Breakout Session 102

Diving into Supporting Clinical Plausibility in Lifetime Survival Extrapolations

The Need for Structured Tools to Guide HTA Submissions

ISPOR Europe, Vienna, 7th November 2022

Moderator
Nick Latimer
Professor of Health Economics, Yorkshire Cancer Research Senior Fellow, University of Sheffield, UK

Panelist
Bart Heeg
Vice President, Global HEOR, Cytel, Netherlands

Panelist
Mario Ouwens
Senior Statistical Science Director, AstraZeneca, Sweden

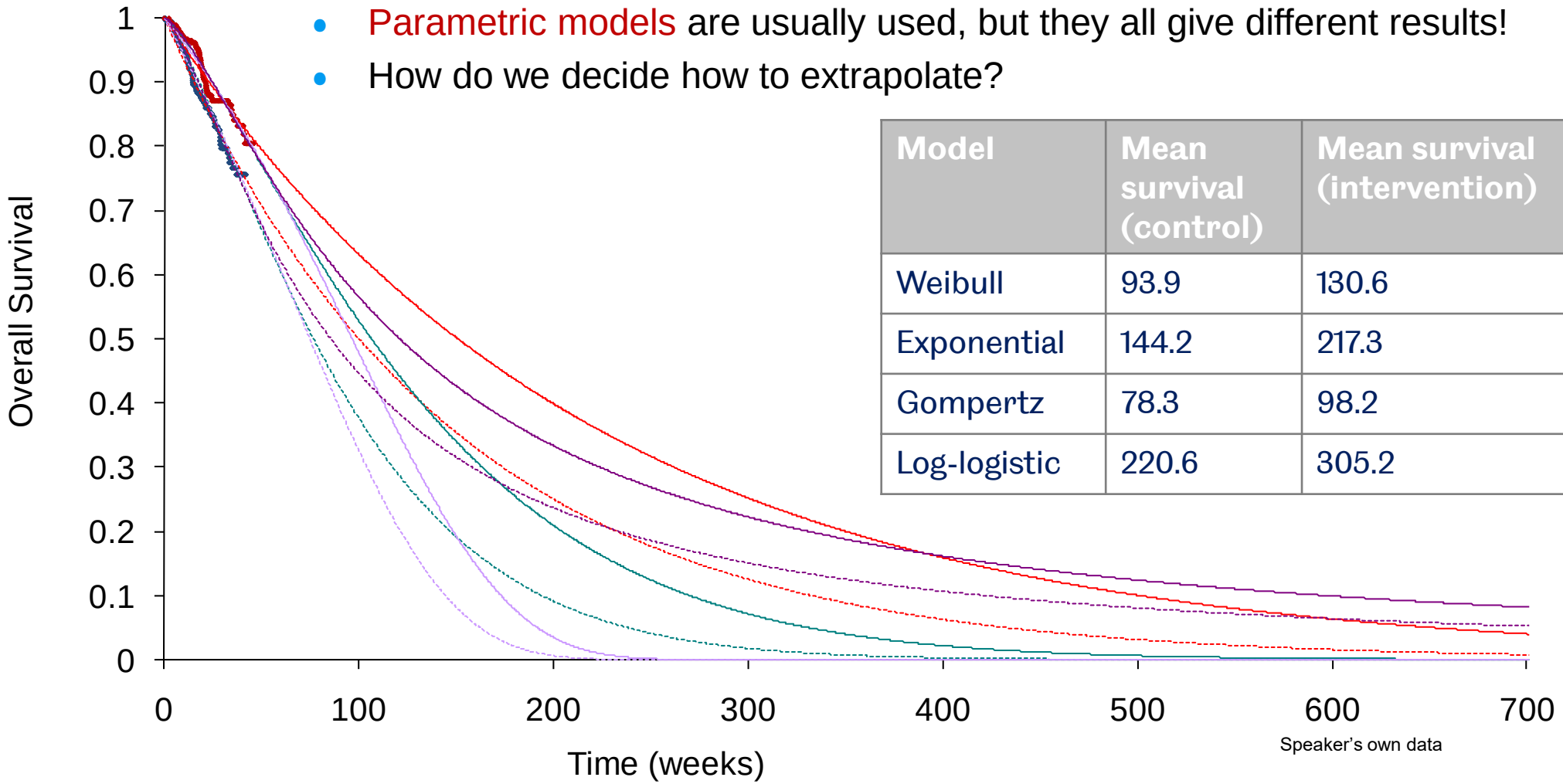
Panelist
Dalia Dawoud
Associate Director (Research) National Institute for Health and Care Excellence (NICE), UK

Disclosures

I am a member of NICE Appraisal Committee B and have authored or co-authored the NICE Decision Support Unit technical support documents on survival analysis

Extrapolation

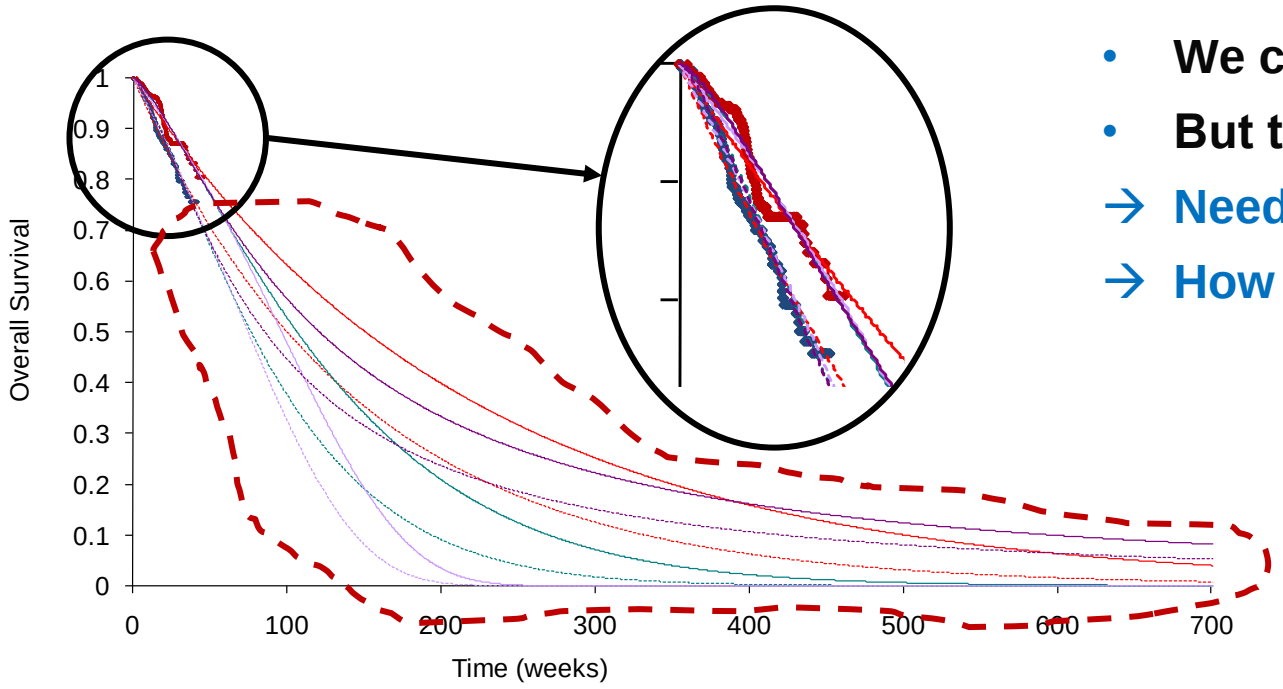
- **Problem** – censored data due to limited trial follow-up
- Parametric models are usually used, but they all give different results!
- How do we decide how to extrapolate?



Model	Mean survival (control)	Mean survival (intervention)	Mean survival gain
Weibull	93.9	130.6	36.8
Exponential	144.2	217.3	73.1
Gompertz	78.3	98.2	19.9
Log-logistic	220.6	305.2	84.6

Speaker's own data

How do we decide how to extrapolate?



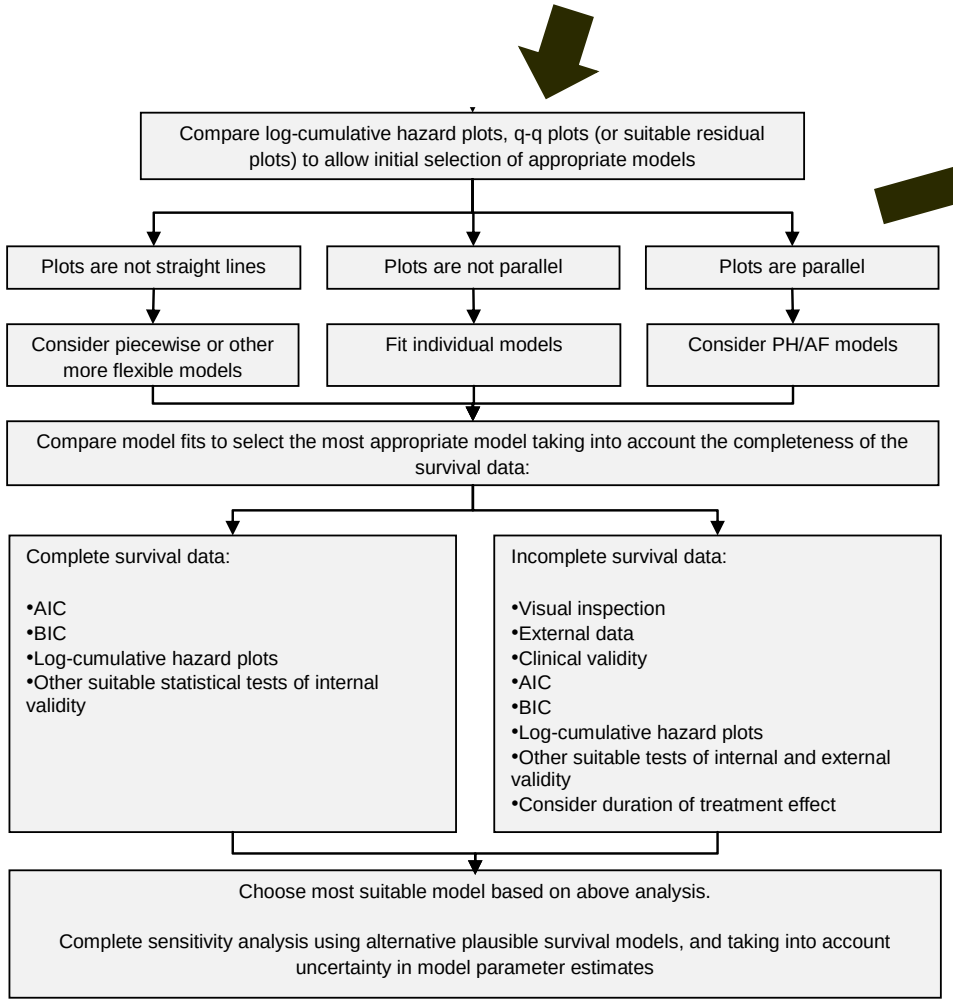
- We can look at fit to the data
- But this isn't enough!

→ Need to consider the plausibility of the extrapolation

→ How do we do that?

Guidance: NICE DSU technical support document 14

➔ **Survival modelling for economic evaluation process chart (SMEEP)** (DSU Technical Support Document 14)



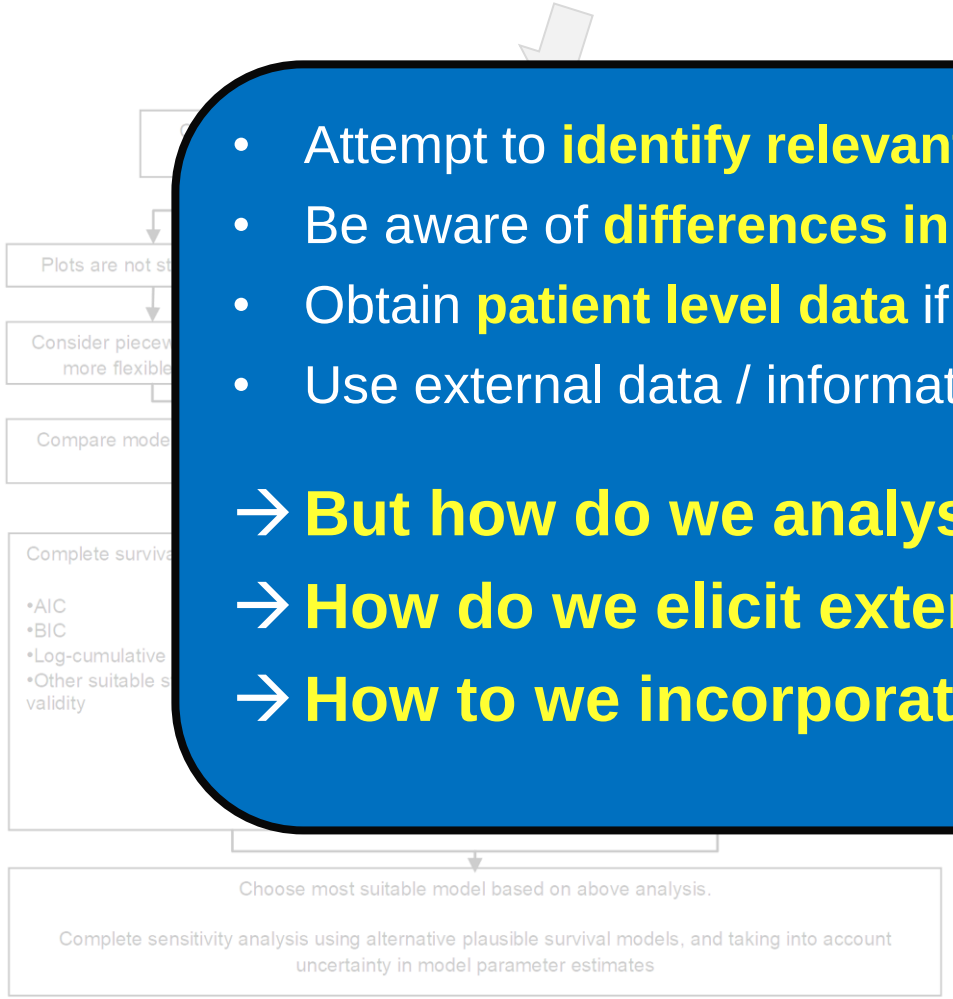
1. Assess internal validity of models (stats tests)
2. Assess external validity (external data, clinical plausibility)
3. Present sensitivity analysis using alternative models

TSD 14 was limited in scope:

- Focused on standard parametric models
- Aim was to encourage consistency in survival analysis
- **Did not attempt to say much about *how* to assess external validity**

Guidance: NICE DSU technical support document 14

→ Survival modelling for economic evaluation process chart (SMEEP) (DSU Technical Support Document 14)



- Attempt to **identify relevant external data** sources or information
- Be aware of **differences in patient characteristics** between data sources
- Obtain **patient level data** if possible, to allow adjustment
- Use external data / information to **validate or calibrate** models

→ **But how do we analyse the external data?**

→ **How do we elicit external information?**

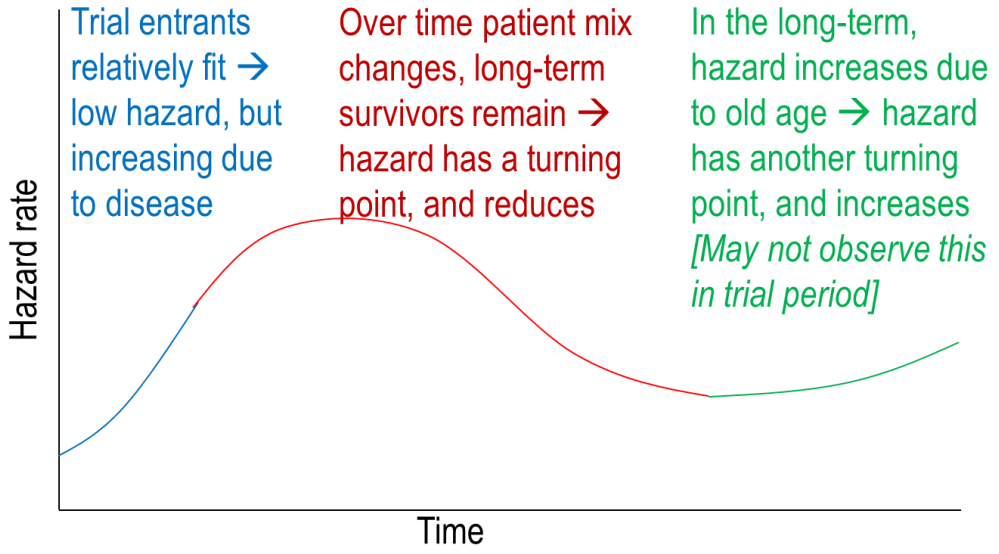
→ **How to we incorporate it?**

Guidance: NICE DSU technical support document 21

- **Encouraged to think about hazards**

→ Standard parametric models are limited, we might need more complex models

- **Complex survival models**
  - Piecewise models
  - Flexible parametric models
  - Cure models
  - Mixture models
  - Landmark response models
- Makes **model specific recommendations**
- Makes **recommendations on plots to present**
  - Hazard plots
  - Implied treatment effects



- **Does say more about external information and data, but not that much...**

Guidance: NICE DSU technical support document 21

- **External data crucial for some complex methods** (cure, relative survival)
  - Should be considered for *all* models
- **Incorporating background mortality** within models is key
  - At least compare predicted hazards to general population hazards
- **Consider using registry data** to inform long-term hazards
- Consider **characteristics of patients in different datasets**
- And whether **study population reflects broader population** with the disease
- Briefly discusses including external information in a **Bayesian framework**

Guidance: NICE DSU technical support document 21

- External data crucial for some complex methods (cure, relative survival)
  - Should be considered for *all* models

- **External information is clearly important**
- **But TSD states that research is ongoing and cannot make firm recommendations**
- **Still not much on how we analyse external data, how we elicit information, how we do all this systematically**

- And whether study population reflects broader population with the disease

- Briefly discusses including external information in a Bayesian framework

The University Of Sheffield.

yorkshire cancer research

Saving Yorkshire Lives

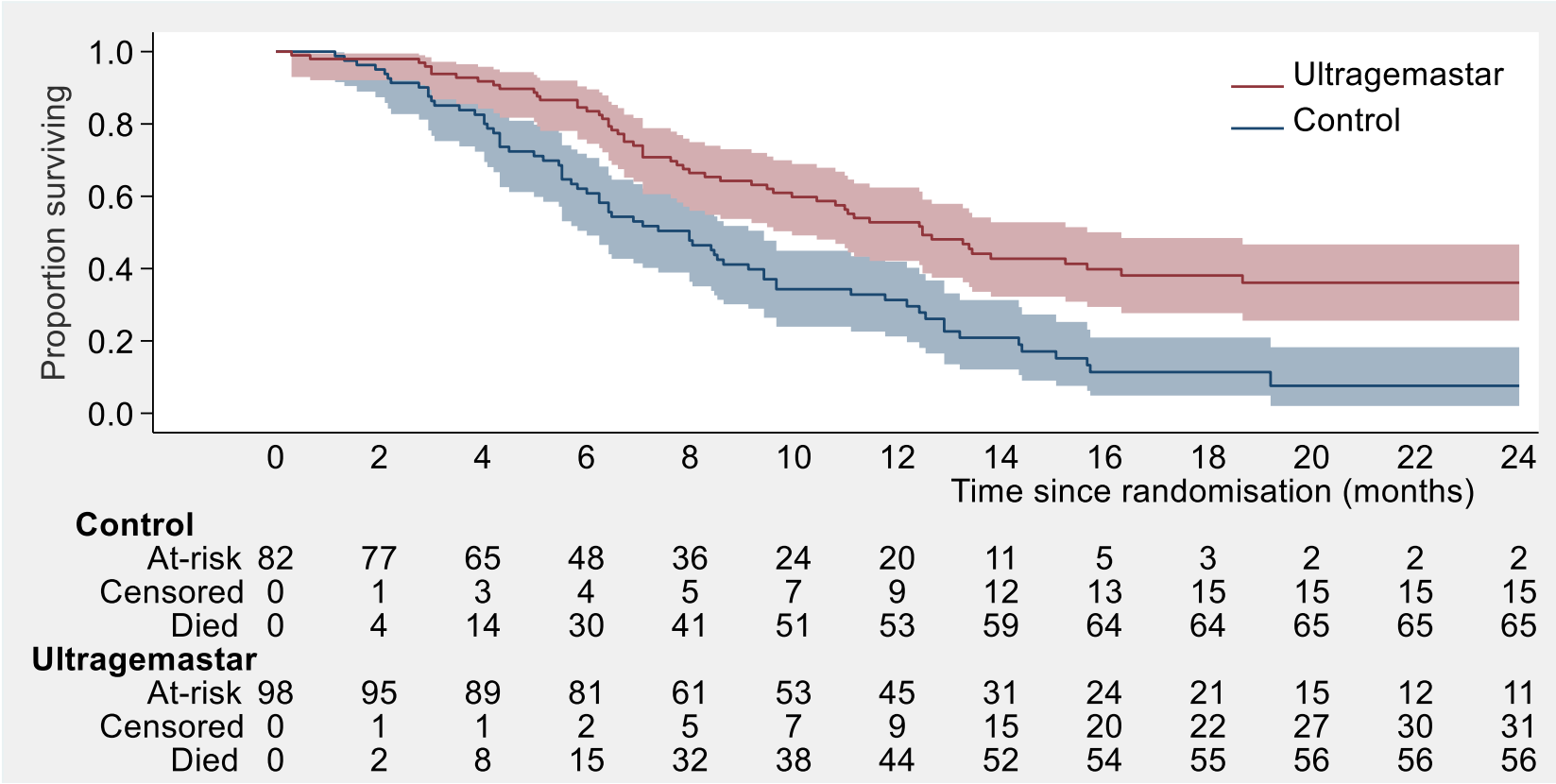
Polls – What do you think?

Poll #1: Can we adequately estimate long-term survival benefits of treatments without having long-term trial data (e.g. 80% events observed)?

a) Yes, we can make treatment recommendations confidently

b) No, we can't make treatment recommendations confidently

c) We need managed access



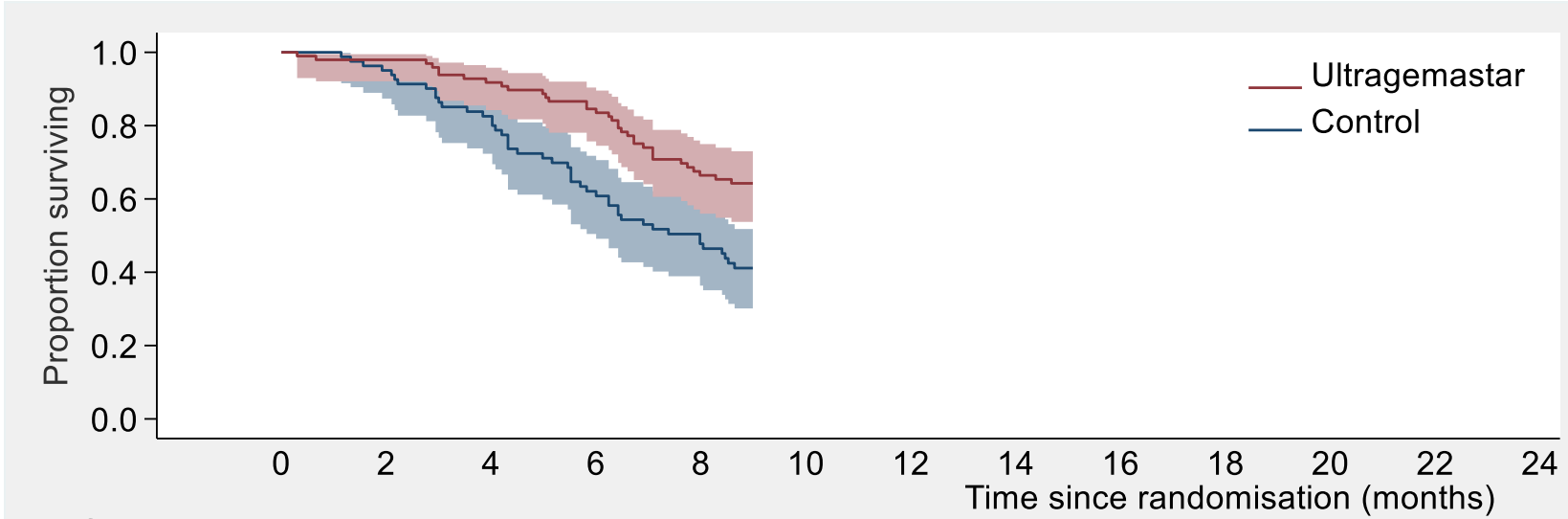
Control													
At-risk	82	77	65	48	36	24	20	11	5	3	2	2	2
Censored	0	1	3	4	5	7	9	12	13	15	15	15	15
Died	0	4	14	30	41	51	53	59	64	64	65	65	65
Ultragemastar													
At-risk	98	95	89	81	61	53	45	31	24	21	15	12	11
Censored	0	1	1	2	5	7	9	15	20	22	27	30	31
Died	0	2	8	15	32	38	44	52	54	55	56	56	56

Poll #2: Can we adequately estimate long-term survival benefits of treatments without having long-term trial data (e.g. 50% events observed)?

a) Yes, we can make treatment recommendations confidently

b) No, we can't make treatment recommendations confidently

c) We need managed access



Control					
At-risk	82	77	65	48	36
Censored	0	1	3	4	5
Died	0	4	14	30	41
Ultragemastar					
At-risk	98	95	89	81	61
Censored	0	1	1	2	5
Died	0	2	8	15	32

Poll #3: Should real world data be used to inform extrapolations?

a) Yes
b) No

Poll #4: Is it clear *how* real world data should be used to inform extrapolations?

a) Yes

b) No

Poll #5: Do you think real world data should be used to validate extrapolations, or to actually inform the model (i.e. included within the model building process)?

a) Validate the extrapolations

b) Actually inform the model