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Smarter Screening For Cancer: The Possibilities And Challenges Of Personalization

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Why Personalize Screening?

An important emerging model for screening and many preventive strategies is *personalization*. This approach uses individual patient characteristics to project the benefit of screening for a given patient and has the potential to improve cancer outcomes while reducing the probability of harm and preserving scarce healthcare resources. Yet, all too often, the existing healthcare system fails to personalize screening in even the most rudimentary way. A recent study found that 75 year-olds with severe comorbidities were nearly two times more likely to be screened for colorectal cancer than 76 year-olds with no comorbidities, even though healthy 76 year-olds tend to live longer and gain greater benefit from screening.¹ In another study, 48% of primary care physicians reported that they would recommend breast cancer screening for women diagnosed with terminal lung cancer, a group in whom screening cannot provide any benefit, may cause harm, and is undoubtedly a waste of resources.² While most clinicians would agree that cancer screening should target patients most likely to benefit, these and other studies clearly demonstrate that the U.S. healthcare system is failing to achieve this goal of personalized care.

If most clinicians agree that cancer screening should be personalized, why is such an approach not implemented in practice? Numerous studies have demonstrated how the benefits of preventive services such as cancer screening change over the lifespan. Others have shown how the benefits vary by other factors, such as screening history and comorbidity status. Yet, these data alone are clearly not enough. Indeed, a more systematic approach to synthesizing these data for clinical use and developing systems of care that support their implementation is needed. In this Viewpoint, we provide an overview of how personalized recommendations for cancer screening can be developed and discuss challenges to implementation that must be overcome if clinicians are to provide the best possible care for their patients.

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How To Achieve Personalized Screening Recommendations

The benefit of a given screening test for a given patient is a function of two key variables: cancer risk and life expectancy. However, evidence suggests that unaided clinical judgment is not reliable when it comes to estimating these variables and integrating them into an appropriate screening recommendation for an individual patient. Fortunately, clinicians have at their disposal multiple prediction tools for both of these variables.^{3,4} Yet, despite their availability and potential usefulness, these tools are rarely used. One reason they are not used more frequently is that these tools do not provide clinically meaningful information needed for personalization. For instance, if prediction tools indicate that an individual has a four-fold increased risk of developing lung cancer within the next 5 years and a life expectancy of 8 years, how should this information be used to arrive at a screening decision? For risk models to be useful in practice, a way is needed to translate simple risk estimates into clinically meaningful estimates of benefit, which can then be used to guide individual clinical decisions.

Clinical trials, which are commonly used to study screening tests, are not aimed at individual decision-making, instead establishing overall causality and average efficacy. Thus, alternative methods are needed to personalize estimates of screening benefit. One alternative approach involves disease simulation modeling.^{5,6} Simulation models have the ability to simultaneously incorporate cancer risk, life expectancy, and screening efficacy, and, while less familiar to many clinicians than clinical trials, have been used to inform U.S. Preventive Services Task Force (USPSTF) screening recommendations. Even though validated simulation models are available for a variety of screen-detectable cancers,⁵ the capability of these models to provide personalized recommendations for screening has not yet been fully exploited.

Colorectal Cancer Screening: An Example Of How Simulation Models Can Be Used

As an example, we used MISCAN-Colon, a widely cited simulation model of colorectal cancer screening, to illustrate how the benefit of screening (cancer deaths prevented per 1,000 individuals screened) can vary according to characteristics such as age, sex/race, screening history, comorbidity status, and exposure to risk factors for colorectal cancer (“background risk”) (Figure 1). The left-most column in the figure (labeled “reference cohort”) shows the benefit of screening colonoscopy for an average-risk 75 year-old white female with no comorbid medical conditions who underwent a negative screening colonoscopy 10 years prior (3.7 cancer deaths prevented per 1,000 individuals screened). Subsequent columns then illustrate how screening benefit varies as each of these factors (age, sex/race, screening history, comorbidity status, and background risk for cancer) is modified one-at-a-time. For example, all other factors being equal, a recently screened, average-risk 75 year-old white female with *no* comorbidities is nearly twice as likely to benefit from screening as one who has *severe* comorbidities (3.7 versus 2.2 cancer deaths prevented per 1,000 individuals screened). Yet, health status is not explicitly incorporated into current guidelines for colorectal cancer screening. Moreover, patients at low risk for colorectal cancer (either because of a prior negative screening colonoscopy or a low

background risk for colorectal cancer) are substantially less likely to benefit from screening, but guidelines do not distinguish between individuals based on these factors.

These simple examples do not take into account interactions between cancer risk and life expectancy, but models can quantitatively weigh such complexities. For instance, smoking and obesity are both risk factors for colorectal cancer, but they are also risk factors for early mortality. When weighed together, the model would suggest (somewhat counter-intuitively) that an obese smoker should not be screened for colorectal cancer more aggressively than a non-obese non-smoker.

The Challenges of Implementation

Even with personalized screening recommendations available, this approach is unlikely to be accepted unless the context in which it will be implemented is considered. Patients and physicians may be unreceptive to personalized screening. For instance, personalized screening approaches would recommend against screening in low-benefit individuals. But prior work has demonstrated that many individuals are reluctant to stop screening even if the expected benefit is low.⁷ On the other hand, little is known about how much benefit is necessary for patients to adopt a preventive intervention. For some patients, the necessary degree of benefit is likely to be substantially greater than physicians presume, such that these patients might elect less aggressive approaches than are currently supposed. Moreover, physicians might find personalization time consuming and cumbersome or might simply disagree with personalized recommendations, ultimately failing to incorporate them into their practice. In addition, systems of care may have existing approaches to screening that directly conflict with personalized recommendations. For example, current quality measures for colorectal cancer screening encourage screening individuals up to age 75.¹ A physician who appropriately discourages screening in a 74 year-old with limited life expectancy could be penalized under such age-based quality measures. As a result, physicians in such systems of care may be less likely to embrace a personalized approach.

Efforts at multiple levels are needed to overcome these challenges. At the patient level, personalized information about the benefits and harms of screening need to be incorporated into educational materials. We also need a better understanding of how to communicate such information so that it can be used to aid decision-making. Similarly, physicians need easily accessible, personalized estimates of benefit (ideally embedded into electronic health record systems) to inform patient-physician discussions. Finally, healthcare systems need to be willing to recommend, implement, and support personalized approaches to screening, and establish clinically sensitive, personalized measures of quality. For instance, colorectal cancer screening quality measures, which are currently based primarily on age, could be modified to use both age and health status. Better yet, these measures could consider whether an active discussion about the benefits and harms of screening took place, with an informed decision used as the marker of quality.

Conclusion

Current decisions about cancer screening are often based primarily on age. As a result, some patients who are likely to benefit from screening are not being screened, and others who are not likely to benefit are being screened unnecessarily. Simulation models, integrated with point-of-care decision aids and decision support tools, could help bridge the gap between prediction models and clinical decision-making. Implementing personalized screening recommendations in clinical practice presents many challenges. However, these challenges must be met to provide optimal cancer screening for patients.

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FIGURE 1. Relationship of age, sex and race, screening history, comorbidity status, and background risk for cancer with the lifetime benefit of screening: the example of colorectal cancer screening with colonoscopy

LEGEND:

The “reference cohort” consists of 75 year-old white females with no comorbidities, average colorectal cancer risk, and a negative screening colonoscopy 10 years prior; CRC = colorectal cancer; NSC = negative screening colonoscopy; CM = comorbidity; RR CRC = relative risk of colorectal cancer.

¹Individuals are classified as having moderate comorbidity if diagnosed with an ulcer, rheumatologic disease, peripheral vascular disease, diabetes, paralysis, or cerebrovascular disease and in case of a history of acute myocardial infarction; as having severe comorbidity if diagnosed with chronic obstructive pulmonary disease, congestive heart failure, moderate or severe liver disease, chronic renal failure, dementia, cirrhosis and chronic hepatitis, or AIDS; and as having no comorbidity if none of these conditions is present.

²The range of the background risk for CRC is based on the National Cancer Institute's Colorectal Cancer Risk Assessment Tool. This tool incorporates the following risk factors: the number of relatives with CRC, current leisure time activity, aspirin/ NSAID use, vegetable intake, body mass index, current and past smoking (males only), and estrogen status within the last two years (females only). In white females, the minimum background risk for CRC is 0.5, the maximum background risk in the absence of a family history of CRC is 1.8, and the maximum risk in the presence of a family history of CRC is 3.5.