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National Cancer Policy Forum
October 28, 2024

Multicancer Detection Tests
A Primary Care Perspective

Disclosures

- NIH funding for lung cancer screening projects: 1 RO1HL158850-01A1; 1 R01 CA267820-01A1; 1r44 CA285136-01
- Member, ACS Guideline Development Group
- The views expressed in this presentation are mine alone and do not reflect any organizations with which I am affiliated

My medical career

- Academic General Internist (1992-2023)
  - Worked at 3 University Medical Centers, 2 VA Medical Centers
    - Involved in supporting clinical screening programs
  - Emeritus Professor of Medicine, University of Iowa
    - Former Director, Division of General Internal Medicine
    - Former Co-leader, Cancer Epidemiology and Population Science Program, Holden Comprehensive Cancer Center
  - Currently involved in cancer screening health services research and guideline development

Primary care perspectives

- Experiences with cancer screening
  - Single-cancer testing of asymptomatic persons
    - Breast, cervical, colorectal, prostate, lung
  - Evidence-based guideline support, particularly from USPSTF
    - Insurance coverage
    - Performance measures (breast, colorectal)
  - FDA approval

Primary care perspectives

- Evidence on the benefits of screening
  - Screening reduces cancer mortality and morbidity
  - Cervical and colorectal screening can prevent cancer
- Evidence on potential harms of screening
  - False positives, complications from diagnostic testing and treatment, overdiagnosis, overtreatment, and incidental findings

Primary care perspectives

- We have clear pathways for following up on abnormal tests
  - Referrals to specialists for gold-standard diagnostic testing

Primary care perspectives

- Limitations of current screening programs
  - Most cancers have no screening test, including highly lethal ones such as pancreas, ovary
  - Screening uptake is variable;[1] adherence can be poor;[2] even among screenable cancers, a low proportion are detected by screening[3]
  - Inappropriate screening of persons with limited life expectancy or poor health status[4]

[1]ACS Cancer Prevention & Early Detection Facts and Figures 2023-2024.[2]Shete S. JAMA Netw Open 2021. [3]NORC at the University of Chicago. https://cancerdetection.norc.org/
[4]Royce TJ. JAMA Int Med 2014;174:1558

Primary care perspectives

- Limitations of current screening programs
  - Disparities in screening uptake, diagnostic evaluations, and receipt of treatment[1]
    - Race/ethnicity, socioeconomic status, geography…
  - Even in randomized trials, most cancer deaths cannot be prevented by screening[2-5]

[1]Islami F. CA Cancer J Clin 2022;72:112. [2]Jonas DE. JAMA 2021;325:971
[3]Hugosson J. Eur Urol 2019;76:43 [4]Nelson HD. Ann Intern Med 2016;164:244
[5]Holme O. Cochrane Database System Rev 2013:CD009259

Multicancer detection tests

- A potential paradigm shift for screening
  - Concurrently screen for multiple cancers, majority of which have no screening test
  - Single blood test is convenient to perform, may increase adherence

The Multicancer Early Detection Consortium Care Delivery Workgroup. https://static1.squarespace.com/static/615c87aaea640d19cc9884ob/t/6499fcaddf755715cc844f39/1687813293969/MCED+Consortium+Care+Delivery+Paper_Final.pdf.

Multicancer detection tests

- A potential paradigm shift for screening
  - Decreasing overall incidence of advanced-stage cancers could reduce the aggregate burden of cancer mortality (population perspective)[1]
  - Not able to detect pre-cancers (primary prevention)[2]
  - Relatively poorer sensitivity for early-stage cancer (less aggressive treatment, more curable)[3]

[1,] Neal RD. Cancers (Basel) 2022;14:DOI. 10.3390/cancers14194818.
[2]Rubenstein WS. CA Cancer J Clin 2024;1-15 [3]Klein EA. Ann Oncol 2021;32:1167

Multicancer detection tests

- Uncertainties
  - No randomized trial data that MCD screening reduces cancer mortality or morbidity
    - Vanguard primary endpoint will be cancer mortality;[1] NHS-Galleri primary endpoint is decreased incidence of late-stage cancer[2]--may not reliably predict mortality[3]
  - Optimal diagnostic pathways following a positive MCD test

[1] Rubinstein WS. CA Cancer J Clin 22 March 2024: DOI.10.3322/caac.21833. [2]Neal RD. Cancers (Basel) 2022;14:DOI. 10.3390/cancers14194818. [3]Feng X. JAMA 2024;331:1910.

Multicancer detection tests

- Uncertainties
  - Negative work-up: FP vs. diagnostic testing incomplete or lacked sensitivity?
  - Finding cancers that cannot be effectively treated
  - Availability of high-quality diagnostic and treatment centers, particularly for rarer cancers
  - Advising a cancer patient's family members about assessing and managing their risk for cancer

Providing guidance about MCD testing

- Clinicians
- Patients
- Healthcare systems

Guidance for clinicians

- In addition to the uncertainties surrounding MCD testing, clinicians should be aware that…
  - MCD testing is not covered by insurance
  - The FDA has not approved any MCD tests
  - No guidelines currently recommend MCD testing

Guerra C. Annu Rev Med 2023;75:67. Rubin R. JAMA 2024;331:1077

Guidance for clinicians

- Clinicians considering MCD testing should recognize the importance of…
  - Assessing life expectancy, ability and willingness to undergo invasive diagnostic procedures and treatment[1]
  - Continuing to offer recommended screening tests[2]
  - Emphasizing healthy behaviors[2]

[1]Kotwal AA. Med Clin N Am 2020;104:989
[2]ACS Cancer Prevention & Early Detection Facts and Figures 2023-2024

Guidance for patients

- Educate patients about…
  - Potential benefits and harms of MCD testing
  - Potential downstream outcomes, including the need for invasive diagnostic tests and treatments
  - The need to continue with recommended screenings, healthy behaviors
  - Lack of insurance coverage, out-of-pocket costs

Guidance for patients

- Engage in shared decision making
  - Collaborative process that allows patients and their providers to make health care decisions together, taking into account the best scientific evidence available, as well as the patient's values and preferences[1]
- Provide decision aids (when they become available) which help ensure that patients received balanced information on benefits and harms[2]

[1]Barry MJ. N Engl J Med 2012;366:780.

[2]Stacy D. Cochrane Database Syst Rev 2024. Jan 29;1:CD001431

Guidance for healthcare systems

- Information technology support for tracking results and follow-up
- Multispecialty support for efficient and high-quality diagnostic evaluations and prompt access to treatment

Guidance for healthcare systems

- Patient navigation for persons at risk of not completing diagnostic testing or undergoing treatment due to barriers related to structural or social determinants of health

Conclusions

- My (evidence-based) perspective: MCD tests are not ready for prime time
- My (pragmatic) perspective: deal with it
  - Tests are available[1]
  - Patients report being interested[2]

[1]Guerra C. Annu Rev Med 2023;75:67. [2]Myers RE. J Pers Med 2023;doi.org/10.3390/jpm13111613

Conclusions

- Educate clinicians
- Educate patients
  - Mandate shared decision making
  - Develop effective decision support tools
    - Follow plain language guidance[1]
    - For use at home and in clinical settings[2]
    - Available in multiple languages[3]

[1]Muscat DM. Med Decis Making 2021;41:848 [2]Joseph-Williams N. Med Decis Making 2021;41:907
[3]Chenel V. Patient Pref Adherence 2018:12:321

Conclusions

- Ensure access to appropriate diagnostic testing for those with positive MCD results
- Ensure access to appropriate treatment for those who are found to have cancer
- Obtain data on practice patterns, outcomes, and economic impact from clinical trials, observational studies, and mandated population-based registries

Thank you