Cell-free DNA Approaches for Cancer Early Detection and Interception

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SUPPLEMENTARY MATERIALS

Supplementary Table S1. Summary of cancer screening tests recommended by the United States Preventive Services Task Force (USPSTF)

Cancer	USPSTF Grade*	Target Population	Platform	Test
Breast†	B	Women ages 50-74 years	Mammography	Imaging
Cervix†	A	Women ages 21-65 years	Pap smear	Cytology
Colorectal	A	Adults ages 50-75 years	Colonoscopy; fecal immunochemical test	Imaging; stool analysis
	B	Adults ages 45-49 years		
Lung	B	Adults ages 50-80 years with 20 pack-year smoking history and quit <15 years ago	Low-dose computed tomography	Imaging
Prostate	C	Men ages 55-69 years	Prostate-specific antigen test	Plasma protein

*Grade A = The USPSTF recommends the service. There is high certainty that the net benefit is substantial. Grade B = The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial. Grade C = The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.

†As of 01 June 2022, the USPSTF recommendations for this cancer screening are in the process of being updated.

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Supplementary Table S2. Principles of screening at two different points in time with a focus on the disease or condition and the test

Principle Area	Wilson and Jungner (1968)[1]	Dobrow (2018)[29]
Disease or Condition	• The condition sought should be an important health problem. • There should be an accepted treatment for patients with recognized disease. • Facilities for diagnosis and treatment should be available. • There should be a recognizable latent or early symptomatic stage. • The natural history of the condition, including development from latent to declared disease, should be adequately understood.	• The epidemiology of the disease or condition should be adequately understood, and the disease or condition should be an important health problem. • The natural history of the disease or condition should be adequately understood, the disease or condition is well-defined, and there should be a detectable preclinical phase. • The target population for screening should be clearly defined, identifiable, and able to be reached.
Screening Test	• There should be a suitable test or examination. • The test should be acceptable to the population.	• Screening test performance should be appropriate for the purpose, with all key components specific to the test being accurate, and reliable or reproducible. • The test should be acceptable to the target population and it should be possible to perform or administer it safely, affordably, and efficiently. • Screening test results should be clearly interpretable and determinate to allow identification of the screening participants who should (and should not) be offered diagnostic testing and other post-screening care. • There should be an agreed-on course of action for screening participants with positive screening test results that involves diagnostic testing, treatment or intervention, and follow-up care that will modify the natural history and clinical pathway for the disease or condition; that is available, accessible, and acceptable to those affected; and that results in improved outcomes. • The burden of testing on all participants should be understood and acceptable, and the effect of false-positive and false-negative tests should be minimal.

Supplementary Table S3. Principles of screening over time, with a focus on the screening program

Principle Area	Wilson and Jungner (1968)[1]	Dobrow (2018)[29]
Screening Program	• There should be an agreed policy on whom to treat as patients. • The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole. • Case-finding should be a continuing process and not a "once and for all" project.	• There should be adequate existing infrastructure, or a clear plan to develop adequate infrastructure, that is appropriate to the setting to allow for timely access to all components of the screening program. • All components of the screening program should be coordinated and, where possible, integrated with the broader health care system to optimize care continuity and ensure no screening participant is neglected. • All components of the screening program should be clinically, socially, and ethically acceptable to screening participants, health professionals and society, and there should be effective methods for providing screening participants with informed choice, promoting their autonomy and protecting their rights. • The expected range and magnitude of benefits and harms for screening participants and society should be clearly defined and acceptable, and supported by existing high-quality scientific evidence that indicates that the overall benefit of the screening program outweighs its potential harms. • An economic evaluation of the screening program, using a health system or societal perspective, should be conducted to assess the full costs and effects of implementing, operating and sustaining the screening program while clearly considering the opportunity costs and effect of allocating resources to other potential non-screening alternatives for managing the disease or condition. • The screening program should have clear goals or objectives that are explicitly linked to program planning, monitoring, evaluating and reporting activities, with dedicated information systems and funding, to ensure ongoing quality control and achievement of performance targets.

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