https://www.medicalnewstoday.com/articles/blood-test-can-detect-50-different-types-of-cancer

Health Economics of Multi-Cancer Blood Testing

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Introduction

- **I have no relevant financial relationships within the last 24 months**

- Draws on Lipscomb J, Horton S, Kuo A, Tomasetti C. Evaluating the Impact of a Multi-Cancer Early Detection Test on Health and Economic Outcomes: Toward a Decision Modeling Strategy. Draft, 2021: submitted *Cancer.*
- Presentation outline:
  - A short primer on health economics, and the cost-effectiveness of existing cancer screening in the US
  - Potential cost-effectiveness of a Multi-Cancer Blood Test (MCBT)
  - Policy implications – early thoughts

Short primer on health economics

- Cost-effectiveness is widely used in health, to help set priorities
- Depends heavily on the effectiveness of a health intervention
- Most commonly measured by QALYs (quality-adjusted life-years) saved
- Measures additional years of life gained (LYG) by an intervention, adjusted by perceived quality; quality ranges from 0 (worst) to 1 (best)

What is good value for money in health?

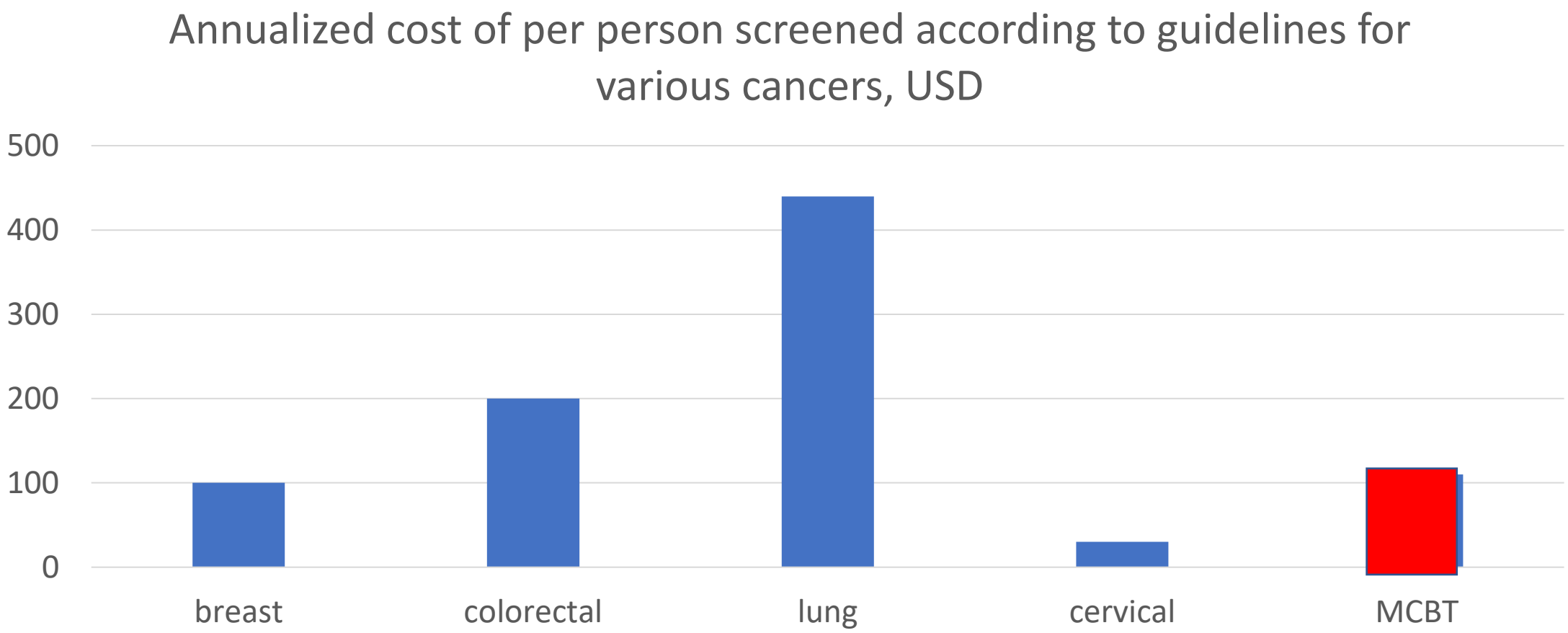
- The lower the cost per QALY for an intervention compared to an alternative e.g. “no intervention”, the more cost-effective it is
- Many countries use a “threshold” – interventions costing more than this threshold are unlikely to be funded
- For the United States, $50,000 is often used as a threshold (per capita Gross Domestic Product, GDP currently is around $64,000)
- The World Health Organization previously suggested that interventions costing less than 1 X per capita GDP were “very cost-effective” – subsequently criticized, but this remains a decent rule of thumb across countries

Current US cancer screening programs

- Breast cancer: mammogram every year age 50-54; every two years 55-69 (CDC)
- Colon cancer: Test ages 50-75; various methods: colonoscopy every 10 years; fecal DNA every 1-3 years (CDC)
- Lung cancer: Test ages 50+ with annual low-dose CT with 20 pack-year smoking history (USPSTF)
- Cervical cancer: Test ages 25-65 every 5 years with primary HPV test, or every 3 years with Pap, or co-test every 5 years (ACS)

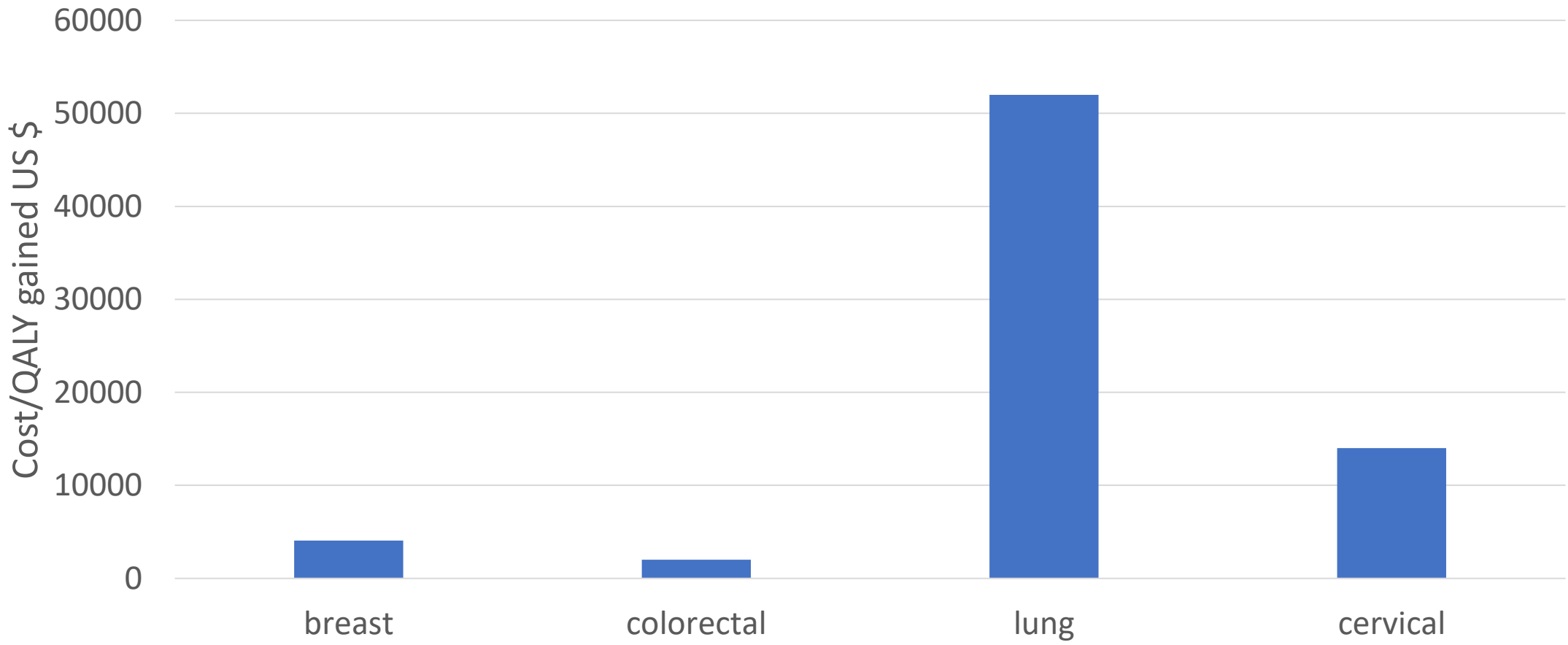
https://www.cedars-sinai.org/programs/imaging-center/exams/ct-scans/lung.html

Estimated annualized cost per person screened of MCBT versus existing cancer screening programs



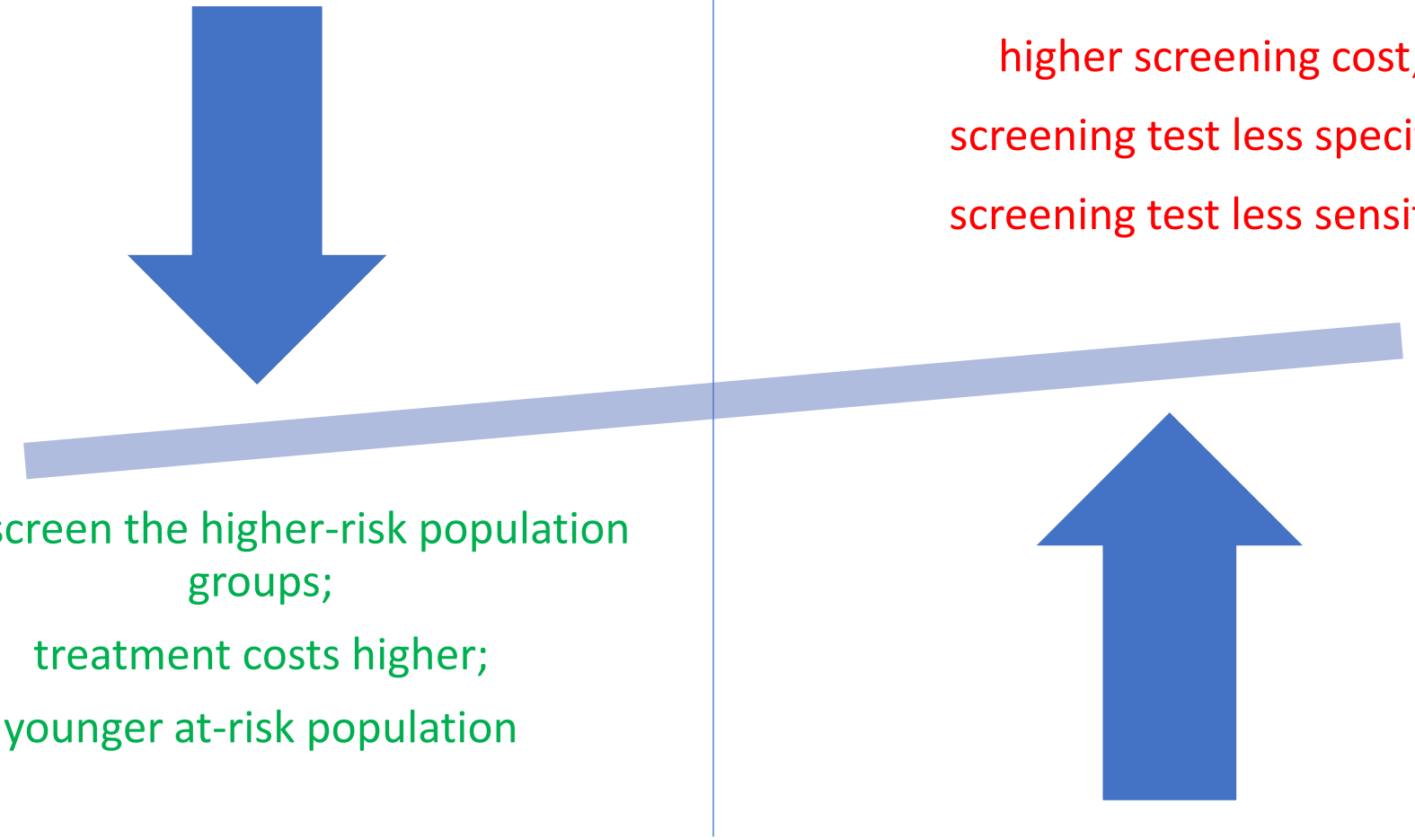
See notes to slide 7. **Cost for MCBT is very preliminary estimate only.**

Cost-effectiveness estimates, existing screening programs, USD (orders of magnitude 2000-2010 $)



Breast: de Koning et al *Int J Cancer* 1991; Colon: Lansdorp-Vogelaar et al *Epidemiol Rev* 2011; Lung: Goffin et al *JAMA Oncology* 2015 for Canada, using $1 CDN = $1 USD in 2008; Cervical: Wright et al *Am J Managed Care* 2016

Factors causing cost per QALY to increase↑ or decrease ↓(become less or more cost-effective)

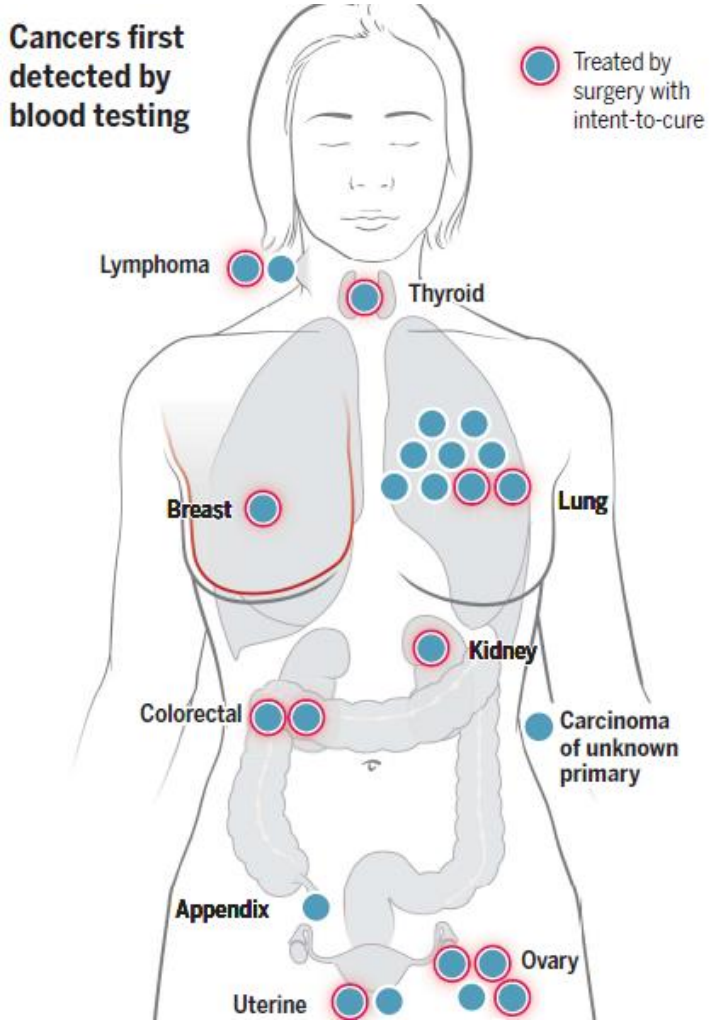


Common cancers in US ranked by incidence and by deaths, and priority for new screening

Incidence	Death	Priority for new screening test?
Breast (11.1%)	Lung (22.6%)	Pancreas
Lung (10.0%)	Pancreas (7.8%)	Liver
Prostate (9.2%)	Breast (7.0%)	Lung
Colon (4.5%)	Colon (6.2%)	Upper GI
Melanoma (4.2%)	Prostate (5.3%)	Ovary
Bladder (3.5%)	Liver (5.1%)	
Non-Hodgkin lymphoma (3.2%)	Upper GI (Oesophagus + stomach) (4.5%)	
Kidney (3.0%)	Leukemia (3.9%)	
Corpus uteri (2.7%)	Non-Hodgkin lymphoma (3.4%)	
Leukemia (2.7%)	Brain, CNS (3.0%)	

Source: Column 1 & 2: Globocan2020 USA Fact Sheet; Column 3 author, ranking (% share deaths/% share new cases >2

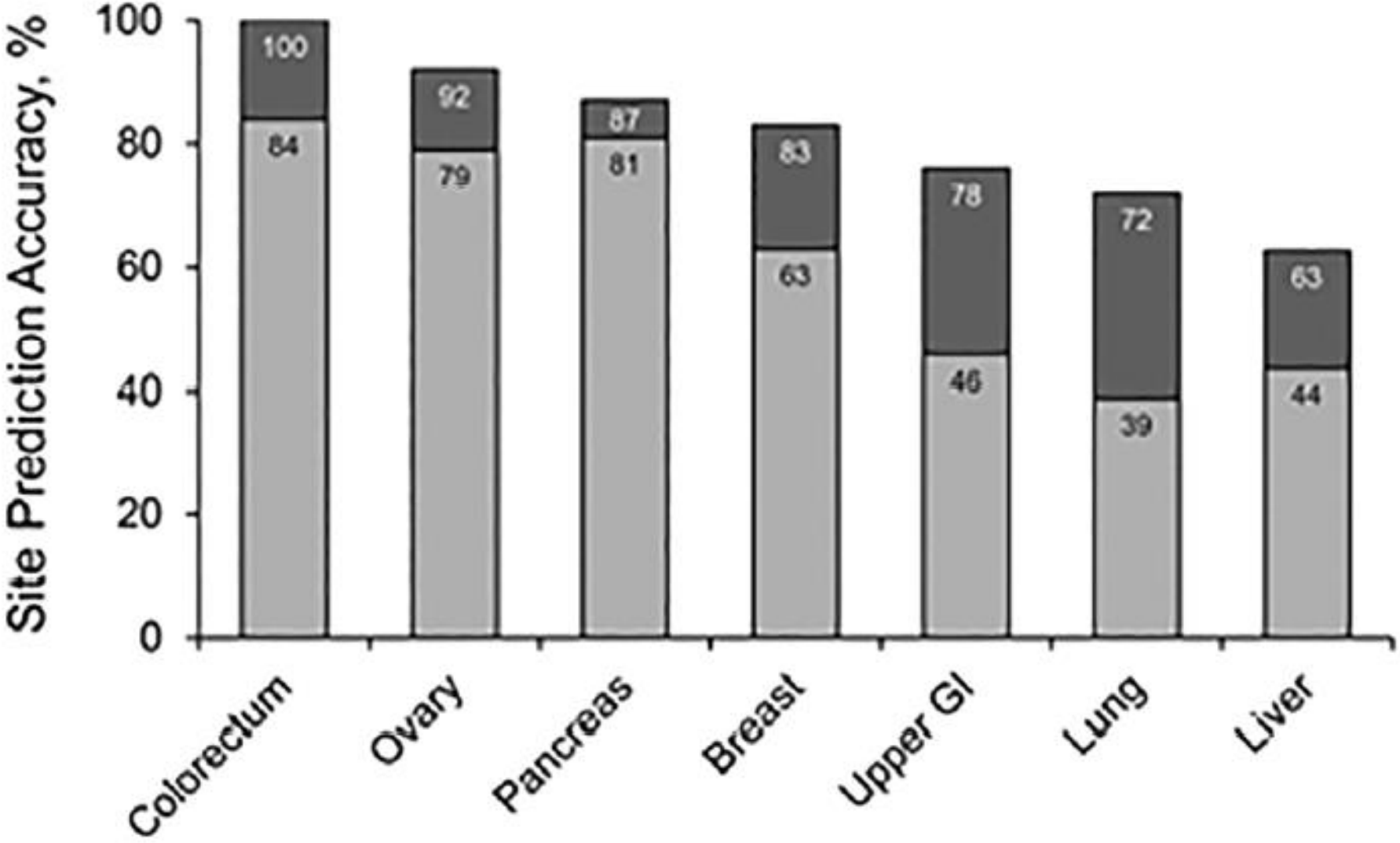
How sensitive is the MCBT?



DETECT-A Trial (AM Lennon et al, Science 349 eabb9601, 2020) concluded that MCBT, in 10,006 women recruited to be followed for 12 months resulted in:

- 26 cases of cancer detected from sequence of 2 blood tests plus follow-up imaging
- Another 24 detected by standard of care screening, and 46 via symptoms
- 17 of 26 were localized/regional disease
- 12 received surgery with curative intent
- 3 false positives that involved minimally invasive follow-up (surgery, bronchoscopy)
- Sensitivity 27-30% (depends on definition)

Detection and site-prediction of surgically resectable cancers



Source: Ahlquist DA *Precision Oncol* 2018

Light bars are where tumor location was correctly classified as most likely site; dark bars one of two most likely sites

Possible new single-cancer blood tests

- Single cancer tests being evaluated include (among others):
  - Ovarian cancer in high risk women (SE Lentz et al, *Gynecol Oncol* 159:804, 2020)
  - Gastric (stomach) cancer in high risk men (R Kapoor et al, *Value Health* 23:1171, 2020)
  - Endometrial (uterine) cancer in high risk population (LJ Havrilesky et al *Am J Obstet Gynecol* 112:526, 2009)
- Some of these tests appear cost-effective in high-risk populations: but screening high-risk populations may miss many cases
- What if a single test (MCBT) could test for several such cancers, i.e. spreading the testing costs over more cancers?

https://www.utoronto.ca/news/evidence-grows-iron-deficiency-screening-childhood-u-t-researchers

Can a Multi-Cancer Blood Test improve on doing several single-cancer tests?

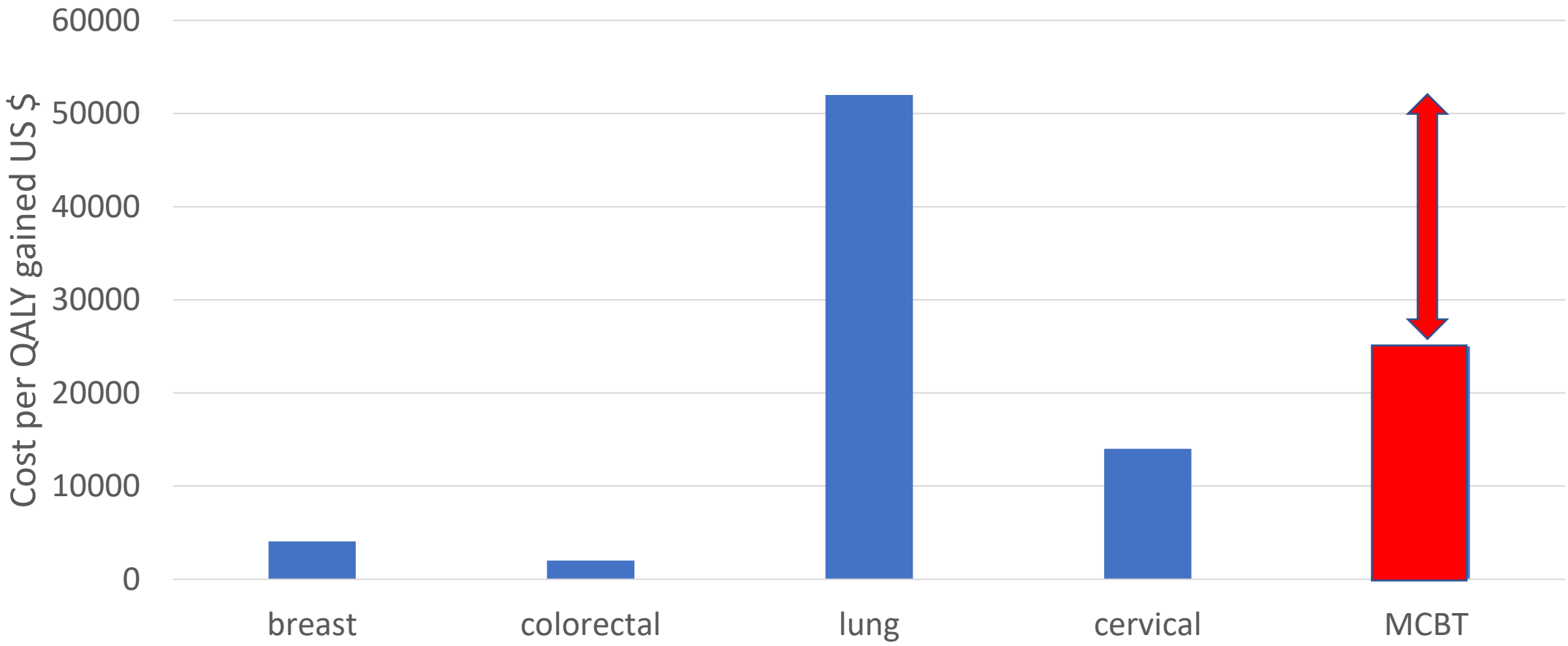
Cancer ID	Similar to:	Assumed MCBT test sensitivity	Assumed survival gains if detected early	Estimated cost-effectiveness, single cancer screening test ($/QALY)
1	Pancreatic cancer	Low (30%)	Low (<1 yr)	Very poor (>$500k)
2	Uterine cancer	High (70%)	High (>20 yrs)	Good (< $50k)
3	Lung cancer	Medium (30%)	Medium (7 yrs)	Poor (>$100k)

We modelled cost-effectiveness of an MCBT for three “baskets” of cancers with different characteristics, including two with no existing approved test, and one (lung) with an existing test

Can a Multi-Cancer Blood Test be cost-effective?

- Assumptions:
  - The test is given once at age 50, and we examine a 2-year interval following the test
  - We use a health sector perspective (i.e. costs of healthcare, but not financial costs of lost work, travel costs for patients etc.)
- Results: **Given our assumptions, the cost-effectiveness of the MCBT is good (cost per QALY is below that of each of the tests separately, and quite well below the threshold of $50,000)**

Cost-effectiveness estimates MCBT versus existing screening programs, USD



See notes to Slide 8 for sources. **MCBT estimate is very preliminary only**.

Limitations of our findings

- The model is complex, even when limited to 3 cancers
- We don’t know as much about cancers which are currently not detected early (e.g. the speed at which they progress)
- For cancers not currently detected early, treatment regimes are likely not well developed and could improve
- Will use of the MCBT make people less likely to adhere to existing screening test guidelines? (bad outcome)
- Or will MCBT increase outreach to those who are not up-to-date with existing screening guidelines (good outcome: in Ontario 1/3 women not up-to-date re breast cancer, 1/3 people not up-to-date re CRC; Litwin, *Gastroenterology* 2016; Cancer Care Ontario Report 2019)

Limitations (cont.)

- Currently we model a one-time only application of the MCBT: for existing cancer screening, cost-effectiveness tends to decline if the test is repeated more frequently (but depends on the speed of progression of the particular cancer)
- Need to update estimate by sex (incidence and response to treatment for some cancers can differ considerably by sex)
- We haven’t modelled the impact on the cost-effectiveness of existing screening programs: cost-effectiveness of these may decline somewhat if (in effect) the same person is being tested twice in the same year for the same cancer

Policy Implications (my opinion)

- I suspect it is unlikely the MCBT would displace existing screening programs where these already exist:
  - MCBT is less sensitive to pre-cancers than existing tests for breast, cervical and colorectal cancers
  - Cervical cancer screening is evolving with HPV vaccination, and possible evolution to DNA testing
- MCBT is also unlikely to reach low- and lower-middle income countries since access to PET-CT for confirmatory testing is limited, as is treatment capability for cancers in general
- More research – and treatment options – may become possible for early stage cancers e.g. stomach, oesophagus, pancreas, liver, ovary, if MCBT improves detection of these at early stages