

COMMENTARY

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Cancer screening: A modest proposal for prevention

I have been assured by a very knowing American of my acquaintance in London, that a young healthy child well nursed is at a year old, a most delicious, nourishing, and wholesome food, whether stewed, roasted, baked, or boiled, and I make no doubt that it will equally serve in a fricassee, or ragout.

—Jonathan Swift, *A Modest Proposal*¹

Large-scale cancer screening programs have the unintended consequences of false-positive results and overdiagnosis, leading to anxiety and overtreatment. The magnitude of these harms continues to be clarified after decades of screening.

Recognizing the trade-off between benefits and harms, the US Preventive Services Task Force (USPSTF) has changed several of its recommendations in recent years. Breast cancer screening recommendations have gone from yearly mammograms starting at age 40 to biennial mammograms starting at age 50 for women at average risk.² Prostate cancer screening is no longer recommended for men age 70 and older, and even for men between 55 and 69, screening is now an individual decision.³

Newer screening programs are targeting high-risk groups rather than the general population, with the aim of increasing the likelihood of benefits and limiting the harms. For example, lung cancer screening is recommended only for current smokers or smokers who have quit within the past 15 years, are between 55 and 80, and have at least a 30 pack-year smoking history.⁴

The movement toward less-frequent screening and screening in a narrower population has evoked strong reactions from advocates of cancer screening. One professor of radiology writes, “It borders on unethical

to suggest that the benefit of having your life saved by screening and living another 40 years can be balanced against the ‘harm’ of being recalled for additional mammographic views for what proves to not be a cancer.”⁵ Another notes, “It does not make any sense to throw away the lives saved by screening to avoid over-treating a small number of cancers.”⁶ Both of these authors defend the position that the goal of screening is to minimize cause-specific mortality, irrespective of overdiagnosis, overtreatment, or false-positive results. In other words, harm should have little to no weight in screening recommendations.

Although the debate on cancer screening is moving toward a more balanced discussion of benefits and harms, many patients are still subjected to screening that is more aggressive than the USPSTF recommends, which may be due to an underlying belief that no harm is greater than the benefit of saving a life.

■ IS MORE-AGGRESSIVE SCREENING THE ANSWER?

Worst of all, when we examine the numbers, cancer screening is not very effective (Table 1).^{2-4,7,8} Even using optimistic estimates of its benefit, it is at best a half measure. Although screening, by detecting more cases of cancer at an early, potentially treatable stage, does save some lives from that cancer, many more people continue to die of cancer *in spite of* screening.

One may wonder if more-aggressive screening could prevent deaths that occur despite standard screening. For example, more-frequent screening or use of additional screening methods such as ultrasonography or magnetic resonance imaging has been suggested for patients at high risk of breast cancer.

Balancing the benefits and the harms of screening can be difficult

TABLE 1

Benefit of cancer screening

Cancer type and method of screening	Per 100,000 person-years			Harms of interventions
	Deaths from cancer	Deaths averted by screening	Deaths not averted by screening	
Breast cancer^a				
Mammography every 2 years				False-positive results Overdiagnosis, overtreatment Radiation exposure
Age 39–49	34	4	30 (88%)	
Age 50–59	54	8	46 (85%)	
Age 60–69	65	21	44 (68%)	
Age 70–74	62	13	49 (79%)	
Age 50–69	58	13	45 (78%)	
Colon cancer^b				
One-time flexible sigmoidoscopy	44	12	32 (73%)	Complications of procedure Overdiagnosis, overtreatment
Guaiaec fecal occult blood test once a year	44	4	40 (91%)	False-positive results Overdiagnosis, overtreatment
Colonoscopy every 10 years ⁸	69	9	60 (87%)	Perforation of the colon
Prostate cancer^c				
Prostate-specific antigen test once a year	48	10	38 (79%)	False-positive results Overdiagnosis, overtreatment
Lung cancer^d				
Low-dose computed tomography once a year	309	59	250 (81%)	False-positive results Overdiagnosis, overtreatment

^aBreast cancer numbers are based on risk ratio in Table 5 of reference 2.

^bEffects of sigmoidoscopy are based on 4 large randomized trials with 11- to 12-year follow-up. Colon cancer mortality without screening is calculated as the average mortality of the control groups in the 4 randomized trials (Table 1 of reference 7). Incident rate ratio of 0.73 was used to calculate colon cancer deaths avoided with screening with sigmoidoscopy. Effects of guaiac fecal occult blood testing are based on 5 randomized trials with 11- to 30-year follow-up (also Table 1 of reference 7). Relative risk of 0.91 was used to calculate effects of screening. The US Preventive Services Task Force (USPSTF) estimated the relative risk of 0.91 after 19.5 years of screening and 0.78 after 30 years of screening. Colonoscopy effects are based on Table 3 and Table 4 of referenced modeling study representing 40-year follow-up of 1,000 men and women.⁸ The modeling study is designed to compare different screening modalities; all participants are screened regardless of life expectancy, and calculations are based on 100% adherence to screening. Therefore, numbers cannot be directly compared with other cancer screening programs.

^cProstate cancer numbers are based on the table in reference 3 on 13-year follow-up of 1,000 men invited to screening.

^dLung cancer numbers are based on National Lung Screening Trial of lung cancer mortality and relative risk of 0.81 from USPSTF meta-analysis.

■ A MODEST PROPOSAL

If one holds the view that benefits alone should be considered when writing recommendations about screening, the logical conclusion extends beyond screening. We would therefore like to propose a different approach to reducing cancer deaths in the general population:

Why not just remove everybody's breasts, prostate gland, and colon before cancer arises?

■ TO CUT IS TO PREVENT

Currently, we offer prophylactic surgery to patients at high risk of cancer. For example, women with *BRCA1/BRCA2* mutations are offered prophylactic mastectomy as one of several options for reducing risk of breast cancer. In 2013, the first case of prophylactic prostatectomy was performed in a man who had a *BRCA1/BRCA2* mutation. Total colectomy is considered in men and women who have he-

editary nonpolyposis colon cancer, instead of segmental resection, to prevent future cancer.

If prophylactic surgery were extended to the general population, it would greatly reduce the number of cancer deaths. Assuming that removing an organ almost always precludes development of cancer, we may predict that prophylactic mastectomy, prostatectomy, or colectomy would save the lives of most of the patients who are still dying of cancer of these organs. The effectiveness rates would approach, but not reach 100%; such is the case with prophylactic mastectomy.

Consider prostate-specific antigen (PSA) screening. Even using the favorable estimate of the impact of PSA screening, arising from the European Randomised Study of Screening for Prostate Cancer trial, 27 men have to be diagnosed, most undergoing local therapy (the trial was conducted before active surveillance became routine), to avert 1 death from prostate cancer over 13 years.⁹

Contrast this “number needed to diagnose” with the number needed to treat for a strategy of routine prostate removal at age 45 or 50. Given that the lifetime risk of death from prostate cancer approaches 3%, and few cases arise before this age, a prophylactic surgical strategy would avert 1 death per 33 operations. If proponents of screening are willing to accept a number needed to diagnose of 27 over a 13-year interval, they may be willing to consider a number needed to treat of 33 over a lifetime.

There may be harms such as perioperative and postoperative complications. Mastectomy could lead to emotional stress from altered body image. Prostatectomy can have long-term complications such as urinary incontinence and sexual dysfunction. Nevertheless, prophylactic organ removal would save far more lives than current screening practices. It also could decrease mental burden, as patients could rest assured that they will never develop cancer, whereas screening often involves ambiguous test results, follow-up tests, and interventions, increasing patient anxiety.

■ FINDING THE BALANCE BETWEEN BENEFITS AND HARMS

In truth, we do not really advocate universal mastectomy, prostatectomy, and colectomy

to prevent cancer, no more than Swift¹ really wanted to eat the children of Ireland to alleviate poverty and famine in that country. Rather, we use it as an extreme proposal to highlight the scope and depth of harms that inevitably arise from screening.

If proponents of aggressive screening believe that the goal is to reduce cause-specific mortality as much as possible, giving little weight or consideration to overdiagnosis and overtreatment, then they ought to embrace universal prophylactic surgery as well. Recognition of this logical consequence reminds us that we must make screening recommendations that balance benefits and harms.

Considering an extreme perspective can help in recognizing our bias toward saving lives from cancer and discounting the harms. Aggravating this bias, it is impossible to know whether an individual patient has avoided fatal cancer or undergone unnecessary treatment. Moreover, changing practice is more difficult if it involves rolling back interventions that were once the standard.

Balancing benefits and harms is especially difficult when trying to compare the benefit of preventing a single cancer death against a harm that is less serious but more common. Medicine has always involved difficult trade-offs, as seen in cost-benefit analysis of new treatments or balancing quality of life with quantity of life in a single patient. In addition, each individual may place different values on benefits of screening and avoiding possible harms.

There is an undeniable trade-off with screening, and we must make a conscious decision on where to draw the line when harms outweigh the benefits. We must proceed with caution when subjecting large numbers of men and women to the possibility of psychological burden and decreased quality of life.

Given the growing appreciation of the harms of screening, it is likely that future guidance will continue to move toward less-frequent screening or focusing resources on high-risk populations, where the absolute magnitude of benefit is greater. Cancer screening is also likely to become an individual decision based on personal values and informed decisions. ■

The effectiveness of prophylactic surgery would approach 100%

REFERENCES

1. **Swift J.** A Modest Proposal for Preventing the Children of Poor People in Ireland, from Being a Burden on Their Parents or Country, and for Making Them Beneficial to the Publick. Dublin: S. Harding, 1729.
2. **Nelson HD, Cantor A, Humphrey L, et al.** Screening for breast cancer: a systematic review to update the 2009 US Preventive Services Task Force Recommendation. www.ncbi.nlm.nih.gov/books/NBK343819/. Accessed February 13, 2019.
3. **US Preventive Services Task Force; Grossman DC, Curry SJ, Owens DK, et al.** Screening for prostate cancer: US Preventive Services Task Force Recommendation Statement. *JAMA* 2018; 319(18):1901–1913. doi:10.1001/jama.2018.3710
4. **Humphrey L, Deffebach M, Pappas M, et al.** Screening for lung cancer: systematic review to update the US Preventive Services Task Force Recommendation. www.ncbi.nlm.nih.gov/books/NBK154610/. Accessed February 13, 2019.
5. **Kopans DB.** A review of: "Tipping the balance of benefits and harms to favor screening mammography starting at age 40 years." www.sbi-online.org/Portals/0/downloads/documents/pdfs/A%20review%20of%20Tipping%20the%20Balance%20of%20Benefits%20and%20Harms%20to%20Favor%20Screening%20Mammography%20Starting%20at%20Age%2040%20Years%20-%20Kopans.pdf. Accessed February 13, 2019.
6. **Yaffe M, Gordon P.** Routine mammograms do save lives: U of T expert. U of T News. www.utoronto.ca/news/routine-mammograms-do-save-lives-u-t-expert. Accessed February 13, 2019.
7. **Lin JS, Piper MA, Perdue LA, et al.** Screening for colorectal cancer: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2016; 315(23):2576–2594. doi:10.1001/jama.2016.3332
8. **Knudsen AB, Zauber AG, Rutter CM, et al.** Estimation of benefits, burden, and harms of colorectal cancer screening strategies: model-based study for the US Preventive Services Task Force. *JAMA* 2016; 315(23):2595–2609. doi:10.1001/jama.2016.6828
9. **Schröder FH, Hugosson J, Roobol MJ, et al; ERSPC Investigators.** Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up. *Lancet* 2014; 384(9959):2027–2035. doi:10.1016/S0140-6736(14)60525-0

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