

Methods for eliciting Bayesian informative priors to inform multi-cancer natural history modelling

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Disclaimer

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Project background

Galleri® (GRAIL) blood test: a multi-cancer early detection (MCED) test that detects circulating tumour DNA (ctDNA) signals shared by over 50 cancer types.

NHS-Galleri trial

- Asymptomatic population 50–77 years
- Three annual screens with (passive) follow-up of 1 additional year (compared to current care)
- Outcome: late-stage (stage III or IV) cancer incidence, 3-4 years after randomisation

Independent analysis will estimate the clinical and cost-effectiveness analysis of the Galleri test by modelling outcomes in individual cancer types.

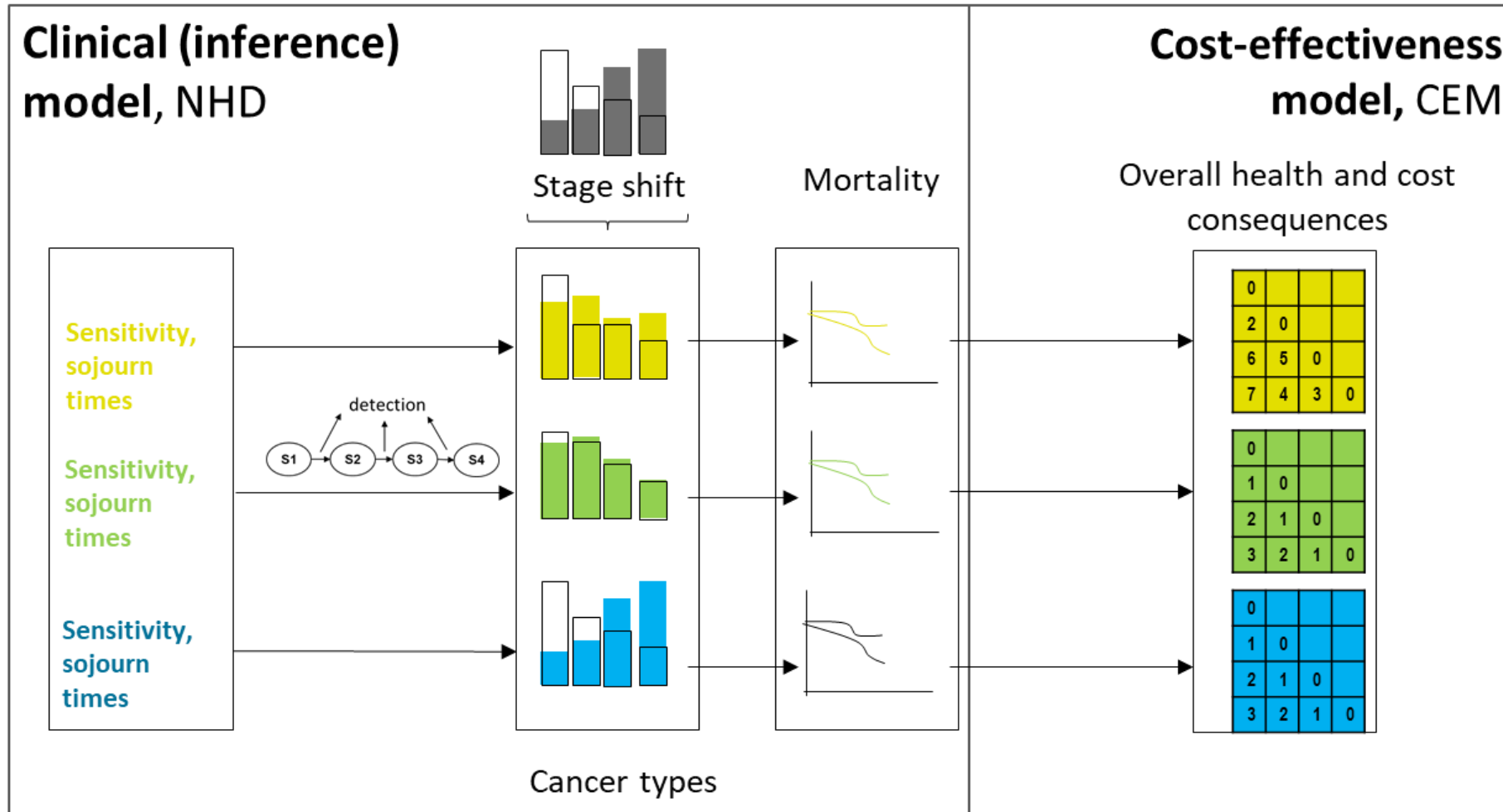
Natural history of disease (NHD) model: cancer sojourn times

Overall mean sojourn time (OMST): mean (across all individuals that develop cancer) duration of time that cancers are detectable (as cancer) before being detected or before death.

Stage-sojourn time: duration of time cancers spend in different stages before they progress to a later stage, are detected or death.

- Early-stage mean sojourn time (EMST) – stages I and II
- Late-stage mean sojourn time (LMST) – stages III and IV

Approach to modelling natural history of disease (NHD)



Empiric estimates of cancer sojourn times

Sojourn time is inherently unobservable and not directly estimable.

Mathematical models can be used to make inference from screening data.

- Primary data from screening trials or routine data on screening programmes
- Data on detection at multiple screening rounds and detection between screening rounds and/or in the absence of screening used to mathematically estimate sojourn times
- Account for complexities such as imperfect screening test sensitivity

Empirical estimates of sojourn times

review of mathematical estimates

We updated a published literature review (Geurts et al., 2022) to 2025

Cancer type	Original review	Update	Total
Breast	12	7	19
Lung	0	1	1
Colon/Rectum	2	1	3
Ovary	0	2	2
Prostate	0	1	1
Liver	0	1	1
Total	14	13	27

Why use structured expert elicitation?

Evidence gaps in screening literature:

- OMST available for 6 cancer types only
- Variation in OMST across studies, generalizability to England unclear
- Only one study on stage-sojourn times
- No studies on ctDNA cancers

The aim of our study was to use structured expert elicitation (SEE), supported by best available evidence, to elicit informative priors for sojourn times across cancer types in England.

Approach to structured expert elicitation

Who is an expert?

Practicing clinicians who have good knowledge of screening research (specialists and generalists)

Elicitation Method

Chips and bins

Mode of delivery

Remote, live video conference sessions lasting up to two hours. Answers collected in a bespoke web app. Training delivered via PowerPoint and practice example.

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Practice question: What is the average number of rainy days in York during October?

I believe that it's very unlikely that:

- the number of days is less than

,

- the number of days is greater than

.

Practice question: What is the average number of rainy days in York during October?

I believe that it's very unlikely that:

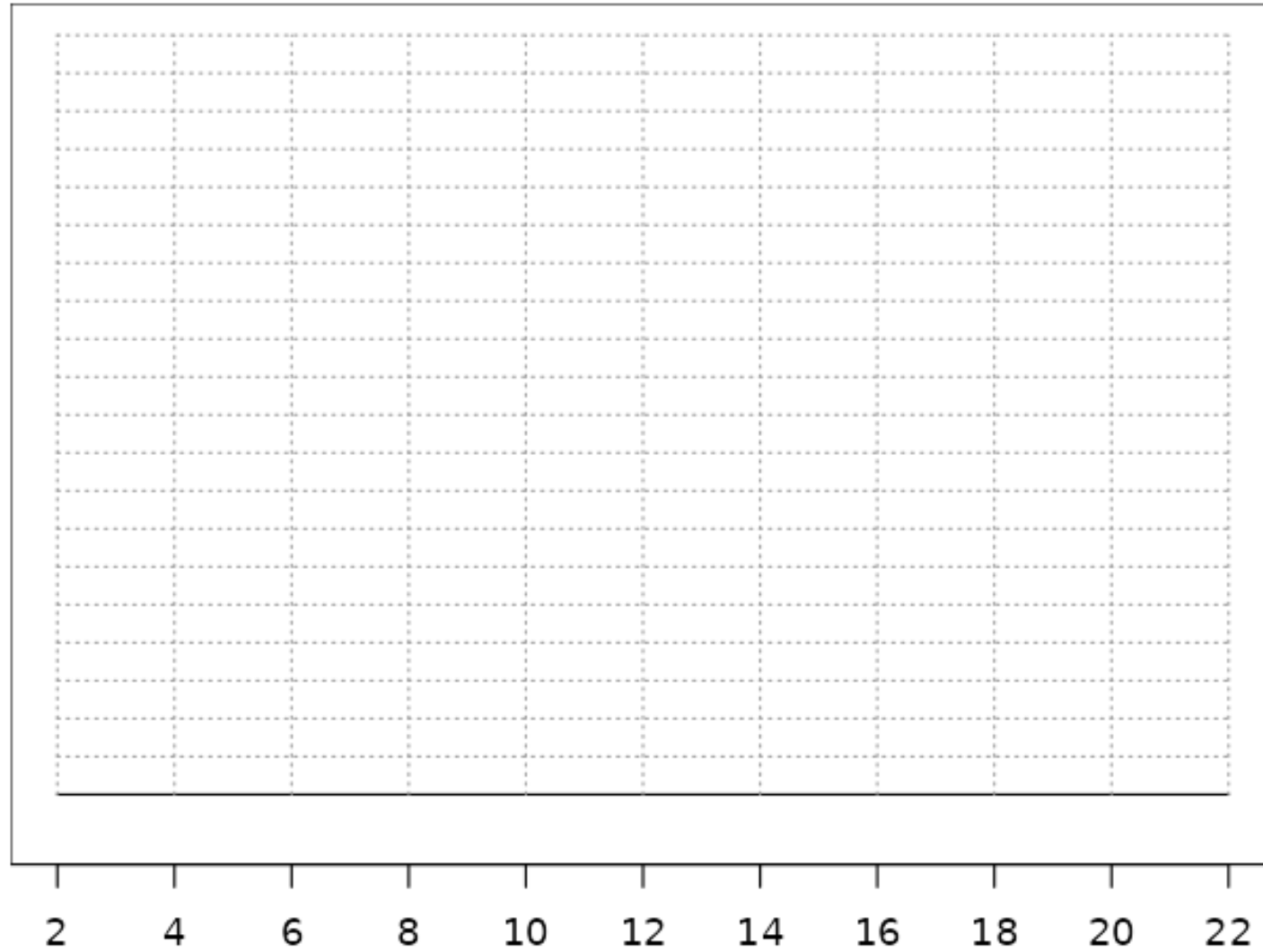
- the number of days is less than

,

- the number of days is greater than

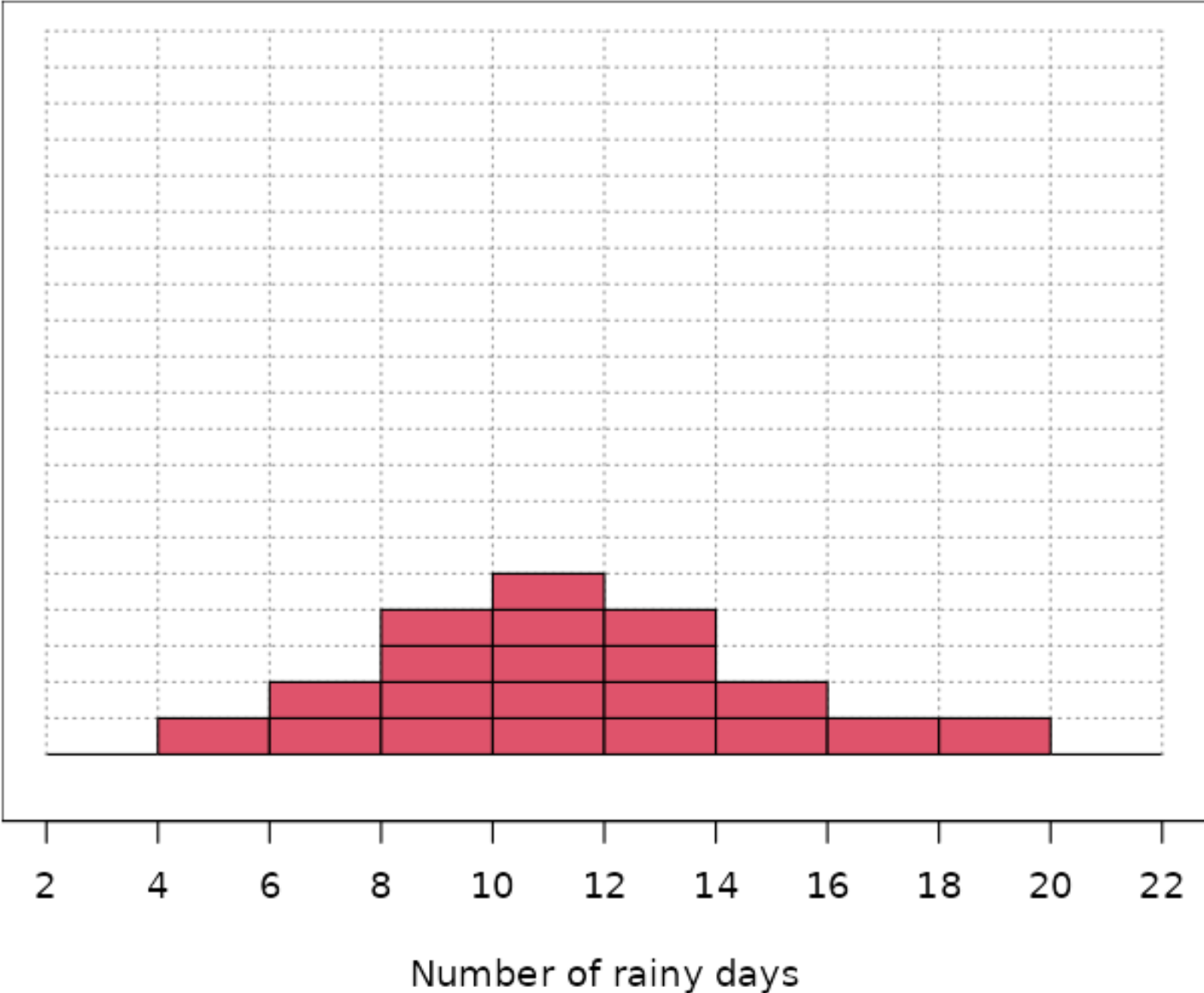
.

You can use **20** more chips.



Number of rainy days

You can use **0** more chips.



Approach to structured expert elicitation

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Elicitation Method

Chips and bins

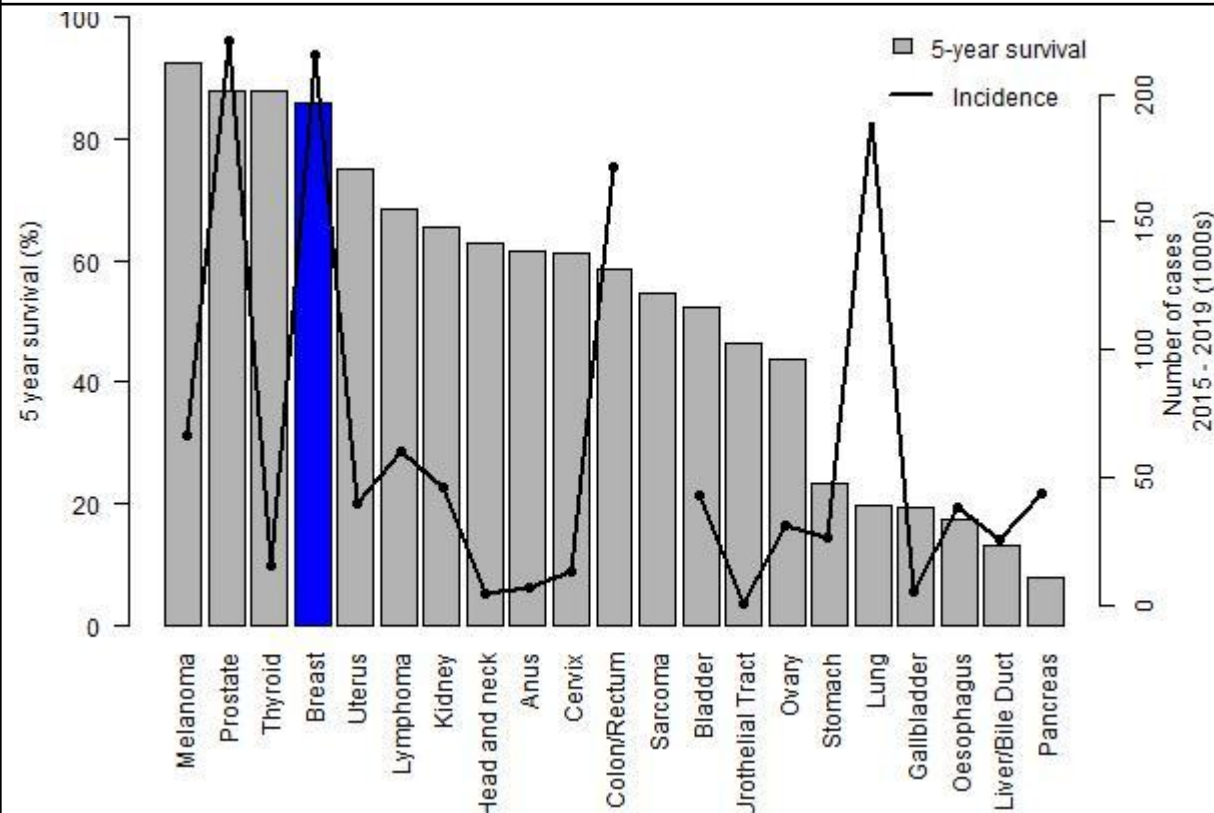
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Remote, live video conference sessions lasting up to two hours. Answers collected in a bespoke Shiny app. Training delivered via PowerPoint and practice example.

Breast cancer prognosis in England

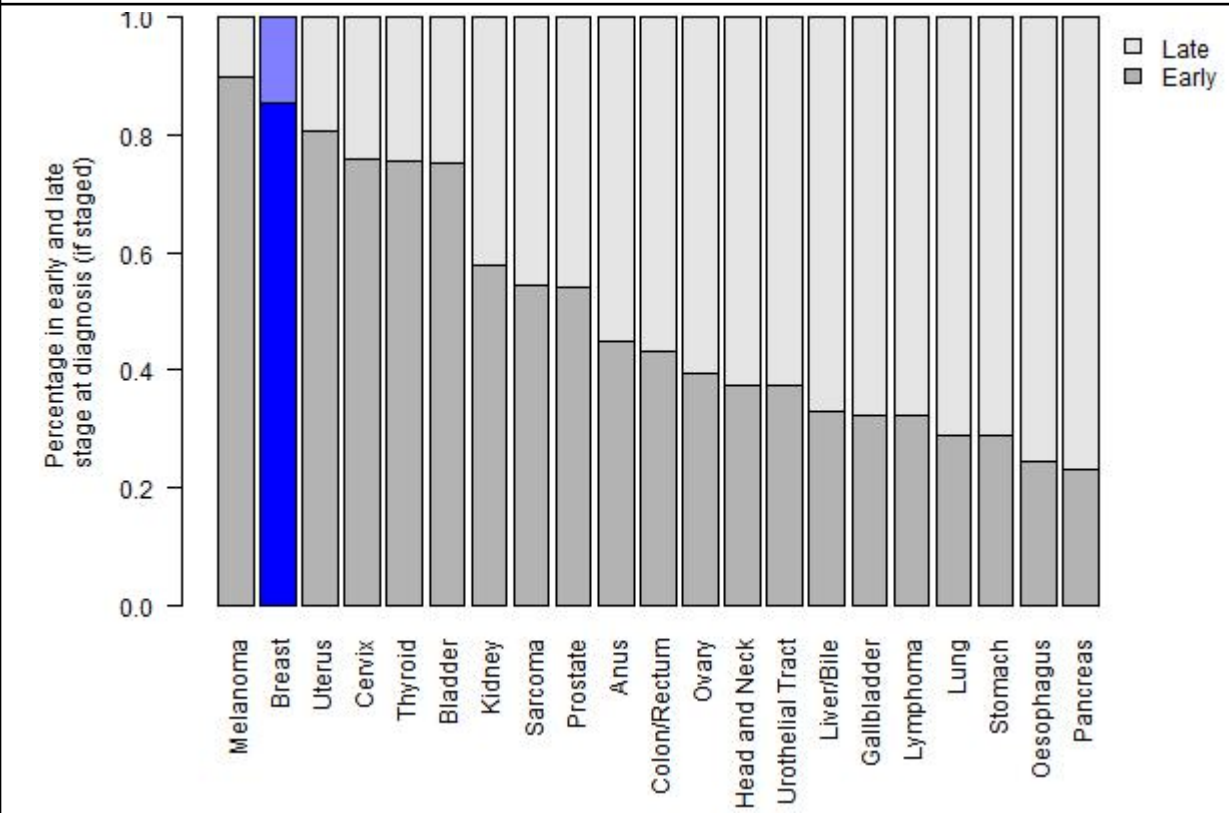
Five-year survival (bar, left-side axis) and number of cases between 2015-2019 (line, right-side axis).

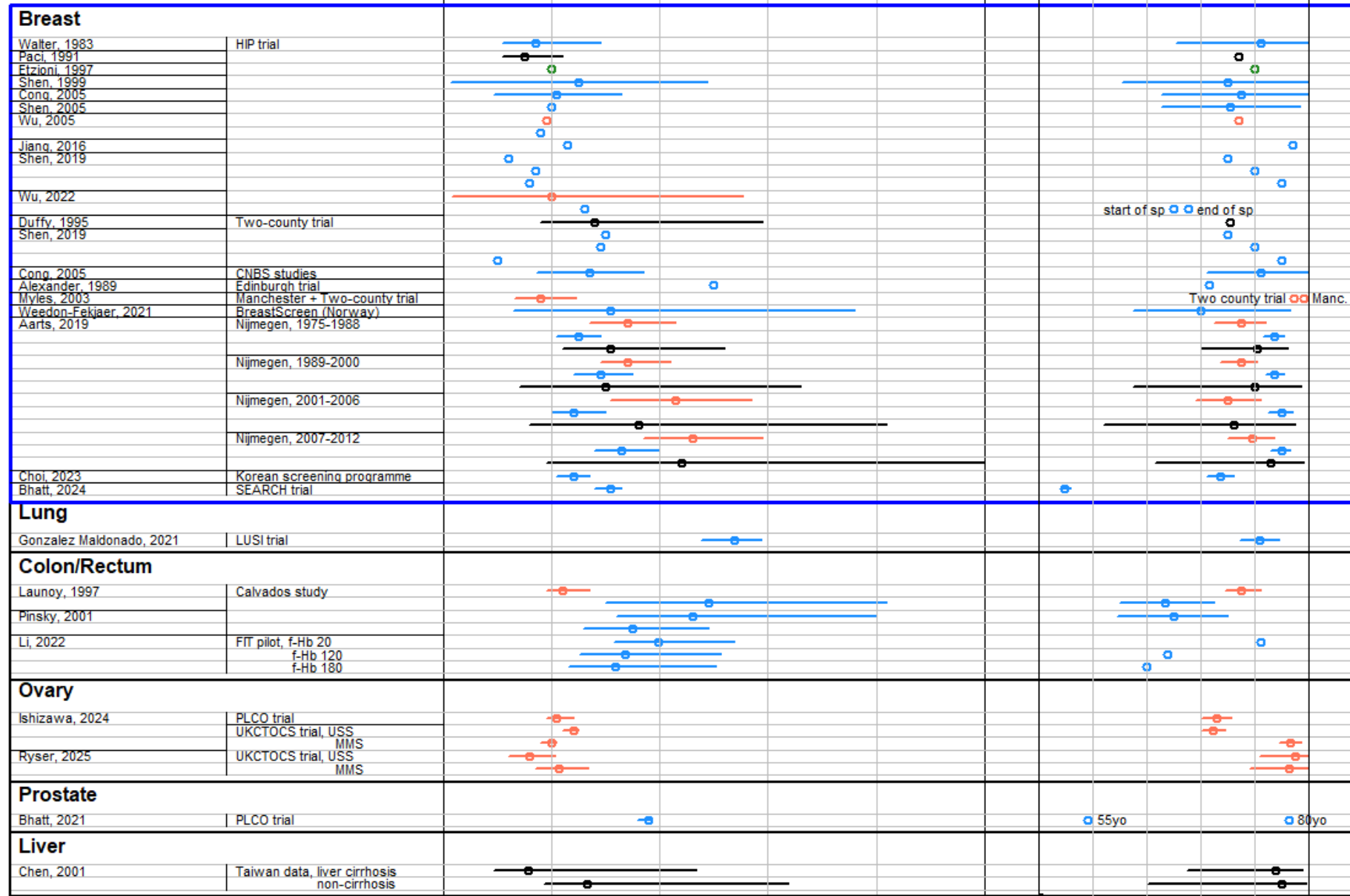
Cancer types ordered by largest to smallest survival



Breakdown of early vs. late stage at diagnosis

Cancer types ordered from largest to smallest proportion of early-stage cancers at diagnosis





- Mean
- 95% CI (where available)
- Bayesian
- MLE
- EMA
- ROE

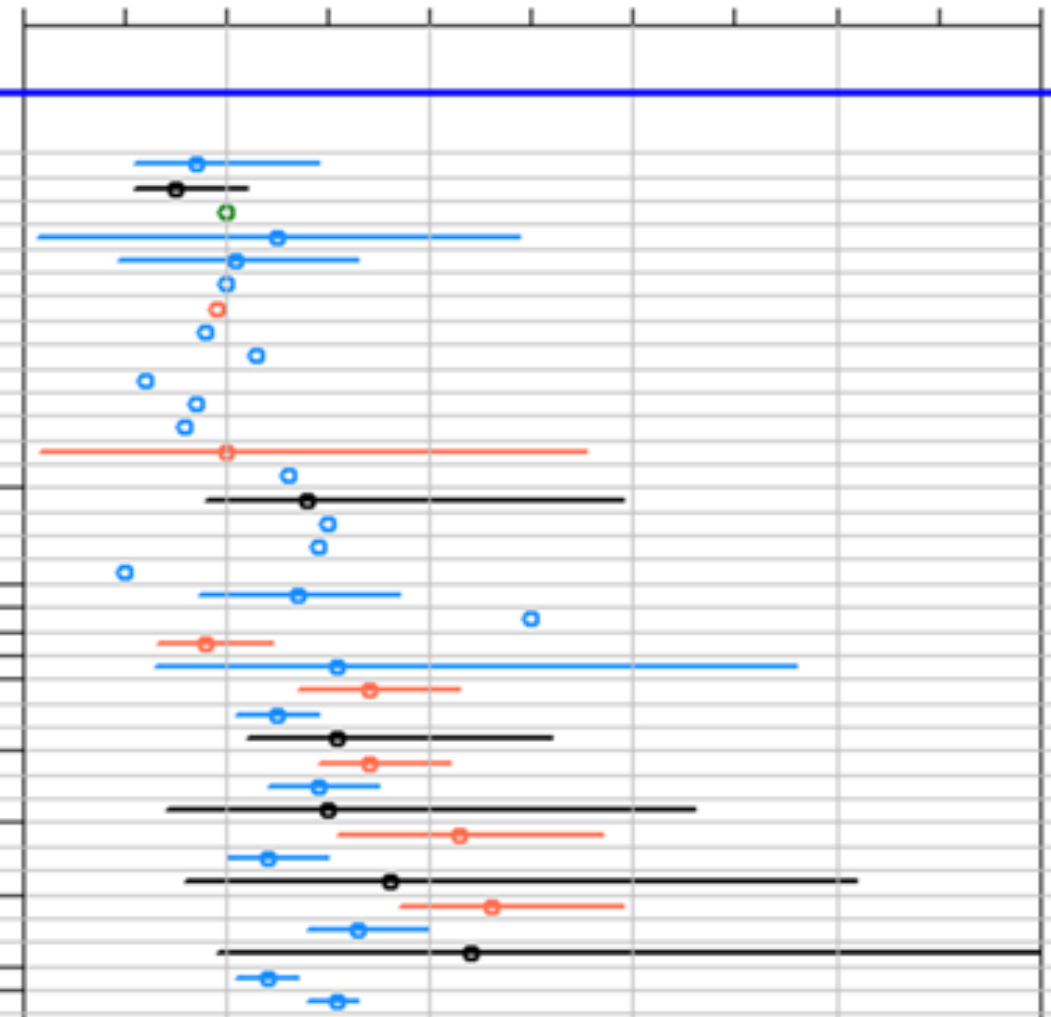
0 1 2 3 4 5 6 7 8 9 10 0 20 40 60 80 100
OMST (years) Sensitivity (%)

0 1 2 3 4 5 6 7 8 9 10

0 20 40 60 80 100

Breast

Walter, 1983	HIP trial
Paci, 1991	
Etzioni, 1997	
Shen, 1999	
Cong, 2005	
Shen, 2005	
Wu, 2005	
Jiang, 2016	
Shen, 2019	
Wu, 2022	
Duffy, 1995	Two-county trial
Shen, 2019	
Cong, 2005	CNBS studies
Alexander, 1989	Edinburgh trial
Myles, 2003	Manchester + Two-county trial
Weedon-Fekjaer, 2021	BreastScreen (Norway)
Aarts, 2019	Nijmegen, 1975-1988
	Nijmegen, 1989-2000
	Nijmegen, 2001-2006
	Nijmegen, 2007-2012
Choi, 2023	Korean screening programme
Bhatt, 2024	SEARCH trial



Lung

Gonzalez Maldonado, 2021	LUSI trial
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Colon/Rectum

Question 1a: OMST (with uncertainty)

Q1a: What is the overall mean sojourn time (OMST) of clinically detected breast cancers in England?

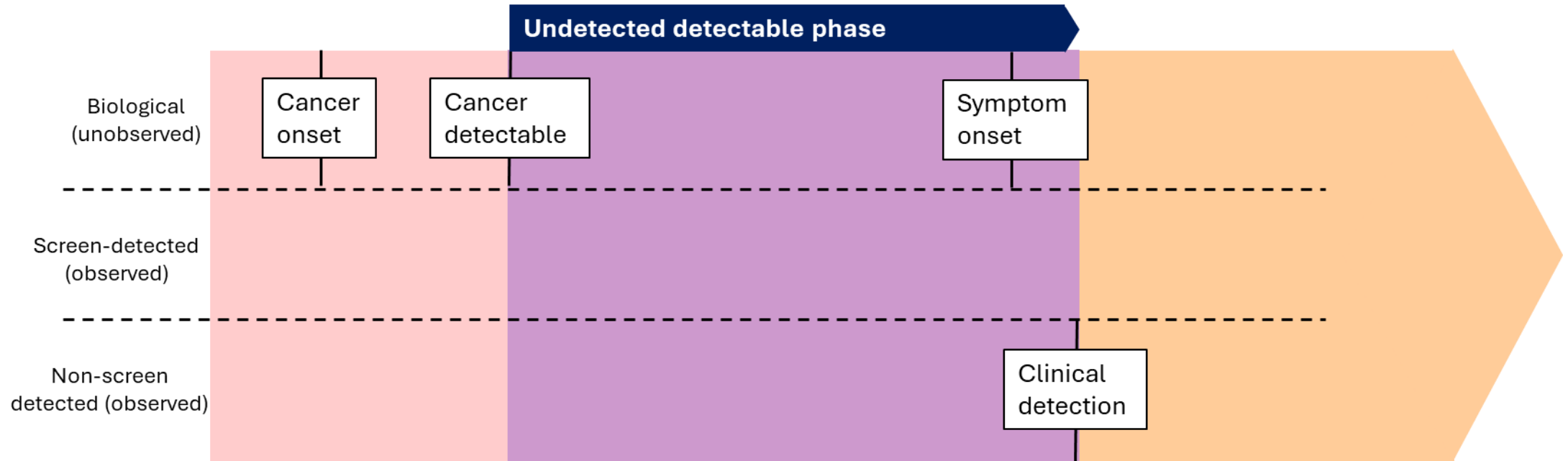
Aim: to generalise the empiric estimates to England.

Q1b: What is the overall mean sojourn time (OMST) of all breast cancers in England?

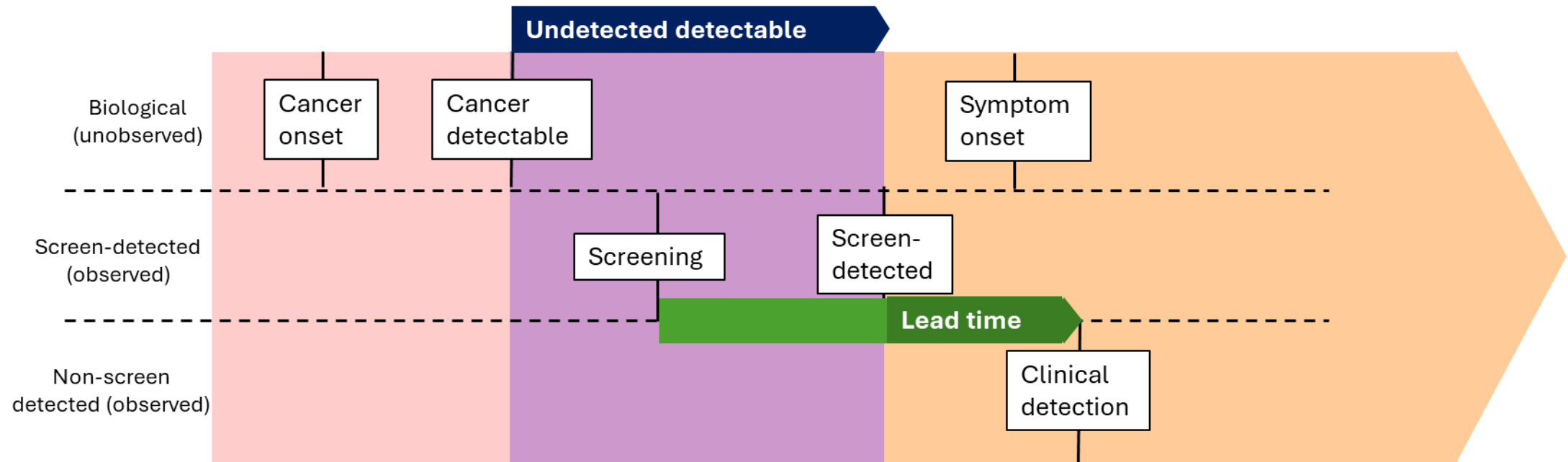
This includes clinically and screen-detected cancers.

Aim: to inform OMST of all cancers in England, in absence of the Galleri test

OMST with symptomatic detection



OMST with screen-detection



Only applicable to cancers with existing screening programmes (colon/rectum, breast, cervix).

Question 1a: OMST (with uncertainty)

Q1a: What is the overall mean sojourn time (OMST) of clinically detected breast cancers in England?

Aim: to generalise the empiric estimates to England.

Q1b: What is the overall mean sojourn time (OMST) of all breast cancers in England?

This includes clinically and screen-detected cancers.

Aim: to inform OMST of all cancers in England, in absence of the Galleri test

Question 1c: sojourn time in cancers with the shortest sojourn time

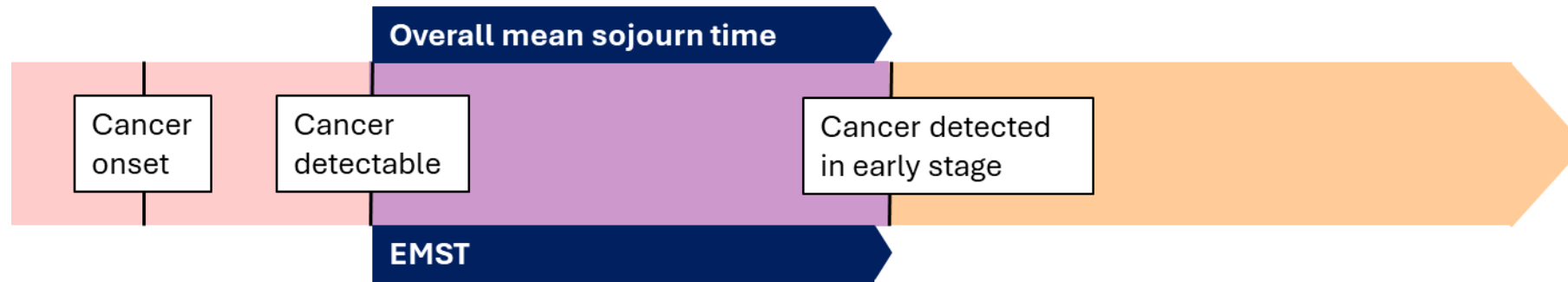
I believe that, if OMST for all cancers is 3.5 years, then the 25% of patients with the fastest-progressing cancers (shortest sojourn time) will have a sojourn time of _____ years or shorter.

Aim: to understand how overall sojourn time differs between cancers of the same type.

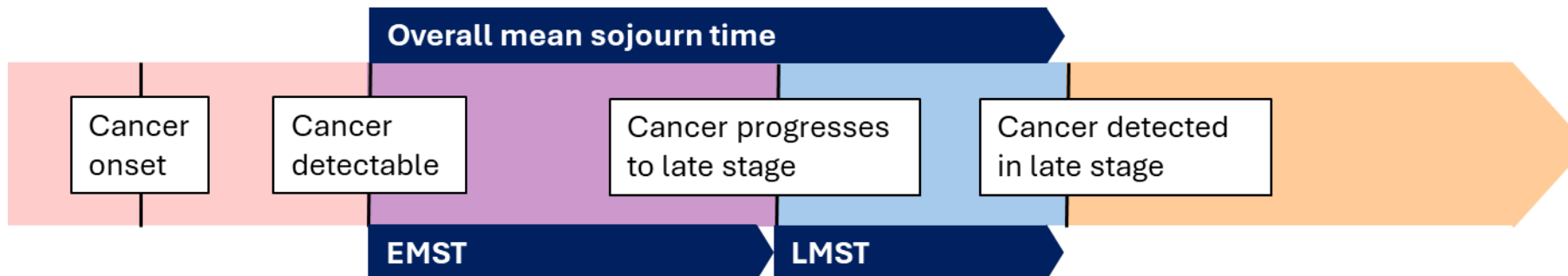
- Informs the distribution of sojourn times (usually assumed to be exponential)

Question 2: stage sojourn times

... for cancers identified in early stage, $OMST = EMST$



... for cancers identified in late stage, $OMST = EMST + LMST$



Question 3: What is the OMST of ctDNA cancers?

- A. Do you believe that the ctDNA cancers detected by Galleri have the shortest sojourn time of all breast cancers?**

Question 3: What is the OMST of ctDNA cancers?

A. Do you believe that the ctDNA cancers detected by Galleri have the shortest sojourn time of all breast cancers?

B. [If yes to Q3A]

Galleri test sensitivity for breast cancer is 30%, indicating they are ctDNA positive cancers (20% of cancers in early stages, 87% of cancers in late stages).

The predicted sojourn time for the 30% fastest progressing breast cancers (using a statistical model applied to your answer to question 1C) is **1** year or less.

Is this value reflective of your beliefs on the OMST of the ctDNA cancers detected by the Galleri test?

Question 3: What is the OMST of ctDNA cancers?

C: [If no to either of the above].

If OMST for all breast cancers (ctDNA and non-ctDNA) is 3.5 years, what do you believe is the OMST of ctDNA breast cancers?

- Elicited with uncertainty

Simplifications for generalists

Questions	Cancer types
OMST and stage-OSMT for all cancers, OMST for ctDNA cancers	Six cancer types for which empiric estimates of OMST are available: breast, lung, colon/rectum, prostate, ovary, liver/bile duct
OMST for all and ctDNA cancers	Five further cancer types in which screening with the Galleri test is expected to produce the highest health gains: cervix, head and neck, lymphoma, oesophagus, pancreas
Multiple choice questions about OMST	Remaining ten cancer types: anus, bladder, gallbladder, kidney, melanoma, sarcoma, stomach, thyroid, urothelial tract, uterus

Progress to date

- 15 experts recruited, 9 elicitations conducted
- One generalists, 8 specialists (16 cancer types)
- Good engagement, positive feedback
- Differences in opinions but no statistically incoherent priors

Thank you!!!