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Lung Cancer Screening: Promise and Pitfalls

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Abstract

OBJECTIVES—To provide an overview of the status of lung cancer screening.

DATA SOURCES—Published articles, book chapters, websites, and research studies on lung cancer screening.

CONCLUSION—Screening with chest x-ray and sputum cytology has not been shown to be effective in reducing lung cancer mortality. Although screening with helical CT is currently under investigation in randomized clinical trials, observational studies have not shown evidence that it can detect lung cancer that is curable.

IMPLICATION FOR NURSING PRACTICE—As healthcare educators and caregivers, nurses should be informed of the status and current controversies associated with lung cancer screening.

Keywords

lung cancer screening; helical CT; low-dose CT; spiral CT; cancer screening clinical trials

Lung cancer will claim more than 160,000 lives in 2007, out of the approximately 213,000 new cases of lung cancer that will be diagnosed in the United States.¹ Despite major advances in medical technology and therapies, the overall five-year survival rate for all lung cancers is approximately 15%. However, the five-year survival rate for lung cancer diagnosed in its earliest stages may be as high as 70%.^{2–4} Therefore, strategies to improve early detection may be helpful, but as with many aggressive malignancies even small tumors have high metastatic potential.⁵ With over 90 million current and former smokers in the United States, the validation of an effective screening test, in conjunction with effective treatment, would have major public health implications.

In the past, randomized screening trials evaluated chest x-ray and sputum cytology as an early detection test, but did not find either to be effective in decreasing mortality rates. More recently, a newer imaging technology has emerged as a potential screening test for lung cancer. Low-dose computed tomography (CT), or helical CT, can detect tumors well under one cm in size. By contrast, x-ray detects tumors approximately one to two cm in size. Observational studies

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of helical CT have shown increased survival rates.⁴⁻⁶ What remains to be determined, however, by ongoing studies is whether the early detection of smaller tumors will in fact lead to a decrease in mortality rates.

This article provides an overview of the elements of a screening trial, data from historical clinical trials, the status of ongoing studies, and a discussion of the controversies related to helical CT. Also, an overview of the National Cancer Institute (NCI)-sponsored National Lung Screening Trial, a large randomized controlled screening study for males and females at risk for developing lung cancer, is provided.

UNDERLYING CONCEPTS OF CANCER SCREENING

In order to understand and interpret findings from screening trials, one must be familiar with certain underlying concepts associated with screening. First, are the concepts of incidence and prevalence. In order for screening to lead to significant public health benefits, the target disease should have high incidence and prevalence rates in the screened population. Incidence refers to the number of cancer cases that develop during a defined *period* of time, and is expressed as cases per year per 100,000 individuals in the population.⁷ Prevalence is the number of cancers that exist in a defined population at a given *point* in time, and is commonly expressed as cancers per 100,000 individuals in the population.⁷

Second, an effective screening test should detect disease at an early stage, while the individual is asymptomatic and while cure may be possible with treatment.⁵ In other words, the test must lead to a decreased mortality rate. The test itself should be safe, inexpensive, and possess sufficient sensitivity (able to identify individuals *with* disease), and specificity (able to identify individuals *without* disease). To bring about a decrease in the mortality rate, an effective treatment must be available to those diagnosed following a positive screen. Effective screening tests, in conjunction with effective treatment then, have the ability to effect a change in the natural history of the disease in a positive manner.

Third, the benefits of screening must outweigh the risks.^{7,8} For instance, the incidence of false positives and false negatives must be evaluated against potential benefits. False positives can result in unnecessary surgeries, treatments, anxiety, and public health costs. False negatives, on the other hand, can lead to undetected disease which progresses beyond the benefits of available interventions.

Fourth, survival and mortality are two inter-related but often misunderstood concepts that are important in understanding the relative effectiveness of lung cancer screening techniques. Survival rates reflect the number of individuals alive at a given time relative to their diagnosis. Although frequently reported in observational screening studies, survival rates alone are not an adequate measure of screening benefit. The measure can be misleading because of several confounding biases, lead-time bias, length bias, and over-diagnosis. It is important to note, however, that survival *is* appropriately used to compare the benefits of one form of treatment or intervention to another.⁹

Lead-time refers to the period of time from cancer detection to the time symptoms would have occurred had the individual not been screened (Figure 1).¹⁰ Essentially the survival rate is artificially lengthened with the addition of the lead-time. In effect, earlier detection prolongs survival independent of a delay in death. For an example, if two individuals (one screened, one not screened) die of lung cancer at the same age, the screened individual's survival time is lengthened because his cancer was detected earlier (lead-time), while he was still asymptomatic. The unscreened individual's cancer would have gone undiagnosed until symptoms occurred. The screened individual appears to have a longer survival time because of the addition of the lead-time, but the mortality is the same. Such findings run counter to the

often held view that cancer is a consistently progressive disease. Research in screening has found that cancer encompasses a wide range of biologic behavior: some cancers progress rapidly to death, some more slowly, and some not at all.¹¹ Length bias refers to the tendency of a screening test to detect indolent, rather than aggressive tumors (Figure 2).¹⁰ Slow growing cancers are more likely to have a prolonged pre-symptomatic period, allowing greater opportunity for detection. This extended period does not necessarily represent an actual improvement in survival, but rather reflects the underlying behavior of the cancer itself. The individual with an indolent disease would in many instances die from other causes first.

A related concept is overdiagnosis, which is of particular interest in CT screening trials because advanced technology allows identification of many non-cancerous abnormalities, including some benign lesions (Figure 3).¹⁰ In fact, recent studies indicate that 20% to 60% of helical CT scans of smokers and former smokers will show abnormalities.^{12–14} Most abnormalities are generally scars from smoking, areas of inflammation, or other non-cancerous conditions. The downstream effects of over-diagnosis cannot be overstated. Individuals may be subjected to the morbidity associated with chemotherapy or surgical interventions for cancers that would otherwise not have become symptomatic or progressive. A relevant example from a different cancer is the Quebec Neuroblastoma Screening Project, conducted from 1989 to 1994. Researchers first identified the rate of death due to neuroblastoma, then compared that rate with the rates in several unscreened control populations born during the same period.^{15,16} The results of the study indicated that screening infants for neuroblastoma did not appear to reduce mortality compared to the control groups due to overdiagnosis. Similarly, overdiagnosis is of particular concern for helical CT, because it can detect far more abnormalities than chest X-rays.

Finally, mortality is the number of disease-specific deaths relative to the total number of individuals screened.⁷ The goal of lung cancer screening is to reduce mortality, thus an effect on mortality is vital to the validation of potential screening methods.

CHEST X-RAY SCREENING TRIALS

In the 1970s, the National Cancer Institute (NCI) sponsored three randomized clinical trials to evaluate the effectiveness of chest x-ray and sputum cytology for lung cancer screening: the Mayo Lung Project, the Johns Hopkins Lung Project, and the Memorial Sloan-Kettering Lung Project.^{17–19} The primary endpoint of all three studies was mortality. Approximately 10,000 male smokers and former smokers were enrolled at each site. The John Hopkins and Memorial Sloan-Kettering studies randomized individuals to receive annual chest x-ray (control) or annual chest x-ray plus sputum cytology every four months (intervention). Results showed no differences in the number of cancers detected in the two groups and no mortality benefit.^{18, 19}

The Mayo Lung Project randomized individuals to an intervention (screened) group to receive chest x-ray and sputum cytology every four months for six years, or to a control group which received guidance to have chest x-ray and sputum cytology annually for six screens.^{17,20} There were 206 lung cancer cases in the intervention group, and 160 cases in the control group. The 5-year survival rate for lung cancer was 40% in the screened group and 15% in the control population. However, there was no difference in lung cancer *mortality* between the groups. Marcus et al re-evaluated this study in extended follow-up in 2000. Again, no difference in mortality was identified between the two groups.²¹

A fourth study conducted in Czechoslovakia randomized 6346 high risk male participants to an intervention arm consisting of chest x-ray and sputum cytology every six months, or to a control group receiving a prevalence screening x-ray and sputum cytology followed by another screen three years later.²² Both groups received annual chest x-ray for an additional three year

period. Results showed a significant increase in the number of cancers detected in the intervention group, including more instances of early stage disease. However, as in the previously cited studies, no difference in mortality was found between the two groups. In 2000, Kubik et al published a 15-year follow-up to the study. The follow-up concurs there is no evidence that lung cancer screening by chest x-ray decreases mortality.²³

More recently, beginning in 1992, the Prostate, Lung, Colorectal, and Ovarian (PLCO) Trial was initiated to further evaluate chest x-ray as a screening test for lung cancer. PLCO, sponsored by NCI, is a large, multi-center, randomized clinical trial involving 154,942 male and female participants between the ages of 55 and 74.²⁴ The control group consists of 77,477 individuals who received no screening. In the intervention group, which consists of 77,465 individuals, smokers and former smokers received single-view, posterior-anterior chest x-ray followed by three annual screens, and non-smokers received prevalence screening followed by two annual screens. Of the 5991 individuals with a baseline positive screen, 126 were diagnosed with cancer within 12 months of the initial screen. Higher rates of cancer were detected in current and former smokers who had smoked within the previous 15 years. Of the cancers detected, 44% of the cancers were stage I. Whether this early detection results in lower mortality rates has yet to be determined.

LOW-DOSE HELICAL CT

Low-dose helical CT, also referred to as low-dose spiral CT, is a scanning technology in which the CT scanner rotates around the subject, who is positioned on a table which then passes through the center of the scanner. Computer-generated images are assembled into a three-dimensional model of the thorax. Helical CT possesses a number of benefits and risks. Helical CT allows a low-resolution image of the entire thorax in a single breath-hold, the duration of which is only 7 to 15 seconds, reducing therefore the likelihood of motion artifact. The narrower, thinner slices of the helical CT image also permit a more accurate evaluation. Lastly, the radiation dose is only one-tenth of a diagnostic CT.

False positives represent the major risk associated with helical CT, which result in unnecessary invasive procedures (such as percutaneous lung fine needle aspiration, bronchoscopy, video assisted thoracic surgery; and thoracotomy), increased anxiety for individuals undergoing diagnostic testing, and exposure to radiation during the screening and subsequent diagnostic tests. In addition, the overall public health costs associated with the unnecessary procedures, based on false positives, represent a significant concern.

OBSERVATIONAL CT STUDIES

In 1996, Sone, et al., screened 5483 individuals from the general population in Matsumoto, Japan, using low-dose helical CT.²⁵ In addition to CT, 3967 subjects received chest x-ray, and individuals with a history of smoking received sputum cytology. Participants had previously received annual screening with chest x-ray and sputum cytology. Of the 5483 participants, 3967 underwent both x-ray and helical CT. Based on the results of the CT, 2524 (64%) were classified as normal, 1047 (26%) were noted to have non-significant abnormalities, 173 (4%) had non-cancerous lung lesions, 59 (1%) had suspicious lesions determined to be non-cancerous; 84 (2%) had lesions suspicious for cancer; and, 80 (2%) subjects had indeterminate small lung nodules. Of the 19 lung cancers diagnosed, 16 were stage I and three were stage IV disease. The study illustrated the increased sensitivity of helical CT over x-ray. Four lesions were ≤ 1 cm, and 14 were between 1 cm and 2 cm. Only one tumor that measured 2 cm was detected on chest x-ray. One lesion was undetected by either chest x-ray or helical CT, and was diagnosed by sputum cytology. Overall, the rate of lung cancer detection by helical CT was 0.4%, which was significantly higher than the 0.03–0.05% previously seen in screenings in the same area.

In 1999, Henschke, et al, in the Early Lung Cancer Action Project (ELCAP) reported results from a single-arm study designed to evaluate low-dose helical CT in a high-risk cohort.⁴ Annual low-dose helical CT and chest x-ray were performed in 1000 individuals with a history of at least 10 pack-years of cigarette smoking. Suspicious (non-calcified) nodules were detected by baseline helical CT screen in 233 individuals, while only 68 were detected by chest x-ray. Of the suspicious nodules found by low-dose helical CT, 27 (2.7%) were malignant and one was benign. Only seven of the 27 malignant nodules found on helical CT were detected on chest x-ray. Stage I disease was diagnosed in 23 (85%) of the cases. Overall, malignancy was identified four times more frequently with low-dose helical CT than with chest x-ray. Based on the results of this study, the investigators proposed universal screening.

Recently, the International Early Lung Cancer Action Project (I-ELCAP), a follow-up study to ELCAP, published results of annual CT screening on over 31,000 high-risk subjects.⁶ This single-arm study enrolled more than 25,000 participants worldwide. Lung cancer was diagnosed in 484 cases, of which 412 (85%) were stage I. The 10-year survival rate for stage I disease was estimated at 88%.

In 1999, Swenson, et al, conducted a five-year prospective study evaluating low-dose helical CT in a cohort of individuals at high risk for developing lung cancer.¹² The study enrolled 1520 male and female smokers and former smokers, aged 50 and older, with a smoking history of 20 pack-years. This single-arm study evaluated the effects of low-dose helical CT annually for five years. 3356 non-calcified nodules were detected in 1118 (74%) participants, and 68 primary lung cancers were diagnosed in 66 (4%) participants. Although survival was increased, mortality rates were not significantly decreased when compared to historical data from the Mayo Lung Project. The authors of the study raised the concern that screening may actually do more harm than good, because of false positives and overdiagnosis.

In 2007, Bach, et al, used a validated prediction model to evaluate the effects of annual CT screening in a high-risk cohort across three studies conducted at Instituto Tumori in Milan, Italy, the Moffitt Cancer Center in Tampa, FL, and the Mayo Clinic, Rochester, MN as discussed above.⁹ The total number of participants at all three institutions was 3246. Lung cancer was detected with CT screening in 144 individuals, 96 (67%) of which were early stage disease. Bach's analysis of the studies showed an increased detection of early stage disease. However, results did not indicate a decrease in the diagnosis of *advanced* lung cancer, or a decrease in mortality, thus calling into question the results of earlier studies of helical CT and increasing the significance of the randomized controlled screening trials currently underway.

THE CURRENT U.S. RANDOMIZED CONTROLLED SCREENING TRIAL

The National Lung Cancer Screening Trial (NLST) is a major NCI-sponsored study, initiated in 2002, designed to compare helical CT and chest x-ray to determine if either is effective in decreasing lung cancer mortality^{10,26}. 53,364 men and women, between the ages of 55 and 74 were enrolled within 18 months of study activation. The subjects were current or former smokers with a history of 30 or more pack-years, but who were at the time asymptomatic. Former smokers must have quit smoking within the previous 15 years and must not have a history of lung cancer or any other type of cancer within the past five years (except skin or localized prostate cancer, or cervical carcinoma *in situ*). In addition, subjects must not have had a CT scan of the chest within the previous 18 months.

The NLST randomized individuals to receive either helical CT or chest x-ray. Both groups received a prevalence screen and annual screens for the following two years. Interim analyses began in 2006 and will continue annually, with final results expected in 2010. An independent Data and Safety Monitoring Board (DSMB) has been established for the trial which meets bi-annually to ensure the safety of all study participants. The DSMB analyzes trial interim data

to make recommendations on trial design if interim data reflect significant differences between the two study arms in either efficacy or toxicity.

Among the additional questions to be addressed by NLST are the following:

- At what stage is lung cancer when it is diagnosed in the screened population?
- How well does the screening test detect early lung cancer? All lung cancer?
- What diagnostic tests are conducted when CT screening or chest x-ray are positive?
- How cost effective is lung cancer screening?
- How does lung cancer screening affect quality of life between early detection and diagnosis?
- How does lung cancer screening influence smoking behavior and beliefs?
- Will additional research on collected blood, urine, or sputum be able to help to predict lung cancer in high risk groups?

NLST, beyond its immediate importance for cancer screening, represents the highest and most appropriate standard for research, the randomized controlled clinical trial. Though these trials require a larger number of participants than observational studies, take longer to conduct, and require significant allocation of scarce resources, RCTs have the benefit of providing definitive results to inform the standard of practice. Additional smaller randomized clinical trials are underway in Europe and will serve as comparators to the NLST. Meta-analyses may also eventually be conducted (Personal communication with Christine D. Berg, March 2007).

In September of 2007, the American College of Chest Physicians published updated guidelines recommending that lung cancer screening with helical CT should not be offered outside the context of a well-designed clinical trial with appropriate human subjects protections.²⁷ This recommendation is based on findings that screening with helical CT has not been proven to decrease mortality. A number of other organizations are awaiting the results of the NLST prior to publishing new or updated screening guidelines.

DISCUSSION

As noted above, observational studies of helical CT initially produced encouraging results. However, because the studies considered only survival and not mortality, their utility in evaluating the ultimate effectiveness of the screening technology is limited. The more recent analysis of three studies by Bach et al (9), by examining the impact on mortality through modeling, provides a more valid basis for evaluating the benefits and risks of helical CT.

Neither the observational studies nor the studies in Bach's analysis, however, were randomized controlled clinical trials, and are, therefore, unable to definitively inform the standard of practice. The NLST, on the other hand, by virtue of its larger number of participants and randomized design, is designed to answer questions beyond the scope of previous studies.

NURSING IMPLICATIONS

Oncology nurses have frequent opportunities to inform and educate both patients and fellow nurses and health care workers with regard to the scientific status of lung cancer screening. Based on the review above, one clear conclusion is that helical CT has yet to be fully evaluated as an effective screening tool. While the current randomized screening trial (NLST) is underway, oncology nurses should remain current on its status and its implications for patient

care, in particular, stressing the importance of the randomized clinical trial—and its basis in the scientific process—on future cancer detection and treatment possibilities.

With respect to individuals under their care, oncology nurses have the opportunity to influence behavior by encouraging patients to avoid smoking. This behavioral change alone would be more effective than any type of screening technology in prolonging life expectancy and improving quality of life.²⁸ Tobacco accounts for nearly 90% of all lung cancers. Former smokers benefit from smoking cessation, but remain at increased risk for the disease. For example, an adult smoker who quits at age 50 still retains a 6% risk of developing lung cancer by age 75. The risk for a lifelong non-smoker of the same age is less than 0.5%.²⁹

The ongoing research on lung cancer screening presents challenges and opportunities for nursing. Quality of life issues, health outcomes weighed in the context of cost-benefit analyses, and their impact on public policy all have direct bearing on the nursing profession and must inform the national research agenda.

REFERENCES

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics. *CA Cancer J Clin* 2007;57:43–66. [PubMed: 17237035]
2. Flehinger BJ, Kimmel M, Melamed MR. The effect of surgical treatment on survival from early lung cancer. Implications for screening. *Chest* 1992;101:1013–1018. [PubMed: 1313349]
3. Nesbitt J. Survival in early-stage lung cancer. *Ann Thorac Surg* 1995;60:466–472. [PubMed: 7646126]
4. Henschke CI, McCauley DI, Yankelevitz DF, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. *Lancet* 1999;354(9173):99–105. [PubMed: 10408484]
5. Patz EF Jr, Goodman PC, Bepler G. Screening for lung cancer. *N Engl J Med* 2000;343:1627–1633. [PubMed: 11096172]
6. Henschke CI, Yankelevitz DF, Libby DM, Pasmantier MW, Smith JP, Miettinen OS. Survival of patients with stage I lung cancer detected on CT screening. *N Engl J Med* 2006;355:1763–1771. [PubMed: 17065637]
7. Clark, R.; Reintgen, D. *Cancer Screening*. Reintgen, D.; Clark, R., editors. St. Louis: Mosby; 1996. p. 1–20.
8. Miller, A. *Cancer Epidemiology and Prevention*. Schottenfeld DaF, JF., editor. New York: Oxford University Press; 1996. p. 1433–1452.
9. Bach PB, Jett JR, Pastorino U, Tockman MS, Swensen SJ, Begg CB. Computed tomography screening and lung cancer outcomes. *JAMA* 2007;297:953–961. [PubMed: 17341709]
10. US Department of Health and Human Services (US DHHS). National Lung Screening Trial-What is the appropriate measure of screening effectiveness?. [Accessed September 12, 2007]. Available at: <http://www.cancer.gov/nlst/what-is-nlst#10b>
11. Bach PB, Kelley MJ, Tate RC, McCrory DC. Screening for lung cancer: a review of the current literature. *Chest* 2003;123(1 Suppl):72S–82S. [PubMed: 12527566]
12. Swensen SJ, Jett JR, Hartman TE, et al. CT screening for lung cancer: five-year prospective experience. *Radiology* 2005;235:259–265. [PubMed: 15695622]
13. Gohagan JK, Marcus PM, Fagerstrom RM, et al. Final results of the Lung Screening Study, a randomized feasibility study of spiral CT versus chest X-ray screening for lung cancer. *Lung Cancer* 2005;47:9–15. [PubMed: 15603850]
14. Gohagan J, Marcus P, Fagerstrom R, Pinsky P, Kramer B, Prorok P. Baseline findings of a randomized feasibility trial of lung cancer screening with spiral CT scan vs chest radiograph: the Lung Screening Study of the National Cancer Institute. *Chest* 2004;126:114–121. [PubMed: 15249451]
15. Tuchman M, Lemieux B, Auray-Blais C, et al. Screening for neuroblastoma at 3 weeks of age: methods and preliminary results from the Quebec Neuroblastoma Screening Project. *Pediatrics* 1990;86:765–773. [PubMed: 2152340]
16. Woods WG, Tuchman M, Robison LL, et al. A population-based study of the usefulness of screening for neuroblastoma. *Lancet* 1996;348(9043):1682–1687. [PubMed: 8973429]

17. Fontana RS, Sanderson DR, Woolner LB, Taylor WF, Miller WE, Muhm JR. Lung cancer screening: the Mayo program. *J Occup Med* 1986;28:746–750. [PubMed: 3528436]
18. Tockman MS. Survival and Mortality from Lung Cancer in a Screened Population: The Johns Hopkins Study. 1986NEED PUBLISHER AND LOCATION
19. Melamed MR, Flehinger BJ, Zaman MB, Heelan RT, Perchick WA, Martini N. Screening for early lung cancer. Results of the Memorial Sloan-Kettering study in New York. *Chest* 1984;86:44–53. [PubMed: 6734291]
20. Sanderson D. Lung Cancer Screening: The Mayo Study. *Chest* 1986;89:324. [PubMed: 3512185]
21. Marcus PM, Bergstralh EJ, Fagerstrom RM, et al. Lung cancer mortality in the Mayo Lung Project: impact of extended follow-up. *J Natl Cancer Inst* 2000;92:1308–1316. [PubMed: 10944552]
22. Kubik A, Polak J. Lung cancer detection. Results of a randomized prospective study in Czechoslovakia. *Cancer* 1986;57:2427–2437. [PubMed: 3697941]
23. Kubik AK, Parkin DM, Zatloukal P. Czech Study on Lung Cancer Screening: post-trial follow-up of lung cancer deaths up to year 15 since enrollment. *Cancer* 2000;89(11 Suppl):2363–2368. [PubMed: 11147613]
24. Gohagan JK, Prorok PC, Hayes RB, Kramer BS. The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial of the National Cancer Institute: history, organization, and status. *Control Clin Trials* 2000;21(6 Suppl):251S–272S. [PubMed: 11189683]
25. Sone S, Takashima S, Li F, et al. Mass screening for lung cancer with mobile spiral computed tomography scanner. *Lancet* 1998;351(9111):1242–1245. [PubMed: 9643744]
26. Greenwald P. A favorable view: progress in cancer prevention and screening. Recent results *Cancer Res* 2007;174:3–17. [PubMed: 17302181]
27. Bach PB, Silvestri GA, Hanger M, Jett JR. Screening for Lung Cancer: AACP Evidence-Based Clinical Practice Guidelines. *Chest* (2nd Edition) 2007;132(3):69S–77S. [PubMed: 17873161]
28. Humphrey, L. Lung cancer screening: An update for the U.S. Preventive Services Task Force. Rockville: Agency for Healthcare Research and Quality (AHRQ); 2004 May.
29. Peto R, Darby S, Deo H, Silcocks P, Whitley E, Doll R. Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies. *Bmj* 2000;321(7257):323–329. [PubMed: 10926586]

FIGURE 1.

Lead-time bias. Lung-cancer-specific survival is measured from the time of diagnosis of lung cancer to the time of death. Screening may appear to prolong survival even though death may not be delayed. Effective screening tests should detect disease before signs or symptoms occur and *must* lead to decreased mortality. Adapted from US DHHS¹⁰.

Sx = Symptoms

Dx = Diagnosis

FIGURE 2.

Length bias. Screening detects more biologically indolent cancers than aggressive cancers due to a prolonged pre-symptomatic phase. This variability in cancer progression may cause it to appear as though there is a screening-related improvement in survival. Adapted from US DHHS¹⁰.

Sx = Symptoms

Dx = Diagnosis

FIGURE 3.

Overdiagnosis. Screening detects cancer that might remain subclinical (non-lethal) before death from other causes. Adapted from US DHHS¹⁰.

Dx = Diagnosis