommendations within our samples in project 1.1A and 2 is the limited time window of screening captured in both surveys.

Another major limitation of all planned studies is selection bias [67]. More specifically, while the Swiss Health Survey and EHIS utilise randomised sampling to recruit participants, individuals who ultimately agree to partake in health surveys generally differ in meaningful ways to individuals who decline to participate [68]. As such, our study samples are unlikely to be representative of the target populations from which they were derived, which will limit the generalizability of our results [69]. Notably, existing literature suggests that individuals who agree to participate in a health study are generally in better overall health, of higher socioeconomic position, and have more preventive care utilisation than the population as a whole [68]. Our studies are therefore likely to overestimate screening utilisation within our target populations. It should also be noted that this selection bias will also impact our analysis of screening trends in project 1.1B due to declining participation rates in the Swiss Health Survey over time, and in our comparison of screening proportions between countries in project 2 given the varying rates of participation across EHIS countries [65].

Expected results and public health consequences:

As it pertains to projects 1.1A and 2, it is expected that a considerable proportion of the population will be found to have been screened outside of recommended age guidelines. This hypothesis stems mostly from the high frequency of screening outside of age recommendations that has been observed in the United States [35–40], Canada [39,70], and France [54,55]. In turn, if this hypothesis is confirmed, it would suggest that low-value cancer screening is frequent in Switzerland and across European countries, which would thereby indicate a need for public health efforts to deter and de-implement this form of low-value care. We expect this conclusion to be further supported by the results of project 1.1B, where we expect to observe that cancer screening above age recommendations have continuously been frequent, with potential increases over time.

Existing literature also provides a good indication of the results we can expect to find for projects 1.2 and 1.3. More specifically, for the former, existing studies from the United States on cancer screening among older adults according to health status have found that individuals with multimorbidity undergo cancer screening more frequently than their counterparts, while the opposite is true for individuals with functional limitations [41,42]. Therefore, we would expect that the same patterning of screening according to health status will likely be observed in Switzerland as well. Meanwhile, for the latter, existing studies on cancer screening in Switzerland among individuals within recommended age guidelines have observed considerable social inequalities, where people in lower socioeconomic positions and/or from vulnerable populations undergo screening less frequently than their more privileged counterparts [56,57,71,58,59]. It is therefore likely that similar distributions of cancer screening according to social factors also occur among older adults above age recommendations. This hypothesis is further supported by the inverse-care law, where those who need health care services the least use it the most, and those who need health care services the most use it the least [60]. Moreover, regarding the second aim of project 1.3, we expect to find that the

difference in screening between social groups will converge over time owing to the diffusion of innovation theory [72]. Irrespective of the observed findings, however, both projects 1.2 and 1.3 will provide meaningful insights into which groups of older adults undergo cancer screening outside of recommendations the most, which can subsequently help inform the targeting of interventions aimed at reducing the frequency of low-value cancer screening.

Timetable for PhD project and expected publications

	2024					2025										2026										2027																						
	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug											
PhD milestones	(PhD Protocol) Writing and submission																Mid-thesis exam																															
Project 1.1	1.1A) Data management and analysis		1.1A) Writing and submission								1.1B) Data management and analysis		1.1B) Writing and submission																																			
Project 1.2							Data management and analysis		Writing and submission																																							
Project 1.3																					Data management and analysis		Writing and submission																									
Project 2																	Data management and analysis		Writing and submission																													
Research stay abroad																																									Research stay abroad							

Figure 1 – Cancer screening recommendations from the United States Preventive Services Taskforce (USPSTF) prior to 2022

Screening type	Age (years)						
	20	30	40	50	60	70	80
Colorectal				45-49	50-75		76-85
Breast			40-49	50-74			75+
Cervical			21-65				66+
Prostate					55-69		70+

Recommendation grades [15,23–25]:

A	B	C
D	I	

Figure 2 – Cancer screening recommendations from the European Commission

Screening type	Age (years)						
	20	30	40	50	60	70	80
Colorectal				50-74			
Breast				45-74			
Cervical			30-65				

Prostate cancer screening is also recommended to men up to the age of 70; Lung and gastric cancer screening are also recommended in high-risk groups [21]

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