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Journal of Clinical Epidemiology 64 (2011) 231–239

Journal of Clinical Epidemiology

TUTORIALS

Trade-off between benefit and harm is crucial in health screening recommendations. Part I: General principles

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Accepted 27 September 2010

Abstract

Health screening is defined as the use of a test or a series of tests to detect unrecognized health risks or preclinical disease in apparently healthy populations to permit prevention and timely intervention. A health screening strategy consists of the sequence of a screening test, confirmatory test(s), and finally, treatment(s) for the condition detected. The potential benefits of health screening are easy to understand, but the huge potential for physical and psychological harm is less well recognized. Thus, health screening should only be recommended when five criteria are satisfied: (1) the burden of illness should be high, (2) the tests for screening and confirmation should be accurate, (3) early treatment (or prevention) must be more effective than late treatment, (4) the test(s) and treatment(s) must be safe, and (5) the cost of the screening strategy must be commensurate with potential benefit. Direct evidence from screening trials is subject to less bias. In some instances, indirect evidence may be acceptable, e.g., when the condition screened for is a risk factor for a disease rather than the disease itself.

Keywords: Health screening; Diagnostic test; Preventive medicine; Screening test; Screening strategy; Confirmatory test

1. The rationale behind health screening

In the last half century, health care has seen a major shift in philosophy from curative to preventive medicine. Medical education has evolved, societies on preventive medicine have been formed, national and international agencies have been set up, and health budgets have been restructured—all in support of this important shift in medical thinking. The concept of health care has escaped the confines of clinics and hospitals, expanding into the public arena, to include homes, schools, and the workplace.

Four major strategies characterize the rapidly growing field of preventive medicine. These include (1) health screening (performing tests for early detection of a disease or its risk factors), (2) lifestyle change, (3) control of environmental exposures, and (4) immunization against infectious diseases. Health screening is often referred to as the cornerstone of disease prevention [1]. It is the main focus of this tutorial. This review may be useful for students in clinical epidemiology courses and for guideline developers and health policy makers who are evaluating screening tests.

We define *health screening* as the use of a test or a series of tests to detect preclinical disease in apparently healthy populations to permit prevention and timely intervention. This definition is illustrated in Fig. 1, which depicts four stages in the natural course of a disease—from good health, preclinical disease, manifest disease, to disease outcomes. Although ''usual therapy'' begins once a disease becomes manifest, health screening is an attempt to intervene at an earlier point in time. In this review, we refer to the sequence of tests and interventions that follow as a ''screening *strategy*.'' This should be differentiated from a ''screening test'' or the diagnostic test, which is just the first step in this sequence.

1.1. The tests for screening

The first component of the definition refers to the initial tests that will be used. Although laboratory tests are the classic examples, history taking or a physical examination are likewise considered as screening tests. For example, breast cancer can be screened for by (1) asking individuals if they have relatives with this condition (history), (2) doing a proper clinical breast examination (physical examination), or (3) performing radiographic studies (laboratory

The authors declare no conflicts of interests with this article.

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0895-4356/$ - see front matter
doi: 10.1016/j.jclinepi.2010.09.009

What is new?

We propose a definition of screening that distinguishes between screening for early disease and screening for risk factors for disease.

What this adds to what is known

These distinctions help refine our understanding of the balance between benefit and harm of screening strategies. The potential for harm, in particular, is often underemphasized, and is discussed in detail in this paper.

What is the implication and what should change now?

While the five criteria used to weigh the risks and benefits of screening are standard, actual recommendations on screening may differ between countries. Consideration of differences in disease burden should lead to variations in priorities and estimates of cost-effectiveness.

testing). These are important distinctions to make, because laboratory tests are often inconvenient and expensive. The history and physical examination allow us less costly and safer methods for screening. They, therefore, provide standards of cost and safety against which laboratory tests can be evaluated. Whatever procedure is used, it must be recognized that, in a screening strategy, a single test is rarely sufficient to establish a diagnosis. Most screening strategies, therefore, involve at least two tests in sequence—a screening test and a confirmatory test. Screening tests do not define disease but identify populations with a higher likelihood of the disease being present. Thus, people who test positive on a screening test include people who have the condition screened for (true positives) and also a number of those who actually do not (false positives). To distinguish between the two, *confirmatory tests* are done to definitively establish the presence or absence of the disease. This two-step approach has an economic advantage. Confirmatory tests, although more accurate, are usually more expensive and, thus, impractical to perform on large populations. Starting with screening tests (usually less expensive) thus reduces the number of people on whom confirmatory tests need to be done.

In breast cancer screening, for example, when either the mammography or clinical breast examination result is positive, the diagnosis usually needs to be confirmed with a histopathological examination of a biopsy specimen.

1.2. The conditions screened for

The second component of the screening definition is the condition screened for. In the natural history of disease, a stage of preclinical disease follows good health (Fig. 1). This stage must be present for screening to work at all. The longer this stage of preclinical disease, the more opportunities there are to detect and treat it. As such, slow benign diseases (with a long preclinical stage) are more easily detected by screening than malignant diseases (with a short preclinical stage). Unfortunately, it is the latter which is our main concern. This is a flaw inherent in most screening strategies. A major criticism against prostate cancer screening, for example, is that it may detect slow indolent forms of the disease preferentially, while often missing the malignant forms [2].

Our definition of health screening distinguishes two types of preclinical diseases—"unrecognized health risks," such as hypertension, and "asymptomatic disease," such as early breast cancer (Table 1). This distinction is important. Conceptually, "health risk" occurs earlier and allows primary prevention of disease before it even ensues. When "asymptomatic disease" is present, on the other hand, the disease process has already started. Therefore, preventing complications (secondary prevention) is the main goal. Screening and confirmatory tests for "health risk" are generally safer, more accurate, and less costly. Screening for hypertension, for example, requires a simple

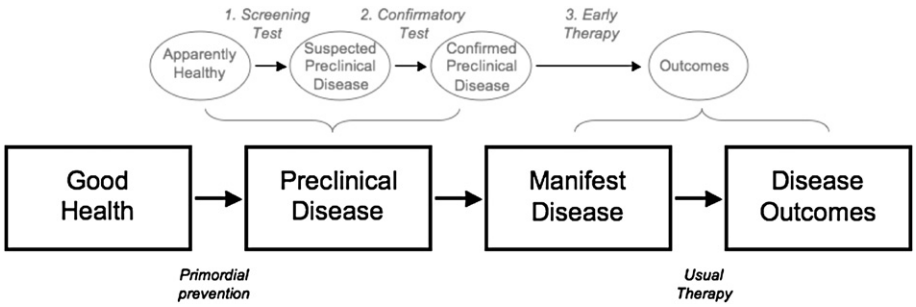

Fig. 1. Interrupting the natural history of disease. The *natural history of disease* (depicted in dark boxes) involves a stage of good health, followed by preclinical disease (e.g., hypertension), manifest disease (e.g., a stroke), and finally, disease outcomes (e.g., death). Primordial prevention interrupts the first step in this progression (e.g., through lifestyle change), and usual therapy tries to achieve this in the last step (e.g., treatment of stroke). In contrast, health screening (depicted in gray ovals) is an attempt to interrupt the natural history by treating disease before it manifests. This entails a 3-part strategy that includes the following: (1) screening tests done on apparently healthy populations, (2) confirmatory tests for those who screen positive, and (3) early therapy to prevent clinical outcomes. Screening strategies or programs should be differentiated from screening tests, which is only the first step in the process.