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In Brief

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Screening is a public health intervention that is a balance of benefit and harm. Appropriate cancer screening and efficacious therapy can reduce cancer-specific mortality, and for some cancers it can reduce the incidence. As with any medical intervention, there is also a potential for harm. Indeed, inappropriate screening can cause tremendous harm. In order to exploit screening and save the most lives, we need to appreciate the potential for harm and the potential for benefit.

Time and time again, a diagnostic test has been widely adopted as a cancer screening test with less-than-adequate evaluation. The result has been harm—including overdiagnosis, unnecessary treatment, and the morbidities associated with that unnecessary treatment. Here, we review the principles of cancer screening and the history of screening for some major cancers.

There are biases associated with observational studies that assess the efficacy of cancer screening interventions and 3, in particular, should be considered carefully: lead-time, length, and selection biases. These biases are discussed further in this monograph. To eliminate the effects of these biases, the efficacy of cancer screening should ideally be determined in randomized controlled trials with all-cause mortality as an endpoint. All-cause mortality is an unambiguous endpoint and eliminates the risk of bias in the assessment of cause of death. Yet, it is not a practical endpoint for a cancer screening trial because it generates a huge (and generally unattainable) sample size requirement. To reduce the sample size requirement, cancer-specific mortality is generally used as the endpoint, but even then, tens of thousands of individuals are generally required for each screening trial. Additionally, 2 forms of assessor bias should be considered whenever cancer-specific mortality is used as an endpoint: sticky-diagnosis bias and slippery-linkage bias.

Randomized trials with cancer-specific mortality as the endpoint have been undertaken to assess screening strategies for breast, colorectal, prostate, lung, ovary, cervix, oral, and liver

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cancers. The historical background leading up to many of these trials and the trials themselves are discussed in this monograph. The results of these trials have had enormous public health implications. These trials have demonstrated that contemporary screening strategies are efficacious for some cancers but not others. Moreover, these trials have shed light on the potential harms of screening. These harms include false-positives, false-negatives, over-diagnosis, and the potential harms associated with the screening interventions.

Newer technologies in imaging and molecular diagnostics are leading to the development of a number of novel screening tests. By appreciating the history of screening, past mistakes will not be repeated as these new technologies evolve. The underlying message here is not that screening is inappropriate; but rather that every cancer must be assessed to determine if it is a screenable cancer, and every putative screening test must be assessed carefully and evaluated before it is widely disseminated. Only then will we not repeat history and harm the patients we want to serve.