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Exact Sciences Comments to the Molecular and Clinical Genetics Panel of the Medical Devices Advisory Committee

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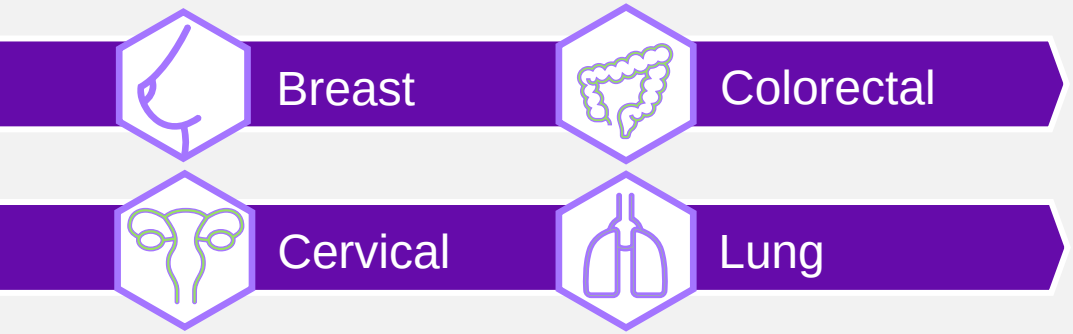
Guideline-recommended screening is available for only a handful of mostly common cancers

Routine screening exists for **only 4** cancer types[2]



2/3rds

of **incident cancers** and **cancer deaths***

are from cancers **without** endorsed **standard-of-care screening**[3]

U.S. data

*Calculated using estimated new diagnoses and deaths from cancers that have standard of care screening: breast, cervical, colorectal and lung (high risk) against all sites

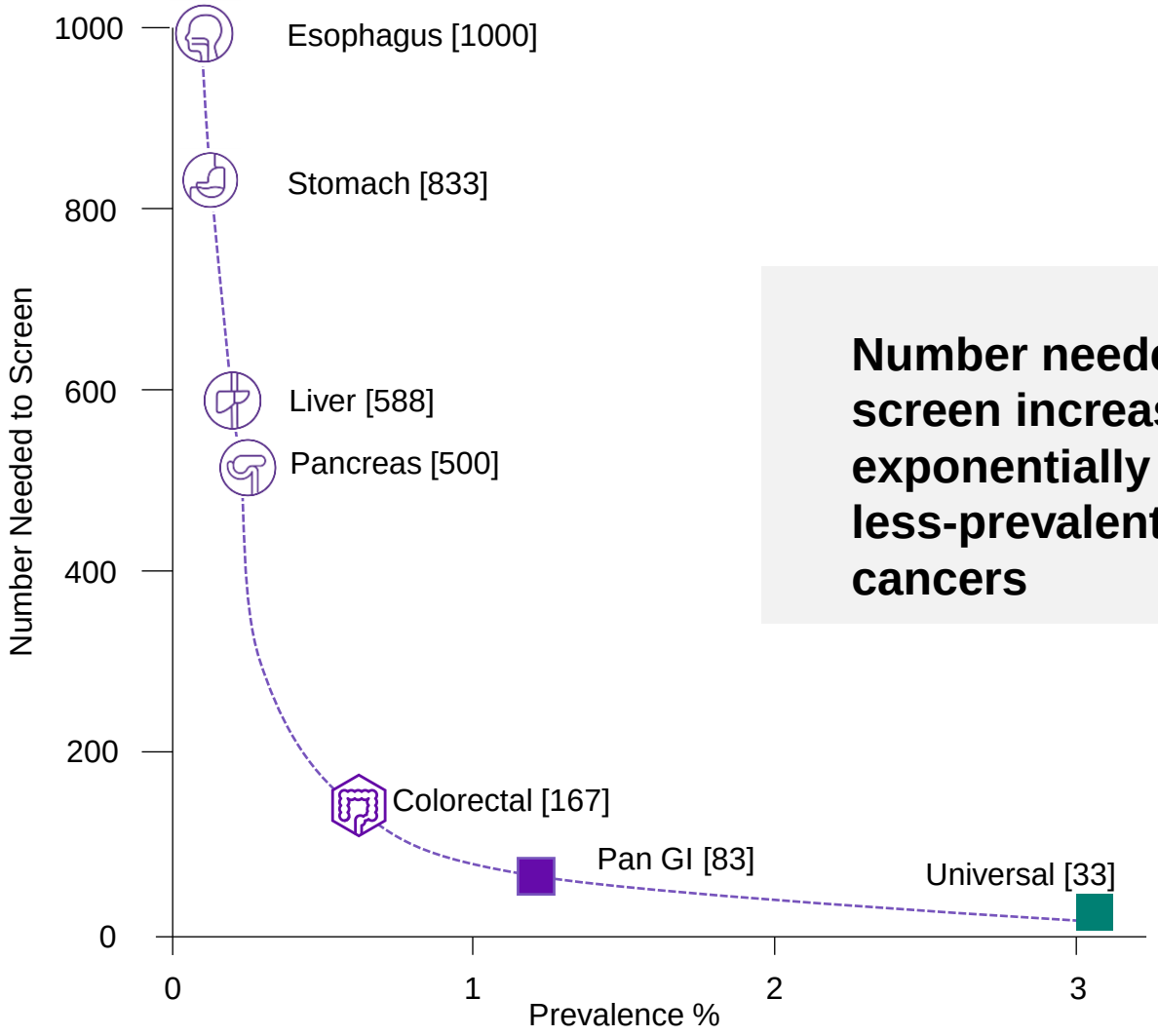
References: 1. Compliance from BRFSS Prevalence & Trends Data. 2015. Accessed April 5, 2023. https://www.cdc.gov/brfss/brfssprevalence/ except LDCT from Zahnd, et al. Am J Prev Med 2019;57(2):250−255. 2. USPSTF. A & B Recommendations. Accessed November 17, 2022. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation-topics/uspstf-a-and-b-recommendations 3. Siegel RL, Miller KD, Wagel NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin*. 2023;73:17-48.

Low prevalence of individual cancers challenges cancer early detection

Screening for less-common cancers <u>individually</u> in average risk people would require:

- Test performance that would be **difficult to achieve**
- **Infeasible** prospective clinical trials
- **Impractical** clinical implementation

Example of the impact of aggregate prevalence on screening efficiency—GI cancers



Number needed to screen increases exponentially with less-prevalent cancers

References: Adapted from Ahlquist, DA. *npj Precis Oncol*. 2018;2:23

A new approach that embraces the concept of multi-cancer testing is needed

Measuring performance across aggregate cancer types, rather than cancer by cancer

Anatomic classification of cancer stems from an era when surgery was the sole treatment option

People cannot predict the cancers for which they may be at risk
- People seek to reduce their personal risk from all cancer
- They are only able to address a portion of their risk through available screening methods

Multi-cancer tests:
- Detect a broad range of cancers by measuring shared cancer signals
- Sum up the prevalence of many cancers
- Include rare cancers, that would have little hope for single cancer screening tests

Evaluating performance in aggregate:
- Aligns with test design and intended use
- Is responsive to the public need for tests that holistically address cancer risk with the patient at the center

Evaluating performance cancer by cancer is not patient-centric and would lead to continued exclusion of uncommon cancers

A least-burdensome regulatory approach is needed to enable the opportunity for substantial public health impact

- Efficacy determined by aggregate cancer detection performance in a prospective randomized trial that reflects the diversity of the US population
  - Comparisons to standard-of-care single cancer screening tests do not reflect intended use
- Safety determined by direct consequences of the test, complications of the diagnostic work-up, and consequences of false positive results
- Clinical utility assessment will largely follow regulatory approval and will require innovative paths to evidence development and may include:
  - Diagnostic yield of clinically significant cancers, including cancers without screening options
  - Clinical outcomes in screen-detected cancers
  - Cancer burden by stage in tested vs. control populations
  - Robust modeling of expected long-term health impacts
- *Innovation in cancer treatment sparked by advances in detection has the potential to deliver greater impacts in the long run—Clinical utility is not static and will evolve*
- *A requirement for cancer-specific mortality measurement would largely halt innovation due to prohibitive time requirements*

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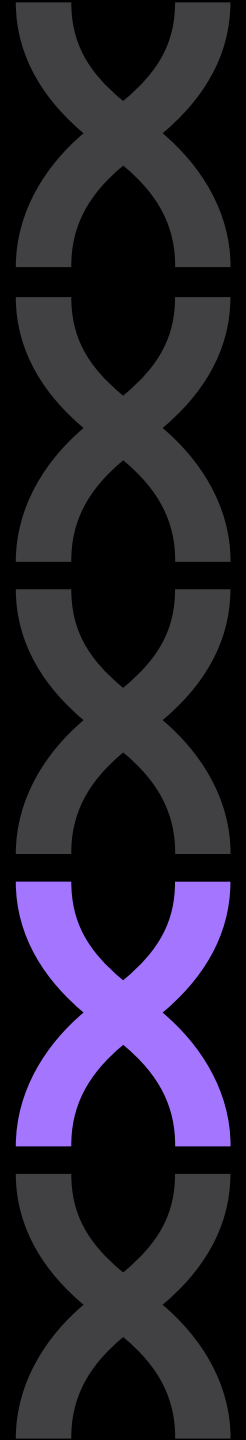
Thank you



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