Principles of Cancer Screening

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KEYWORDS

• Cancer screening • Overdiagnosis • Lead time • Targeted screening
• Number needed to screen • Performance characteristics

KEY POINTS

- Early detection of cancer through screening can reduce cancer mortality; detection of precancerous lesions, achievable currently with colorectal and cervical cancer screening, also reduces cancer incidence.
- Sensitivity and specificity are critical metrics for researchers assessing the predictive ability of a screening modality; positive predictive value (probability of cancer given a positive test) is more relevant for clinicians.
- The gold standard for evaluating cancer screening tests is the randomized controlled trial (RCT). Caution must be taken when using observational data, and especially survival statistics, to assess cancer screening.
- Harms from screening include false-positive tests and their downstream sequellae, including invasive diagnostic tests and complications thereof, and overdiagnosed and overtreated cancers.
- Targeting screening to high-risk subjects is a strategy to make screening more efficient, in terms of optimizing the benefits to harms tradeoff and the cost-effectiveness of screening.

INTRODUCTION

For more than a half century, cancer screening has been an important component of the struggle to reduce the burden of morbidity and mortality from cancer. In certain cases, such as with cervical cancer, the effects have been dramatic, with mortality decreasing more than 80% in the United States after implementation of widespread screening with Pap smears.[1] For most other cancers, however, the effects of screening have been substantially less pronounced. Benefits of screening have generally been on the modest side, and there has been increasing recognition of screening-related harms. The promise of cancer screening still beckons, however, and many new

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technologies continue to be evaluated for their potential to generate new screening modalities.

A standard introduction for a scientific paper concerning cancer screening proceeds as follows: the 5-year survival rate for cancer X is very low. Among stage I cases, however, 5-year survival is much higher; however, few cases are diagnosed in this stage. Therefore, if cancer X could only be detected earlier, the prognosis for subjects diagnosed with cancer X can be much improved.

In a nutshell, this is the basic, and very intuitive, rationale behind cancer screening. Although intuitively appealing, some caveats are in order. First, cancers diagnosed in early stages have a (relatively) good prognosis, but that does not necessarily mean that if those cancers currently diagnosed in late stage were detected earlier they would also have the same favorable prognosis. It is possible, for some cancer types, that inherent properties of late-stage tumors, such as their potential for early metastasis, and not the time of initial treatment, determine their eventual clinical outcome. Second, as a preventive intervention, screening tests are applied to asymptomatic and apparently healthy populations where, because of the relatively low prevalence of any given cancer type, most of those being screened cannot benefit from the screening but can be harmed because of either the screening test itself or of downstream consequences of it.

On the more favorable side for screening, there is the concept of detection through screening of precancerous lesions. Although standard screening programs are an example of secondary prevention, whereby cancer incidence is not reduced but mortality from the cancer is, screening modalities, such as those for colorectal and cervical cancer, that detect early cancers and precancerous lesions provide primary prevention (ie, incidence reduction) and secondary prevention. In addition to incidence reduction being a substantial benefit in itself, in terms of patient well-being and societal costs, screening modalities that reduce cancer incidence have greater magnitude reductions in cancer mortality than those that only provide secondary prevention.

This article provides an overview of some basic concepts and principles in cancer screening. Discussed are performance characteristics of screening tests (related to test accuracy), measures of screening benefit, some potential biases associated with evaluating screening benefits, harms of screening, the concept of cost-effectiveness of screening, and the related concept of targeting screening to high-risk groups. Finally, current recommendations for cancer screening in North America are summarized.

PERFORMANCE CHARACTERISTICS OF SCREENING TESTS

The performance characteristics of a screening test refer to its ability to accurately predict disease state. **Table 1** shows some common test performance characteristics. Sensitivity and specificity, and more generally the receiver-operating characteristic curve of sensitivity at varying levels of specificity for continuous or ordinal valued tests, are critical in the research setting for evaluating the potential of new screening modalities. Positive predictive value (PPV) is more relevant in the clinical setting, in that it assesses the probability that a patient with a positive test has the cancer of interest. Importantly, PPV depends not only on sensitivity and specificity, but also critically on the prevalence of the cancer being screened for (technically, this is the prevalence of underlying, undiagnosed cancer). With fixed sensitivity and specificity, PPV decreases as prevalence decreases. Because cancer prevalence in a screened population is low, even high specificity values can lead to very low values of PPV, regardless of sensitivity. For example, for a prevalence of 0.6% (eg, breast cancer in women