

Cancer screening for older people: to screen or not to screen

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ABSTRACT

In this scoping review, the evidence of the benefits of screening older people for the five most common types of cancer in Hong Kong, namely colorectal, lung, breast, liver, and prostate cancers, is discussed. Although cancer treatments can be extensive and a good prognosis is less likely if cancer is diagnosed at a late stage, screening programmes for older people in primary care remain a matter of contention. The general recommendation for the screening of older people is to adopt an individualised approach that takes account of not only age but also co-morbidity, life expectancy, harms and benefits, and patient's preference.

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Introduction

Cancer, a word that evokes fear in most people, is the second leading cause of death worldwide; 8.8 million of deaths due to cancer are estimated to have occurred in 2015.¹ Globally, the most common types of cancer are lung, breast, bowel, and prostate.² In Hong Kong, the five leading types of cancer (combining both males and females) are, in order of incidence, colorectal, lung, breast, liver, and prostate cancers.³ Because the incidence of cancer increases with age, early detection can help reduce the burden of treatment and is more likely to lead to a better outcome if the cancer is adequately treated. Although there are guidelines on the recommended ages at which to begin screening for different types of cancer, there is less guidance on the screening needs of older adults.⁴

Controversies over cancer screening for older people

Cancer screening for early detection is promoted globally because of the link between an ageing population and an increase in the prevalence of cancer worldwide, on the supposition that this will improve the prognosis of cancer patients and may therefore be beneficial for older people.⁵ Of note, 33 countries have joined the International Cancer Screening Network and are participating in active population-based screening programmes for breast, colorectal, cervical, and lung cancers.⁶ There are practice guidelines recommending the ages at which to start screening for various types of cancer, but there is less information about when

to cease screening, specifically in older people. Epidemiological studies of cancer in people aged 70 years or older are rarely reported in the literature; even if there are such studies, only subgroup analyses are found.⁷ The efficacy of screening older people for cancer remains controversial. Even though cancer rates have increased with age, this does not imply that routine cancer screening is recommended or even appropriate for older people.⁸

The aims of this review were to examine the evidence regarding screening for cancer in older people and to present an overview of the current state of knowledge about controversies and recommendations with regard to screening for the top five most common kinds of cancer in older people in Hong Kong.

Methods

A scoping review was conducted to explicate current discussions of recommendations for screening older adults for cancer. A scoping review was deemed to be appropriate because it is often used to address broad topics, the literature on which may include studies with numerous designs. The approach described by Arksey and O'Malley was adopted.⁹

The databases of MEDLINE, EMBASE, the Web of Science, the Cochrane Library, CINAHL, and SCOPUS were searched using the following strategies:

- Strategy 1—(Elder*) and (Cancer screening or cancer prevention) and (Mortality or morbidity)
- Strategy 2—(Elder*) and (Cancer screening or cancer prevention) and (Effect or efficacy or effective*)

針對老年人的癌症篩查：是否應作普查？

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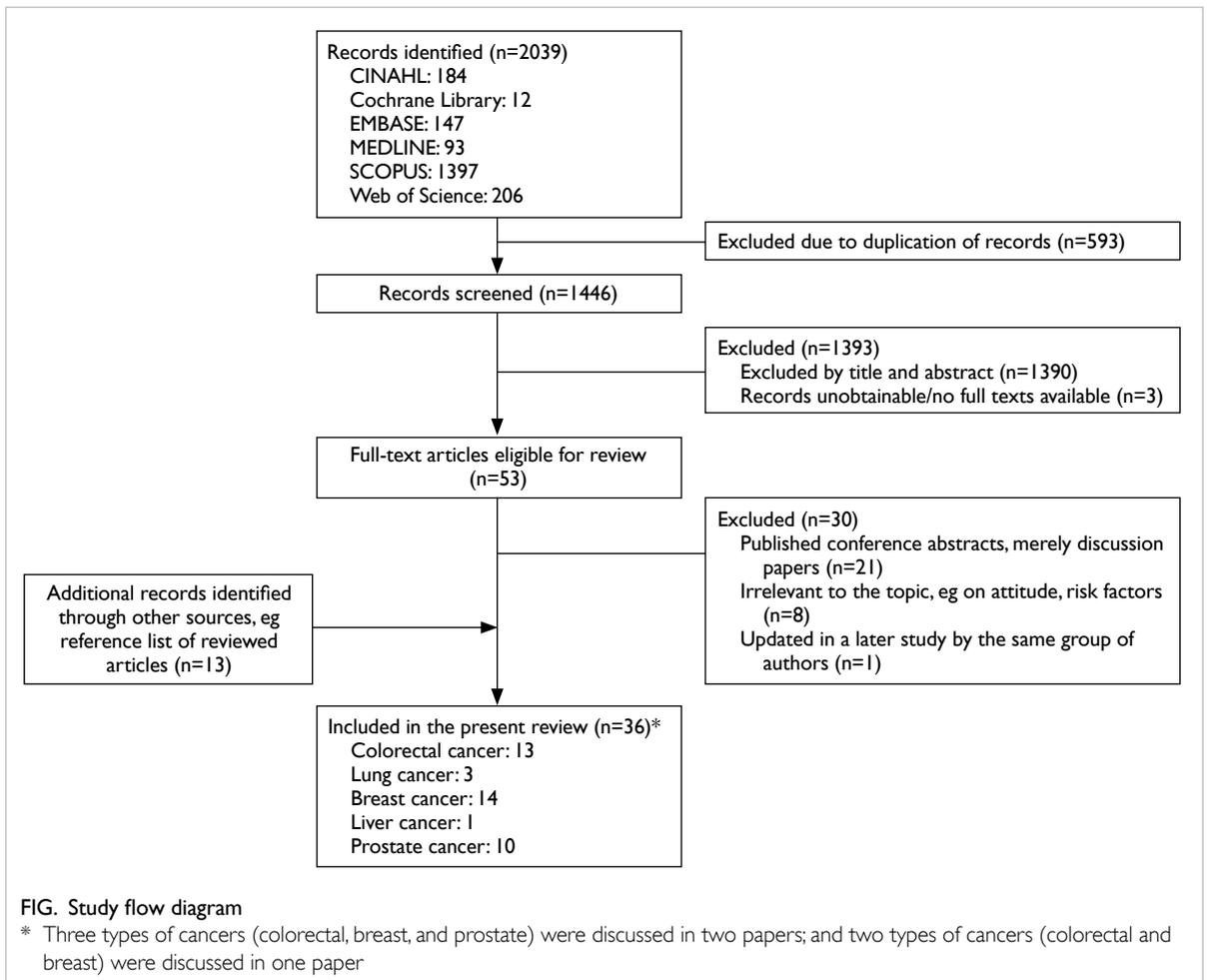
本文獻綜述討論有關癌症篩查為老年人帶來好處的證據，包括以下最常見的五大癌症：結腸直腸癌、肺癌、乳腺癌、肝癌和前列腺癌。縱使癌症治療方法十分廣泛，而且晚期癌症預後較差，但在基層醫療層面為老年人作癌症篩查仍具爭議性。一般針對老年人癌症篩查的建議是採取個人化的方法，即不僅考慮患者的年齡，還要關注其共病、預期壽命、對患者的利弊，以及個人選擇。

Searches were conducted for studies in which the population was restricted to those aged 65 years or above. The search fields included abstracts and titles, studies written in English, and studies published in the last 10 years only (January 2007 to April 2017). We included only studies that evaluated screening for five types of cancer (colorectal, lung, breast, liver, and prostate). Studies that employed retrospective data analysis, simulation modelling, and observational, experimental (randomised controlled trials [RCTs]) or uncontrolled clinical

trials were included. Systematic reviews were also included, but discussion papers that did not describe the process by which the database searches were conducted were excluded. Articles that discussed knowledge or attitudes to cancer screening and surveillance monitoring were also excluded.

Three members of the team screened all of the titles of the papers that were retrieved; papers that were considered irrelevant were discarded. Next, irrelevant papers were also excluded after the abstract and/or the full paper had been reviewed. At least two members independently read the full text of all of the papers that were potentially relevant and selected those that met the criteria for inclusion. The final selection of papers was achieved through a series of virtual online discussions that continued until a consensus was reached.

Other reports relevant to the topic found or cited in text in the reviewed papers were also included. As a result, 13 papers were added to the 23 papers from the scoping search. A total of 36 papers were included for review, with 13, 3, 14, 1, and 10 papers that concerned the screening of colorectal, lung, breast, liver, and prostate cancers, respectively (Fig). Three of the papers examined the evidence of



more than one type of cancer and have therefore been included in different sections for review purposes. Recommendations for screening guidelines from national institutes or professional associations have also been included in each section after discussion of the reviewed papers. In the papers being reviewed, 'benefit' in screening is defined as early detection, survival, or reduced risk in mortality or co-morbidity; 'harm' is defined as mortality (death due to the specific type of cancer under investigation), false-positive and false-negative test results, or over-diagnosis.

Colorectal cancer screening

The faecal occult blood test (FOBT), barium enema, sigmoidoscopy, and colonoscopy are used to screen for colorectal cancer.^{4,10} Quarini and Gosney¹¹ reviewed all available articles on colorectal cancer screening in MEDLINE from 1990 to 2007. They found limited evidence relating to the screening of older people.¹¹

In a recent population-based simulation study, Meester et al¹² analysed the number of deaths from colorectal cancer that were attributable to non-screening in the US; most such deaths were attributable to non-screening. Similar findings have been reported in Germany where screening colonoscopy has been offered since 2002. Brenner et al^{13,14} used simulation modelling based on Germany's national data and found that screening colonoscopies have great potential in the prevention and early detection of colorectal cancer, with a low risk of over-diagnosis. Moreover, the majority of prevented cases would have occurred at the age of 75 years or older.¹⁴ Rozen et al¹⁵ also reported that those aged 75 years or older, rather than younger individuals, could benefit from screening.

Using colorectal cancer-specific mortality data between 1991 and 2001 obtained from the National Center for Health Statistics database in the US, Maheshwari et al¹⁶ compared the impact of prematurely stopping screening with the maximal potential benefit expected from lifelong screening. A total of 80% of the maximal benefit from screening was achieved by screening up to the age of 82 years. Kahi et al¹⁷ examined the survival of older people after colonoscopy using a retrospective cohort analysis of those aged 75 years or above and followed up for a median of 5.95 years. The authors reported that colonoscopy was safe and yielded clinically significant findings in 15% of older patients.¹⁷

van Hees et al¹⁸ used a simulation model to determine up to what age colorectal cancer screening should be considered in unscreened older people with no, moderate, or severe co-morbidity. They concluded that if the physical condition of unscreened older people with different co-morbidity status permits them to undergo a colonoscopy,

screening should be considered up to the ages of 86, 83, and 80 years for no, moderate, and severe co-morbidity, respectively. van Hees' team also reported that fewer co-morbidities were associated with screening at older ages.¹⁹ Lansdorp-Vogelaar et al²⁰ and Gross et al²¹ whose studies are included in this review, also arrived at a similar conclusion.

Not all studies found positive results for colorectal screening. A longitudinal study by Fillenbaum et al²² observed no significant association between cancer screening and population-level health-related outcomes (including mortality).

Over-diagnosis and complications from treatment are often concerns in the promotion of screening. Although colorectal polyps are detected more frequently in older people, especially those over the age of 80 years, the view is that to conduct a colonoscopy in older people is to introduce a higher risk for only a smaller gain in life expectancy (15%) than would be the case with younger people.²³ Cancer screening in people older than 75 years remains controversial because they have not been included in RCTs on the efficacy of screening studies.¹⁰

The guidelines from the National Cancer Institute,²⁴ the American Cancer Society,²⁵ and the US Preventive Services Task Force (USPSTF)²⁶ generally recommend that people who are at an average risk of developing colorectal cancer or who have a family history of colorectal cancer or colorectal polyps begin regular screening for colorectal cancer at the age of 50 years. Specifically, the USPSTF recommends against screening with colonoscopy beyond the age of 85 years.²⁷ The Canadian Task Force on Preventive Health Care recommends against screening with colonoscopy at all ages, but it does support the use of FOBT or faecal immunochemical testing for screening every alternate year and with sigmoidoscopy every 10 years for those aged 50 to 74 years.²⁷

In Hong Kong, the Department of Health launched a 3-year Colorectal Cancer Screening Pilot Programme in 2016 to provide subsidised screening for those born between 1946 and 1948. The Hong Kong Anti-Cancer Society recommends that individuals aged 50 to 75 years with an average risk of developing colorectal cancer should consider undergoing an annual FOBT and flexible sigmoidoscopy every 5 years or a colonoscopy every 10 years.²⁸ Overall, the current literature suggests that colorectal cancer screening is beneficial, but that age as well as morbidity and life expectancy should be considered when determining the age at which screening should stop. Screening colonoscopy in very elderly patients (aged ≥ 80 years) should be performed only after carefully considering the potential benefits and risks, and the preferences of the patient. A summary of the literature review of screening for colorectal cancer is shown in Table 1.^{11-22,27}

TABLE I. Screening for colorectal cancer: summary of literature review^{11-22,27}

Study	Country	Study design	Objective(s)	Sample	Key findings / conclusion
Fillenbaum et al, ²² 2007	US	Longitudinal cohort study (followed up for 4-6 years)	To determine the effect of health behaviours such as cancer screening on population health-related outcomes	A representative community sample of those aged ≥ 71 years (n=2230) from the Duke Established Populations for Epidemiologic Studies of the Elderly	No significant association between cancer screening and population-level health-related outcomes (as measured by functional status, self-rated health, hospitalisations, and mortality rate); disease-specific screens were useful at a personal level but not associated with population-level health
Kahi et al. ¹⁷ 2007	US	Retrospective cohort study	To describe the findings, survival rate, and predictors of mortality of older people post-colonoscopy	Older individuals aged ≥ 75 years (n=404); in two hospitals during 1999-2000	The median survival of those aged 75-79 years was >5 years if their Charlson score was ≤ 4 ; among those aged ≥ 80 years, the median survival was <5 years regardless of Charlson score; age and morbidity were predictors of death
Maheshwari et al, ¹⁶ 2008	US	Life-table analysis of the risks of dying from colorectal cancer or from all causes	To examine the impact of age on the benefits of colorectal cancer screening	Data from the Surveillance, Epidemiology, and End Results programme and the National Center for Health Statistics databases (1991-2001)	Approximately 80% of the maximum benefit from screening was achieved by screening until age 82 years
Quarini and Gosney, ¹¹ 2009	UK (first author)	A methodical approach to searching the literature (1990-2007)	To review the current literature on colorectal cancer screening	Not applicable	Very little research on colorectal cancer specifically in elderly people; present screening programmes did not reflect the health needs of older people
Gross et al, ²¹ 2011	US	Retrospective study using Medicare claims data (1993-2002)	To identify the harms and benefits of screening colonoscopy based on sex, age, and co-morbidity in different older groups	Individuals of 67-94 years old diagnosed with primary colorectal cancer, compared with a subset of 50000 matched non-cancer cases	The positive effect of screening for colorectal cancer was the same for both sexes; screening decisions should not be based solely on age
Rozen et al, ¹⁵ 2011	Israel	Retrospective study using Israel National Cancer Registry data (1980-2008)	To describe the long-term results of colonoscopies and I-FOBTs in those aged ≥ 75 years	Among the patients (n=271), only 6 diagnosed as having colorectal cancer	Approximately 41% of colorectal cancers occurred in those aged ≥ 75 years, who were diagnosed clinically and not by screening; a one-time set of I-FOBTs identified nearly all colorectal cancers in older and in younger patients
Lansdorp-Vogelaar et al, ²⁰ 2014	US	Collaborative modelling using 7 well-established cancer simulation models	To investigate the harms and benefits of cancer screening by age and co-morbidity to inform screening cessation (including mammograms, I-FOBTs, and prostate-specific antigen tests)	Cohorts aged 66-90 years in 2010 with no, mild, moderate, or severe co-morbidity; each cohort was compared with an average-health cohort	Older people with no, mild, moderate, and severe co-morbidities could benefit from screening until the ages of 76-78, 74, 72, and 66 years, respectively, and still experienced similar levels of harm and benefit as individuals of average health up to age 74 years; estimates of harms and benefits by co-morbidity could help doctors and patients to decide on when to cease screening
Brenner et al, ¹³ 2015	Germany	Simulation modelling	To estimate the long-term impact of the country's screening colonoscopy offered to all individuals of age ≥ 55 years since 2002	A total of 4408571 first-time screening colonoscopy for the period 2003-2012 (data from the German national screening colonoscopy registry)	Number of prevented colorectal cancer cases projected to increase from <100 in 2005 to approximately 6500 cases in 2015; the screening programme would lead to significant reductions in the burden of care despite modest participation rates
Brenner et al, ¹⁴ 2015	Germany	Simulation modelling (note: same study as Brenner et al ¹³ but with another question studied)	To quantify the effect of screening colonoscopy on prevention, early detection, and over-diagnosis in the last 10 years	(As above)	Colonoscopies had the advantages of prevention and early detection, with a low risk of over-diagnosis; 180000 colorectal cancers are estimated to have been prevented (97% were prevented by screening colonoscopies done up to age 75 years); 1/121 screening colonoscopies were early detected up to age 80 years (89% by screening colonoscopies up to age 75 years); over-diagnosed in 1/1089 screening colonoscopies (58% arose from screening colonoscopies done on those age >70 years)

Abbreviation: I-FOBTs = immunochemical faecal occult blood tests

TABLE I. (cont'd)

Study	Country	Study design	Objective(s)	Sample	Key findings / conclusion
van Hees et al, ¹⁸ 2014	US	Microsimulation modelling	To examine up to what age colorectal screening should be conducted among the unscreened elderly with no, moderate, and severe co-morbidity	A total of 45 cohorts simulated for each age between 76 and 90 years with no, moderate, and severe co-morbidity; each cohort comprised 10 million cases	Colorectal screening needed to be considered up to the ages of 86, 83, and 80, for those with no, moderate, and severe co-morbidity, respectively
van Hees et al, ¹⁹ 2015	US	(As above; note: same study as van Hees et al, ¹⁸ 2014)	To identify the determinants of benefits for older people of colorectal cancer screening; to examine the maximum age for screening to remain cost-effective	A total of 19200 cohorts simulated based on age, gender, race, screening history, background risks, and co-morbidity status; each cohort consisted of 10 million individuals	Screening colorectal cancer based on age was inefficient; individual factors should be considered
Meester et al, ¹² 2015	US	Microsimulation modelling analysis designed for the period 1980-2030	To estimate the number of colorectal cancer deaths attributable to non-screening	A virtual population created based on US census data (similar to the population in life expectancy, and in the natural history and occurrence of colorectal cancer)	More than half of current US colorectal deaths could be attributed to not screening; increasing screening uptake in the population was beneficial
Tazkarji et al, ²⁷ 2016	Canada (first author)	A methodical approach to search the literature (2006-July 2016)	To guide family doctors in devising screening and treatment plans for older patients	Not applicable	Needed to consider age, life expectancy, co-morbidities, functional status, risk and benefits, and patient preferences when recommending preventive health measures to patients

Lung cancer screening

Chest X-rays, sputum cytology, and low-dose computed tomography (CT) have been used to screen for lung cancer.²⁹ Although chest X-rays or sputum cytology have been used to check for signs of lung cancer, there is less evidence from RCTs to show that using them can lead to a reduction in the number of associated deaths.²⁹ There is, however, some evidence from large-scale RCTs that low-dose CT screening can reduce lung cancer deaths.³⁰

Oken et al³¹ compared annual chest radiographic screening with the usual care in the Prostrate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial. The participants were aged 55 to 74 years and were heavy smokers. Radiographic screening did not reduce lung cancer mortality when compared with the usual care. Aberle et al's National Lung Screening Trial³² in the US examined the effects of lung cancer screening by low-dose CT for participants aged 55 to 74 years who were either current or former (within the past 15 years) heavy smokers (at least 30 packs of cigarettes/year). An annual low-dose CT for 3 years reduced 20% of deaths from lung cancer when compared with chest radiography.

Using simulation modelling, McMahon et al³³ examined the potential benefits (life years saved or lung cancer deaths avoided) of 576 lung cancer

screening programmes that included a variety of screening criteria in terms of age, smoking history, and the number and frequency of CT screenings. They concluded that it would be more efficient (measured in terms of the number of cancer deaths compared with no screening) if screening were extended to the age of 80 or 85 years. The potential harm of low-dose CT, however, should also be noted, such as false-positive and false-negative results, over-diagnosis, exposure to radiation, and an emotional toll on the individual concerned.

Based on the National Lung Screening Trial,³² a systematic evidence review³⁰ and modelling studies, the USPSTF has updated their guidelines. They now recommend that people aged 55 to 80 years who currently smoke or who have quit smoking within the past 15 years should undergo annual screening with low-dose CT.³⁴ The USPSTF also recommends that screening be discontinued for those who have quit smoking for 15 years or who have developed a health problem that substantially limits their life expectancy or their ability or willingness to undergo curative lung surgery.³⁰ The Hong Kong Anti-Cancer Society does not recommend any routine screening for the general population. Considering both life expectancy and co-morbidity status would help physicians to decide the necessity of screening in different individuals.³⁵ A summary of the literature

review of screening for lung cancer is shown in Table 2.³¹⁻³³

Breast cancer screening

Clinical breast examinations and breast self-examinations, mammograms, ultrasound, and magnetic resonance imaging, are all measures to screen for breast cancer, with the mammogram being the most widely used test.

A systematic review by Galit et al³⁶ suggested that with a reasonable life expectancy and without severe co-morbidities, women aged 75 years or above are likely to benefit from mammography. Mo et al³⁷ found that mammography screening alone for Chinese women over the age of 70 years with positive clinical breast examination results would save on the cost of ultrasonography without any loss in the effectiveness of screening. When co-morbidity and screening are considered, Lansdorp-Vogelaar et al²⁰ showed that the benefits of a biennial mammography existed until the median ages of 76, 74, 72, and 66 years for older women with no, mild, moderate, or severe co-morbidity, respectively.

The EUROSCREEN Working Group reviewed observational studies and reported that the reduction of the breast cancer mortality rate was 38% to 48% for women who had actually been screened, with

the rate of over-diagnosis of only 6.5%.^{38,39} They argued that the current controversy is related to the use of inappropriate methods that are incapable of revealing the true effect of screening, and that population-based mammography screening is of greater benefit than harm.

Using simulation modelling, Tejada et al⁴⁰ evaluated seven screening policies to determine which combination of upper age limit and screening interval could maximise screening benefits for older women. Annual screening with an upper age limit of 80 years was found to be most effective in increasing the survival rate.⁴⁰ Similarly, Sanderson et al⁴¹ found a significant reduction in the breast cancer mortality rate of older women who underwent an annual mammography compared with those who underwent a biennial or irregular mammography.

Some researchers have nonetheless taken a contrary view. Fillenbaum et al²² found no significant association between breast cancer screening and health-related outcomes such as self-rated health and mortality. Similarly, the benefits of screening were found to be limited due to a huge number of cases of over-diagnosis in the older population.⁵ Mandelblatt et al⁴² evaluated the effectiveness of 20 different mammography screening programmes using six established models of cancer incidence and mortality trends in the US. They reported that

TABLE 2. Screening for lung cancer: summary of literature review³¹⁻³³

Study	Country	Study design	Objective	Sample	Key findings / conclusion
Aberle et al, ³² 2011	US	Randomised controlled trial	This NLST aimed to determine whether annual screening with low-dose CT for 3 years could reduce mortality from lung cancer	Participants from 33 medical centres (n=53 456); aged 55-74 years with a history of heavy smoking (30 packs/year or had quit within 15 years); low-dose CT group (n=26 722) and chest radiography group (n=26 732) followed up until 2009	A 20% decrease in mortality from lung cancer found in the low-dose CT group when compared with the radiography group; annual screening with low-dose CT for 3 years reduced mortality from lung cancer in the sample; there was also a high rate of false-positive results in the low-dose CT group
Oken et al, ³¹ 2011	US	Randomised controlled trial	Radiographs were used in a PLCO cancer screening trial to determine the outcome (mortality) of annual screening (1993-2001) for lung cancer of those who currently smoke 30 packs/year or who had quit within 15 years	Participants aged 55-74 years (n=154 901) followed up until 2009; annual screening group (n=77 445) and usual care group (n=77 456); data from a subset of participants for the NLST were also analysed	Annual screening with chest radiographs over a 4-year period did not significantly decrease lung cancer mortality compared with usual care, neither in the PLCO as a whole nor in the subset of participants who would have been eligible to enrol in the NLST
McMahon et al, ³³ 2014	US	Microsimulation modelling	To examine the potential benefits (life years saved or lung cancer deaths avoided) of 576 lung cancer screening programmes that had variable screening criteria (age, smoking history, number and frequency of CT screenings)	Models adopted the natural history parameters of lung cancer calibrated to the NLST to simulate the life histories of US men and women born in 1950	Annual screening based on age and smoking history in the NLST was inefficient; screening up to ages 80 or 85 years would be more efficient

Abbreviations: CT = computed tomography; NLST = National Lung Screening Trial; PLCO = Prostate, Lung, Colorectal, and Ovarian

if the age of cessation was set at after 69 years, the reduction in mortality would be slight.

A Cochrane review examined the effect of mammography screening in terms of mortality and morbidity in a total sample of 600 000 women.⁴³ Screening led to a 15% reduction in mortality but the over-diagnosis and over-treatment rate was 30%. The authors suggested that screening might not be doing more good than harm.⁴³ Of note, only one trial in this Cochrane review included women up to the age of 69 years. In their retrospective cohort study, Parvinen et al⁴⁴ found that a mammography screening programme for women up to the age of 74 years effectively reduced mortality rates in the older population, but that the reduction in rate was only 20%. Their conclusion was that the gain in benefits may not justify the harm from screening.

Mammography screening is unlikely to benefit those with a life expectancy of less than 5 years as reported in Tazkarji et al's study.²⁷ Braithwaite et al⁴⁵ found that the benefits of screening decrease with increasing age and co-morbidity. Their sample of women aged 65 years or above without severe co-morbidity showed only a slight improvement in life expectancy. They, too, argued that the magnitude of the benefit may not justify screening given the potential harm. Citing the Canadian National Breast Screening Study with 25 years of follow-up, the National Cancer Institute in the US concluded that the benefits of mammography screening are uncertain.⁴⁶

In summary, the overall effect of breast cancer screening in older women remains a controversial topic. Currently, the American Cancer Society suggests that women who are at an 'average risk' of developing breast cancer have an annual mammogram starting at the age of 40 years, with no specific age mentioned as the marker for discontinuation, while the USPSTF now suggests that regular screening should start from the age of 50 years and end at the age of 74 years. The Hong Kong Breast Cancer Foundation recommends that women over the age of 40 years consider undergoing a mammography every 2 years.⁴⁷ A summary of the literature review of screening for breast cancer is shown in Table 3.^{5,20,22,27,36-45}

Liver cancer screening

There are no widely recommended tests to screen for liver cancer among the general public except for those who are at a high risk of developing the disease. Alpha-fetoprotein (AFP) and abdominal ultrasound are the two most common tests in use. Nonetheless the sensitivity and specificity levels of AFP are unsatisfactory.⁴⁸ This protein has also been shown to be unreliable in detecting small liver cancer.

There is hardly any evidence of the benefits of screening older people for liver cancer. Huang

et al⁴⁹ conducted a two-stage community screening programme (first with blood tests and then by ultrasonogram for identified high-risk cases) on a sample of 1002 people with a mean age of 68.3 years for women and men in an area where the hepatitis C virus is endemic. They observed that older patients who had early-stage hepatocellular carcinoma and who were being treated had a good prognosis for survival.

Currently, the American Cancer Society offers no recommendations for liver cancer screening in the general population. Cancer Research UK recommends a liver screening test only for high-risk individuals.⁵⁰ Similarly, the Hong Kong Department of Health does not recommend routine cancer screening for people at 'average risk'—only for those at high risk, such as carriers of the hepatitis B and/or C viruses and those with cirrhosis.⁵¹ In summary, screening tests for liver cancer should not be performed in a routine manner but should be recommended only for people who are at a high risk of developing the disease. A summary of the literature review of screening for liver cancer is shown in Table 4.⁴⁹

Prostate cancer screening

Prostate-specific antigen (PSA) testing, digital rectal examination, and prostate biopsy are the three main approaches usually used in combination with screening prostate cancer.⁴ There is no single effective and reliable test to screen for early prostate cancer in healthy men.⁵⁰ It is not uncommon for men to have some cancer cells in their prostate by the age of 80 years although only one in 25 will actually die from prostate cancer.⁵⁰ To date, the debate over PSA screening remains heated even though screening was first introduced in the late 1980s.

Konety et al⁵² reported the work of a 30-member panel of US experts who recommended that the initiation of screening for prostate cancer in men older than 75 years should be undertaken only after careful consideration, and that age-normed PSA values should be used to determine 'normal' levels.

Using mathematical modelling, Etzioni et al⁵³ found that by 2000, 45% to 70% of the observed decline in prostate cancer mortality could be plausibly attributed to screening. They concluded that PSA screening might account for much of the observed drop in prostate cancer mortality. Etzioni et al⁵⁴ also studied the link between PSA screening and the decline in the incidence of late-stage prostate cancer. Their tested model showed that screening explained about 80% of the observed decline in the incidence of distant-stage (as opposed to locoregional stage) prostate cancer. Nonetheless the team suggested that other factors such as awareness and advances in treatment might also play certain roles.

Telesca et al⁵⁵ used data derived from the

TABLE 3. Screening for breast cancer: summary of literature review^{5,20,22,27,36-45}

Study	Country	Study design	Objective(s)	Sample	Key findings / conclusion
Fillenbaum et al, ²² 2007	US	Longitudinal cohort study (followed up for 4-6 years)	To determine the effect of health behaviours such as cancer screening on population health-related outcomes	A representative community sample of those aged ≥ 71 years (n=2230) from the Duke Established Populations for Epidemiologic Studies of the Elderly	No significant association between cancer screening and population-level health-related outcomes (as measured by functional status, self-rated health, hospitalisations, and mortality rate); disease-specific screens were useful at a personal level but not associated with population-level health
Galit et al, ³⁶ 2007	Israel (first author)	Systematic review of studies in MEDLINE up to August 2006	To determine the efficacy of breast cancer screening	Women aged >74 years	Early detection of cancer and reduction of breast cancer mortality associated with a mammography screening programme in women aged ≥ 75 years, with reasonable life expectancy and without severe co-morbidity; data supported screening for those aged ≥ 75 years, based on individual assessments
Mo et al, ³⁷ 2013	China	Uncontrolled clinical trial (2008-2012)	To evaluate the outcomes of using individual and combined breast cancer screening (CBE, mammographies, and ultrasound)	Women aged 35-74 years in a county of Shanghai (n=14 464)	The sensitivity of using CBE, ultrasound, or mammogram alone was 61.4%, 53.7%, and 67.3%, respectively; the sensitivity level improved with the combined use of mammogram and ultrasound; mammography alone for women aged >70 years with positive CBE results would save on the cost of ultrasonography without losing the effectiveness of screening
Mandelblatt et al, ⁴² 2009	US	Simulation modelling	To evaluate the effectiveness of 20 mammography screening strategies with different initiation and cessation ages and screening intervals using 6 established models of cancer incidence and mortality trends in the US	A cohort of women born in 1960 and followed up from age 25 years and throughout their lifetime	Biennial screening achieves a mean of 81% of the benefit of annual screening, but with less harm (50% reduction in the number of false-positive cases); if the cessation age was set at >69 years, a slight reduction in mortality was observed but with increased age, over-diagnoses also increased
Gotzsche and Nielsen, ⁴³ 2011	Denmark (first author)	Systematic review (Cochrane) with meta-analysis of 8 included RCTs	To examine the effect of mammography screening in terms of mortality and morbidity using papers in PubMed up to November 2008	Women who had not had breast cancer in 2 groups (n=600 000): with and without mammography screening; however, only one trial included women aged 45-69 years; most included RCTs had an age range of 45-64 years	Screening led to a mortality reduction of 15% but an over-diagnosis and over-treatment rate of 30%; it is therefore questionable whether screening does more good than harm
Broeders et al, ³⁸ 2012	The Netherlands (first author)	Systematic review of observational studies and meta-analysis of incidence-based mortality and case-controlled studies	To evaluate the impact of mammography screening on mortality rates for breast cancer in Europe using articles in PubMed up to February 2011	Studies that included an analysis of a group aged between 50 and 69 years	Reduction in breast cancer mortality was 38%-48% for women who were actually screened; valid observational designs should have adequately followed up on individual data, including a woman's history of screening and the cause of her death; the current controversy over breast cancer screening was related to the use of inappropriate methods that were incapable of revealing the true effect of screening
Paci, ³⁹ 2012	Italy (first author)	(As above: same study as Broeders et al, ³⁸ 2012 but a different analysis)	To compare and weigh the benefits (mortality reduction) and harms (over-diagnosis, false-positives) of breast cancer screening in Europe	(As above)	7-9 Women saved/1000 women screened biennially from age 50-51 till 68-69 years and followed up for another 10 years; 4 women in this group would be over-diagnosed and 200 women would have a false-negative result; the benefit of population-based mammography screening was greater than over-diagnosis

Abbreviations: CBE = clinical breast examinations; RCT = randomised controlled trial

TABLE 3. (cont'd)

Study	Country	Study design	Objective(s)	Sample	Key findings / conclusion
Tejada et al, ⁴⁰ 2015	US	Simulation modelling	To examine the effect of breast cancer screening policies for women aged ≥65 years	Over 1 million pieces of de-identified data from the Breast Cancer Surveillance Consortium (with data from 7 mammography registries) representative of the female population aged ≥65 years in the country	Annual screening from age 65-80 years was found to be the most effective cancer screening policy in that it increased survival rates and minimised breast cancer mortality
Lansdorp-Vogelaar et al, ²⁰ 2014	US	Collaborative modelling using 7 well-established cancer simulation models	To investigate the harms and benefits of cancer screening by age and co-morbidity to inform screening cessation (including mammograms, faecal immunochemical tests, and prostate-specific antigen tests)	Cohorts aged 66-90 years in 2010 with no, mild, moderate, or severe co-morbidity; each cohort was compared with an average-health cohort	Women with no, mild, moderate, or severe co-morbidities could benefit from screening until the ages of 76-78, 74, 72, and 66, respectively, and still have similar levels of harm and benefit as average-health individuals up to age 74 years; estimates of harms and benefits by co-morbidity could help doctors and patients to decide on when to cease screening
de Glas et al, ⁵ 2014	The Netherlands	Retrospective study using a national cancer registry database	To assess breast cancer incidence (early [stages I, II, or ductal in-situ] and advanced [stages III, IV] stages) pre- and post-implementation of a mass screening programme that had been extended to the upper age of 75 years in 1998	Women aged 70-75 years (n=25 414) diagnosed with breast cancer between 1995 and 2011	An increase of 114.2/100 000 cases of early-stage tumours and a decrease of 6.8/100 000 cases of advanced-stage tumours post-implementation; over-diagnoses implied that the programme was of limited effectiveness
Parvinen et al, ⁴⁴ 2015	Finland	Retrospective cohort study using the Finnish Cancer Registry	To examine the effect of a mammography screening programme in the city of Turku, Finland, by comparing mortality rates with other regions with different screening policies	40.7 Million women aged 40-84 years for the period 1976-2009 (pre-screening era: 1976-1986)	>20% Reduction in mortality found (a) among women aged 60-74 years compared with Helsinki, and (ii) in women aged 75-84 years at death compared with the rest of Finland; findings supported breast cancer screening targeted at women aged 50-74 years
Sanderson et al, ⁴¹ 2015	US	Retrospective study using Medicare claims data (1995-2009) from the Surveillance, Epidemiology, and End Results programme	To explore whether age and race affect the results of mammography screening on mortality among women aged 69-84 years	A total of 64 384 (4886 black and 59 498 white) women with a primary breast cancer diagnosis who had an annual or biennial screening 4 years prior to diagnosis; followed up for 10 years	10-Year mortality risks were 3.3 times higher in whites and 2.2 times higher in blacks with no or irregular screening compared to annual screening
Tazkarji et al, ²⁷ 2016	Canada (first author)	A methodical approach to searching the literature (2006-July 2016)	To guide family doctors in devising screening and treatment plans for older patients	Not applicable	Screening mammography most likely unable to benefit women with <5 years of life expectancy; needed to consider age, life expectancy, co-morbidities, functional status, risks and benefits, and patient preferences when recommending preventive health measures to patients
Braithwaite et al, ⁴⁵ 2016	US (first author)	Systematic review	To review studies (in MEDLINE and EMBASE published from 1980 to 2013) that examined the benefits and harms of mammography screening for women aged ≥65 years	Not applicable	Women aged ≥65 years without severe co-morbidity might have a slightly improved life expectancy from screening; benefits decreased with increases in age and co-morbidity levels; the magnitude of the benefit might not justify screening given the potential harms

TABLE 4. Screening for liver cancer: summary of literature review⁴⁹

Study	Country	Study design	Objective	Sample	Key findings / conclusion
Huang et al, ⁴⁹ 2011	Taiwan	Uncontrolled clinical trial	To determine whether a hepatocellular carcinoma 2-stage screening programme could reduce mortality among elderly patients	Participants (n=1002) from community; mean age 68.3 for females and 65.3 years for males; followed up for 4 years post-screening	Alpha-fetoprotein and platelet count are feasible screening methods to identify risk among the elderly; good prognosis of survival observed in elderly patients at the early stage of hepatocellular carcinoma who accepted curative treatment

Surveillance, Epidemiology, and End Results (SEER) registry of the National Cancer Institute in the US to examine the increase and subsequent decline in the incidence of prostate cancer after the adoption of PSA screening, and arrived at the opposite conclusion. They maintained that the disease would not have continued to increase in incidence in the absence of PSA screening. Also using the SEER data, Welch and Albertsen⁵⁶ used age-specific population estimates from the US Census data to determine the excess or deficit in the number of men diagnosed and treated each year after 1986. Since 1986, an estimated additional 1.3 million men were diagnosed and more than 1 million of them were treated. They concluded that most of the excess incidence must be the result of over-diagnosis.

Two large-scale RCTs published in 2009—the European Randomized Study of Screening for Prostate Cancer⁵⁷ and the US PLCO cancer screening trial⁵⁸—produced conflicting results on screening for prostate cancer with PSA testing, providing fuel for further debate.

Jemal et al⁵⁹ conducted an interesting study that examined changes in the incidence of stage-specific prostate cancer and PSA screening rates for the period 2005 to 2012 using the US National Cancer Institute database. Both the incidence of early-stage prostate cancer and rates of PSA screening had declined, coinciding with the 2012 USPSTF recommendation to omit PSA screening from routine primary care. Nonetheless, the authors also recommended a longer follow-up period to ascertain whether these decreases were indeed associated with mortality trends. Thus, whether reduced screening would lead to reductions in over-diagnoses or to missed opportunities for early detection remains an open question.

The American Cancer Society states that a screening test should not be offered to men who do not have any symptoms of prostate cancer and who have a life expectancy of about 10 more years or less, because of its slow-growing prognosis. The USPSTF and the American Academy of Family Physicians do not recommend the use of the PSA test to screen for prostate cancer, as there is little evidence to show

that the benefits outweigh the harm. They argue against screening for men 75 years of age and older because of a lack of evidence to support screening.

In brief, views about the desirability of prostate cancer screening are polarised, and much confusion over the issue remains.⁶⁰ Observational evidence to date has not always supported the efficacy of PSA screening in reducing mortality; rather, a growing body of observational evidence points to the over-diagnosis and over-treatment of prostate cancer triggered by PSA testing.⁶¹ Randomised trials have produced conflicting results. Thus, the efficacy of prostate cancer screening for old men remains a point of contention. A summary of the literature review of screening for prostate cancer is shown in Table 5.^{20,27,52-59}

To screen or not to screen older people

To screen or not to screen older people for common types of cancer remains controversial, especially for people over the age of 75 years. Screening may reduce the risk that individuals will develop a condition or its complications, but it may not guarantee protection. Most of the papers and guidelines suggested that screening has to be individualised for this particular age-group. Even though the risk of cancer increases with age, it should not be the only factor taken into account when making decisions about screening. Routine cancer screening does not benefit those with a limited life expectancy.⁶² Estimating life expectancy will help guide decision-making for preventive screening and treatment plans.²⁷ Because life expectancy varies in relation to co-morbidity status, taking co-morbidity-adjusted life expectancy into consideration may be helpful to physicians.³⁵

In any screening programme, there is an irreducible minimum of false-positive and false-negative results.²³ The feelings and overall health status of the patient also need to be considered. It may be appropriate to screen patients with a life expectancy sufficiently long to experience the potential benefits of screening. Personalised

TABLE 5. Screening for prostate cancer: summary of literature review^{20,27,52-59}

Study	Country	Study design	Objective	Sample	Key findings / conclusion
Konety et al, ⁵² 2008	US	Review of the literature and expert panel discussions to arrive at a consensus	To develop a consensus recommendations for prostate cancer screening and management	An expert panel consisting of 30 multidisciplinary health care providers (physicians from related specialties, nurses, 1 patient representative, and 1 attorney) in the state of Iowa	The panel supported using greater discretion in screening for prostate cancer in the older population; also agreed that there was a greater need for patient counselling with regard to the harms and benefits of screening after 75 years of age
Etzioni et al, ⁵³ 2008	US	Simulation modelling	To quantify the impact of PSA screening on the decline in mortality from prostate cancer during the 1990s	Used 2 mathematical models to project mortality rates among men aged 50-84 years with or without PSA screening between 1980 and 2000	Projected that 45%-70% of the observed decline in prostate cancer mortality might be attributable to screening; also suggested that other issues such as changes in treatment practices might also play a role in improved outcomes
Etzioni et al, ⁵⁴ 2008	US	Simulation modelling	To examine the link between PSA screening and the decline in the incidence of distant-stage prostate cancer (the authors classified pathological stages into clinical stages of 'locoregional' or 'distant' cancer progression)	Simulated life histories for US men aged 50-84 years between 1980 and 2000; PSA testing was superimposed on a background of natural histories and clinical diagnoses of prostate cancer without screening	The tested model showed that PSA screening explained around 80% of the observed decline in the incidence of distant-stage prostate cancer; other factors including awareness and advances in treatment might also play certain roles
Telesca et al, ⁵⁵ 2008	US	Simulation modelling	To estimate the lead time in diagnoses associated with PSA testing	Data from 9 SEER areas in the US	4.59 Years of lead time for whites and 6.78 years for blacks with a corresponding estimated fairly flat trend of prostate cancer incidence after the introduction of PSA screening; the results implied that the incidence of prostate cancer would level off in line with changes in prostate care in the absence of PSA screening
Welch and Albertsen, ⁵⁶ 2009	US	Retrospective data analysis	To estimate the number of men affected in terms of diagnosis and treatment after the introduction of PSA screening	Data from SEER (1986 as the base year—the year before PSA screening was introduced) plus US census data for estimating the excess number of men diagnosed and treated each year after 1986, up to 2005	In considering the incidence trend in the US for the last 2 decades, an estimated additional 1 305 600 men were diagnosed with prostate cancer, and 1 004 800 of those were treated; the majority of the additional 1 million men did not benefit from early detection
Schröder et al, ⁵⁷ for the ERSPC Investigators, 2009	Finland, Sweden, Italy, The Netherlands, Belgium, Spain, Switzerland	Randomised multicentre trial initiated in the 1990s	To determine the effect of screening with a PSA test on death rates from prostate cancer	Age 50-74 years (n=182 000); screening group: offered PSA screening about once every 4 years and control group: did not receive screening	1410 Men would be required to be screened and another 48 men treated in order to prevent 1 prostate cancer death; screening by PSA test reduced deaths by 20% but was associated with a high risk of over-diagnosis
Andriole et al, ⁵⁸ for the PLCO cancer screening trial, 2009	US	Randomised controlled trial	To investigate the effect of screening with PSA test and digital rectal examinations on mortality rates from prostate cancer	Participants (n=76 693) divided into annual screening group (n=38 343) and usual care group (n=38 350) followed up from 1993-2001	After 7 years of follow-up, the incidence of death from prostate cancer in the annual screening group = 50/10 000 person-years, and in the usual care group = 44/10 000 person-years; the death rate from prostate cancer was very low and there was no significant difference between groups

Abbreviations: ERSPC = European Randomized study of Screening for Prostate Cancer; PLCO = Prostate, Lung, Colorectal, and Ovarian; PSA = prostate-specific antigen; SEER = Surveillance, Epidemiology, and End Results

TABLE 5. (cont'd)

Study	Country	Study design	Objective	Sample	Key findings / conclusion
Lansdorp-Vogelaar et al, ²⁰ 2014	US	Collaborative modelling using 7 well-established cancer simulation models	To investigate the harms and benefits of cancer screening by age and co-morbidity to inform screening cessation (including mammograms, the faecal immunochemical test, and the PSA test)	Cohorts aged 66-90 years in 2010 with no, mild, moderate, or severe co-morbidity; each cohort was compared with an average-health cohort	Older people with no, mild, moderate, or severe co-morbidities could benefit from screening until the ages of 76-78, 74, 72, and 66, respectively, and still have similar levels of harm and benefit as average-health individuals up to age 74 years; estimates of harms and benefits by co-morbidity could help doctors and patients to decide on when to cease screening
Jemal et al, ⁵⁹ 2015	US	Ecological study (retrospective data analysis)	To examine changes in prostate cancer incidence and PSA screening rates with regard to the 2008 and 2012 USPSTF recommendations	Data from SEER registries plus data from men aged ≥50 years without prostate cancer who responded to the 2005, 2008, 2010, and 2013 National Health Interview Survey were used to determine the rate of self-reported PSA testing in the previous year	The incidence of early-stage prostate cancer and PSA screening rates have both declined and coincided with the 2012 USPSTF recommendation not to conduct PSA tests in routine primary care for men; a longer follow-up period was needed to see whether these decreases were associated with mortality
Tazkarji et al, ²⁷ 2016	Canada (first author)	A methodical approach to searching the literature (2006-July 2016)	To guide family doctors in devising screening and treatment plans for older patients	Not applicable	Need to consider age, life expectancy, co-morbidities, functional status, risks and benefits, and patient preferences when recommending preventive health measures to patients

Abbreviations: PSA = prostate-specific antigen; SEER = Surveillance, Epidemiology, and End Results; USPSTF = US Preventive Services Task Force

consideration might benefit older people if the positive impacts can outweigh the negative, even for the oldest-old.

Conclusion

Cancer is common in the older population and, for them, the benefits of screening for common types of cancer remain controversial. The evidence is strongest for the efficacy of colorectal cancer screening, even for older people aged 75 years and beyond. Low-dose CT for screening for lung cancer has benefits for heavy smokers. Liver cancer screening is recommended only for those at high risk of developing the disease. The evidence for screening older people for breast cancer is conflicting; as is the evidence for the effectiveness of PSA tests for screening for prostate cancer. Although some screening tests can bring certain benefits, other factors related to advancing age may be present, such as co-morbidities that may cause harm and would eventually outweigh the benefits of cancer screening. More research is indeed needed to understand the relationship between cancer and ageing, and also the risks and benefits of cancer screening for older people, to ultimately promote good health and functional longevity.

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