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The Harms of Screening
A Proposed Taxonomy and Application to Lung Cancer Screening

Rationale: Making rational decisions about screening requires information about its harms, but high-quality evidence is often either not available or not used. One reason may be that we lack a coherent framework, a taxonomy, for conceptualizing and studying these harms.

Objectives

- To create a taxonomy, we categorized harms from several sources: systematic reviews of screening, other published literature, and informal discussions with clinicians and patients. We used this information to develop an initial taxonomy and vetted it with local and national experts, making revisions as needed.

Results

- We propose a taxonomy with 4 domains of harm from screening: physical effects, psychological effects, financial strain, and opportunity costs. Harms can occur at any step of the screening cascade. We provide definitions for each harm domain and illustrate the taxonomy using the example of screening for lung cancer.

Conclusions and Relevance

- The taxonomy provides a systematic way to conceptualize harms as experienced by patients. As shown in the lung cancer screening example, the taxonomy also makes clear where (which domains of harms and which parts of the screening cascade) we have useful information and where there are gaps in our knowledge. The taxonomy needs further testing and validation across a broad range of screening programs. We hope that further development of this taxonomy can improve our thinking about the harms of screening, thus informing our research, policy making, and decision making with patients about the wisdom of screening.

Methods

- We first reasoned that harms are experienced by patients, and thus the perspective of the taxonomy should be patient centered. We defined harm as any negative effect perceived by patients or significant others resulting from screening compared with not screening. We considered only whether it is reasonable to think that at least some patients would experience the harm as a negative effect in their potential benefits, could encourage clinicians to discuss harms with patients, and could help patients and the public better understand the real trade-offs inherently involved with screening. We have been unable to identify a general taxonomy of the harms of screening.

The purpose of this article is to propose a taxonomy to conceptualize and define the harms of screening. We present this proposed taxonomy in the hope that it stimulates a discussion leading to a generally accepted framework.
lives, not whether the harm is well documented, frequent, or serious in medical terms. Harms are “potential” for an individual, since not everyone experiences them. We defined screening as pertaining to the “screening cascade” (Figure).

We developed an initial taxonomy from several sources: systematic reviews of screening, our own reviews of published literature, and informal discussions with both clinicians and patients. We then vetted the initial taxonomy with multiple groups, including both local and national experts (see the eAppendix in the Supplement), making revisions as needed.

Results

Overview

We arrived at a taxonomy of 4 domains: physical harms, psychological harms, financial strain, and opportunity costs, as defined in the Table. Although benefits from screening can only occur when the entire screening cascade is intact, specific harms within the domains occur at different steps throughout the screening cascade (Figure) and are additive in overall magnitude. We illustrate the taxonomy with the example of screening for lung cancer with low-dose computed tomographic scanning (LDCT), using recent systematic reviews and our own systematic searches to indicate harms for which evidence is or is not available.11,12

Physical Harms of LDCT Screening for Lung Cancer

Physical harms occur primarily when we perform a test or procedure or give a treatment to the patient (Figure). For LDCT screening, the first physical harm is exposure to radiation at the screening step. An individual undergoing annual screening from age 55 years to age 79 years could have as many as 25 LDCT scans, with additional full-dose computed tomographic (CT) scans for positive findings or for surveillance after indeterminate screening results. Over time, and for a large population, this radiation exposure may add up to measurable physical harm.13 Although the exact magnitude of this harm is uncertain, reasonable estimates are available.14

A second physical harm from LDCT screening is in the workup for a positive screening test result. In the largest LDCT screening trial (the National Lung Screening Trial [NLST]), 39.1% of people in the LDCT group had at least 1 positive test result (noncalcified nodule at least 4 mm in diameter) over 3 annual screening tests; 96.4% of the positive results were falsely positive.15 Almost all patients with positive test results had follow-up imaging; 4.2% had a surgical procedure and 2.2% had a biopsy. Although the rate of serious medical complications from this workup was low (approximately 1.4%), the harm associated with the workup goes beyond medical complications. The physical discomfort of having the workup is also a harm, regardless of whether there is a complication. It is also of note that almost twice as many NLST participants in the screening arm experienced a serious complication from the workup as had their lives extended by screening.15 The percentage of people having a serious complication from the workup of a positive LDCT result will likely be greater in settings outside of a clinical trial.16 We found no research evidence on the magnitude or “burden” of the physical harm that patients associate with having these workup procedures, with or without complications.

The third category of physical harm from screening is associated with treatment: either earlier treatment of a person with cancer that would have been found later without screening or overtreatment of a person with cancer that would not have been found without screening. As screening and earlier treatment delays death for only 20% of patients destined to die from lung cancer,17 80% of screened people with fatal cancer will die at the same time they would have without screening. Early detection from screening has caused these patients to live longer with the diagnosis, receiving treatment and follow-up for a longer time. They experience harm rather than benefit from screening. For patients with cancer that would not have become clinically important, screening leads to unnecessary treatment harms. Our best evidence shows that approxi-
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Psychological Harms of LDCT Screening for Lung Cancer

Psychological harms of screening may occur at any of the steps of the screening cascade (Figure) but are especially salient at steps when people are given new information, such as receiving results of screening tests or workup. Overall, we found 13 publications from 11 studies, all with varying limitations, that examined some aspect of the psychological harms of the screening cascade for lung cancer. Anticipation of having a screening test is stressful for some patients. Another stressful period is after the screening test before the patient receives the results.

As noted in the previous subsection, 39% of participants in the NLST had at least 1 positive screening test result, with a noncalcified nodule at least 4 mm in diameter. Many of these patients will have a nodule between 4 mm and 8 mm in diameter, an “indeterminate” category; recommendations are for these patients to undergo periodic repeated imaging to ascertain whether the nodule is growing. This system of surveillance puts the patient (and their significant others) in an uncertain state for a prolonged period. We found no research exploring this harm for LDCT screening.

Some patients develop increased anxiety after receiving a positive or indeterminate screening result, although these anxiety levels may decline with time. A larger number of patients experience other psychological harms, such as condition-specific distress, as thoughts of having lung cancer lead to sleepless nights, intrusive thoughts, and worries about the future. We found only 3 studies that assessed condition-specific distress.

Overlying the psychological harms is the context of the screening situation. In the case of LDCT screening for lung cancer, eligible people, according to the draft US Preventive Services Task Force recommendations, have at least 30 pack-years of smoking history. To the extent that these people see themselves as having a socially unacceptable personal behavior that may have caused lung cancer, they may experience feelings of guilt, shame, and anxiety in anticipation of possibly being diagnosed with lung cancer. We found no studies that examined this issue for LDCT screening.

Another psychological harm from screening is the effect on individuals of receiving a diagnosis of lung cancer. Although we found little research documenting this effect, it is likely that “labeling” the individual in this way plays a major role in how the individual thinks of himself or herself in the future. Labeling is due to screening in the 2 aforementioned situations: earlier detection of fatal cancers for which treatment is ineffective, and overdiagnosis of cancers that would not have caused the patient important health problems. In both situations, screening has caused psychological harm by labeling patients with a potentially fatal diagnosis. Although one can estimate the frequency of these situations, we found no studies of the psychological “burden” of labeling as experienced by patients.

Still another group of patients with an abnormal screening test result who may feel the psychological effects of a workup are those with “incidental” findings on screening CT, findings not indicative of lung cancer but that may indicate some other medical condition. In the NLST trial, more than 10% of all people screened had incidental findings on the first LDCT screen, and approximately 6% had an incidental finding on both screening rounds 2 and 3. Still more people undergoing a workup for lung cancer may have an incidental finding from more intense imaging. Patients with incidental findings often go through a different type of workup, including sometimes invasive procedures, that for lung cancer (Figure). Although some have tried to make the case that these incidental findings could be beneficial, it is much more likely that their overall effect is negative. The burden of proof for any benefit for these incidental findings lies with those proposing the benefit. We found no studies examining the psychological (or physical) effects of workup of incidental findings and discovery of incidental disease.

Finally, there are psychological harms of nonbeneficial treatment due to screening. As noted previously, this occurs with ineffective earlier treatment, with overtreatment in overdiagnosed patients, and in patients undergoing ineffective treatment for an incidental condition found by screening or workup. These treatments may include major surgery, radiation, and chemotherapy, all associated with known psychological harms. The fact that these patients do not know that the harm they are experiencing is unnecessary does not reduce the magnitude of their suffering.

Financial Strain of LDCT Screening for Lung Cancer

Financial strain from screening comes not only from actual financial charges for the screening test, but also from concern about the anticipated financial cost of being diagnosed with and treated for lung cancer. Financial strain may start with the screening test itself and then increase with a positive result and anticipation of the cost of the workup. The patient often does not know ahead of time exactly what the cost will be and may expect the worst-case scenario. If the workup finds lung cancer, financial strain may encompass future lost wages and the effects on one’s family. Previous financial plans may be thrown into disarray. We found no studies examining this type of harm.
Opportunity Costs of LDCT Screening for Lung Cancer

People undergoing LDCT screening and workup may experience harm through missed opportunities. Some of these missed opportunities have to do with health, including distraction from other important healthy activities or visits to clinicians for important health problems. Other missed opportunities may include time with friends and family. Finally, there is the missed opportunity of continuing progress at work and on one’s own projects. We found no research evidence about this type of harm.

Discussion

The taxonomy encourages a systematic approach to thinking about harms, an approach that is needed to move research, discussion, and decision making about screening from an overemphasis on benefits alone to a focus on balancing benefits and harms.

Discussion

There are limitations to our approach. One criticism we have encountered is that our taxonomy overstates the importance of psychological harms. It is not our intention, however, to prioritize one type of harm over another. The effect of a particular harm on a screened population depends on the frequency of the harm as well as its burden for the individuals affected. By making sure that psychological effects are considered along with physical effects, we assert that both domains of harms are worthy of being considered in screening decisions.

Some have questioned our inclusion of financial strain under the rubric of “harm.” For real people, however, the strain of anticipated financial problems can be important in weighing the decision whether to be screened. We believe it is easier to conceptualize financial strain alongside of but separate from other harms. We also distinguish “opportunity costs” from financial strain. By opportunity costs we do not mean financial costs but rather the loss of alternative activities that could have benefited the patient in multiple ways. Part of opportunity costs comes from the time required to participate in the screening cascade. Another part comes from the distraction of screening from other activities, both in terms of health and enjoyment of life.

Some clinicians have commented to us that harms are just the price we pay for the benefits of screening. It may be, however, that we were to fully appreciate the frequency and burden of harms, our enthusiasm for screening would decline. The taxonomy is designed to unveil the true extent of the problem of harms.

Finally, there are still further harms to be considered. For instance, another harm from screening is the strain on the medical care system. Organizing systematic screening requires careful planning and effort, including changing staff roles, increasing patient education, taking clinicians’ time, working out referral patterns and follow-up, considering outreach, and changing documentation. Inevitably, such effort directed to screening means less effort directed toward other health issues. We have not captured this type of harm in our taxonomy.

Conclusions

Our purpose in developing a taxonomy of the potential harms of screening is to help investigators, policy makers, clinicians, and the public think more clearly and systematically about harms and to consider harms equally with benefits in decisions about screening. We do not assert that harms always outweigh benefits, only that it is always necessary to weigh the two. We consider this a draft taxonomy, a work in progress that could contribute to our current public discussion about screening. In the end, we hope that a widely agreed-on taxonomy will eventually lead to more balanced decision making about the wisdom of screening.
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REFERENCES