

# Cost-effectiveness of monoclonal antibodies and maternal vaccination programmes against RSV

David Hodgson

17<sup>th</sup> Vaccine Congress

27<sup>th</sup> September 2023





# Background + Overview

# RSV protection in infants in 2023

## Nirsevimab (Beyfortus, Sanofi)

- Long-acting monoclonal antibody
- Given once before RSV season

74.5% (95 CI 49.6 to 87.1) against MA-LRTI

Hammit et al. 2022. NEJM

The NEW ENGLAND JOURNAL of MEDICINE

### ORIGINAL ARTICLE

## Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants

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## Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Pereras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Gullam, B. Tapiero, R.T. Stein, F.P. Polack, H.J. Zar, N.B. Staerke, M. Duron Padilla, P.C. Richmond, K. Koury, K. Schneider, E.V. Kalinina, D. Cooper, K.U. Jansen, A.S. Anderson, K.A. Swanson, W.C. Gruber, and A. Gurtman, for the MATISSE Study Group\*

Kampmann et al. 2023. NEJM



## RSVPreF (ABRYSVO, Pfizer)

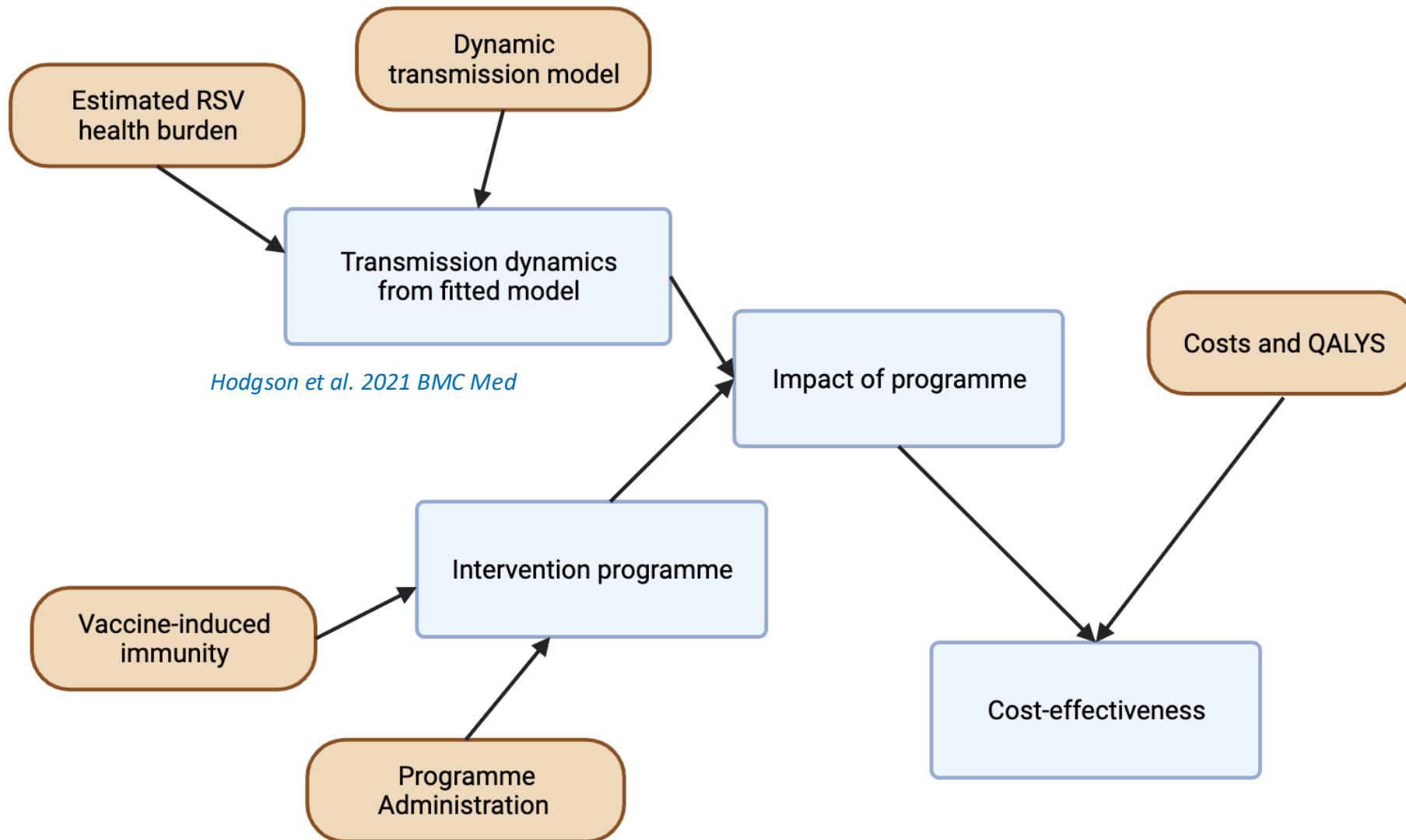
- Maternal vaccine
- Given during third trimester

69.4% 97.58% CI (44.3 to 84.1) against severe MA-LRTI

Both approved for use by FDA/EMHA

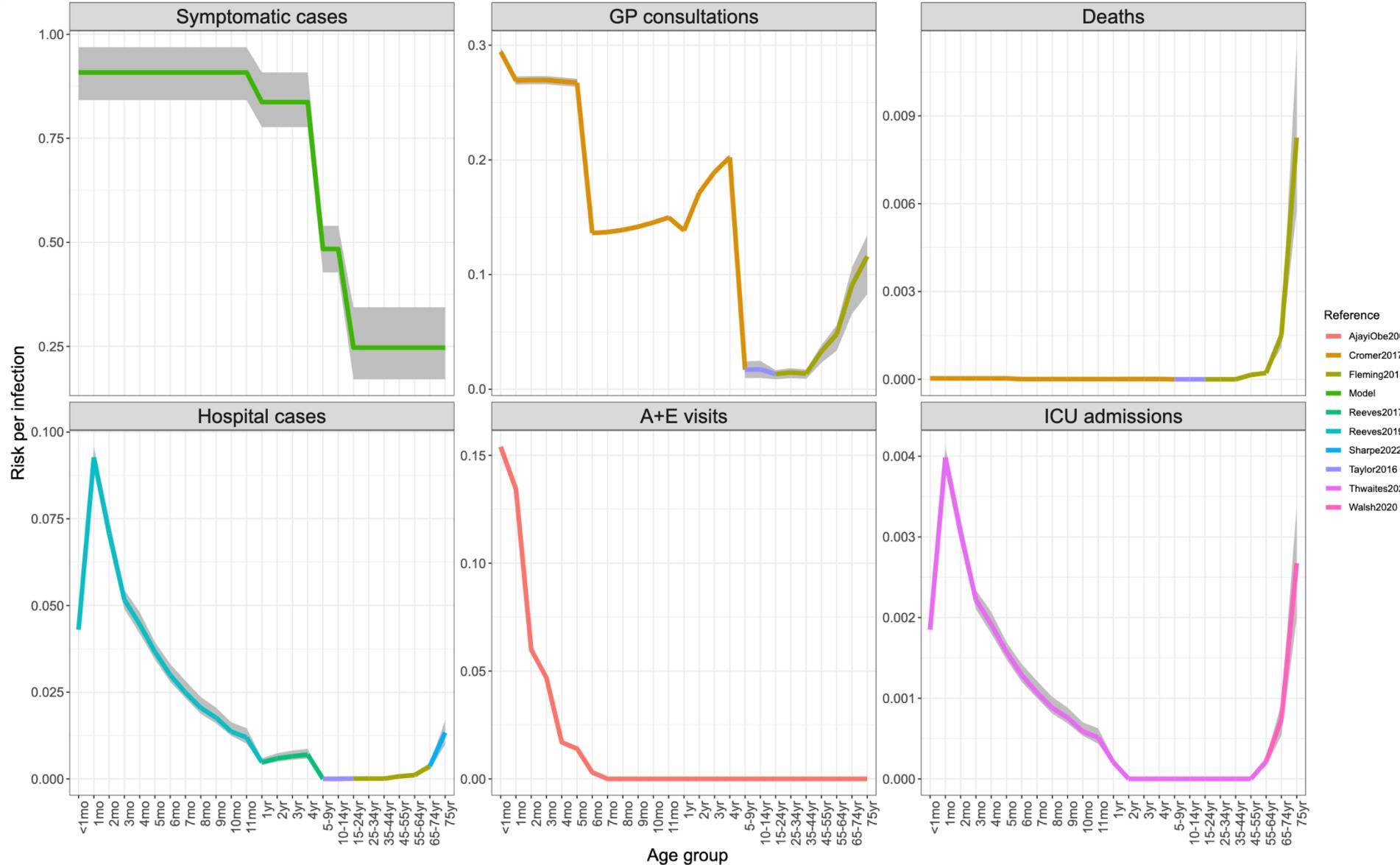
Question for UK: which, if any, of these should we incorporate into the NIP?

# Overview of project



# Risks of healthcare outcomes

**Risk per infection:**  
outcome incidence/  
model predicted  
incidence



# Economic parameters

## COSTS

### GP consultations:

- £36. *Unit costs manual*

### A + E Visits:

- £182.28. *National schedule of NHS costs (T0\_)*

## QALY LOSS

SUBGROUP	QALY LOSS	REFERENCE
< 5 years Symptomatic	$2.336 \times 10^{-3}$ ( $0.269 \times 10^{-3}$ – $9.255 \times 10^{-3}$ )	Hodgson et al. 2020
≥5 years symptomatic	$1.448 \times 10^{-3}$ ( $0.135 \times 10^{-3}$ – $5.928 \times 10^{-3}$ )	
< 5 years hospitalisations	$4.098 \times 10^{-3}$ ( $0.624 \times 10^{-3}$ – $13.141 \times 10^{-3}$ )	
≥5 years hospitalisations	$2.990 \times 10^{-3}$ ( $0.346 \times 10^{-3}$ – $11.387 \times 10^{-3}$ )	

## Hospital cases

AGE GROUP	MEDIAN RSV-RELATED HOSPITAL ADMISSION COST (£, 95% CrI)	
	SHORT-STAY ONLY	SHORT- AND LONG-STAY
<15 years of age	1100.23 (1029.66–1253.16)	1909.86 (1599.19–3711.22)
≥ 15 years of age	652.29 (585.37–740.31)	1753.21 (1233.30–2739.47)

\*Paediatric Acute Bronchiolitis with CC Score 0–5+ (PD15A–PD15D). *National schedule of NHS costs*

\*Unspecified Acute Lower Respiratory Infection with/without Interventions 0–13+ (DZ22K–DZ22Q). *National schedule of NHS costs*

## ICU admissions

AGE GROUP	MEDIAN RSV-RELATED ICU ADMISSION COST (£, 95% CrI)
<15 years of age	2905.20 (2282.80–3862.67)
≥ 15 years of age	2324.80 (1948.25–2653.25)

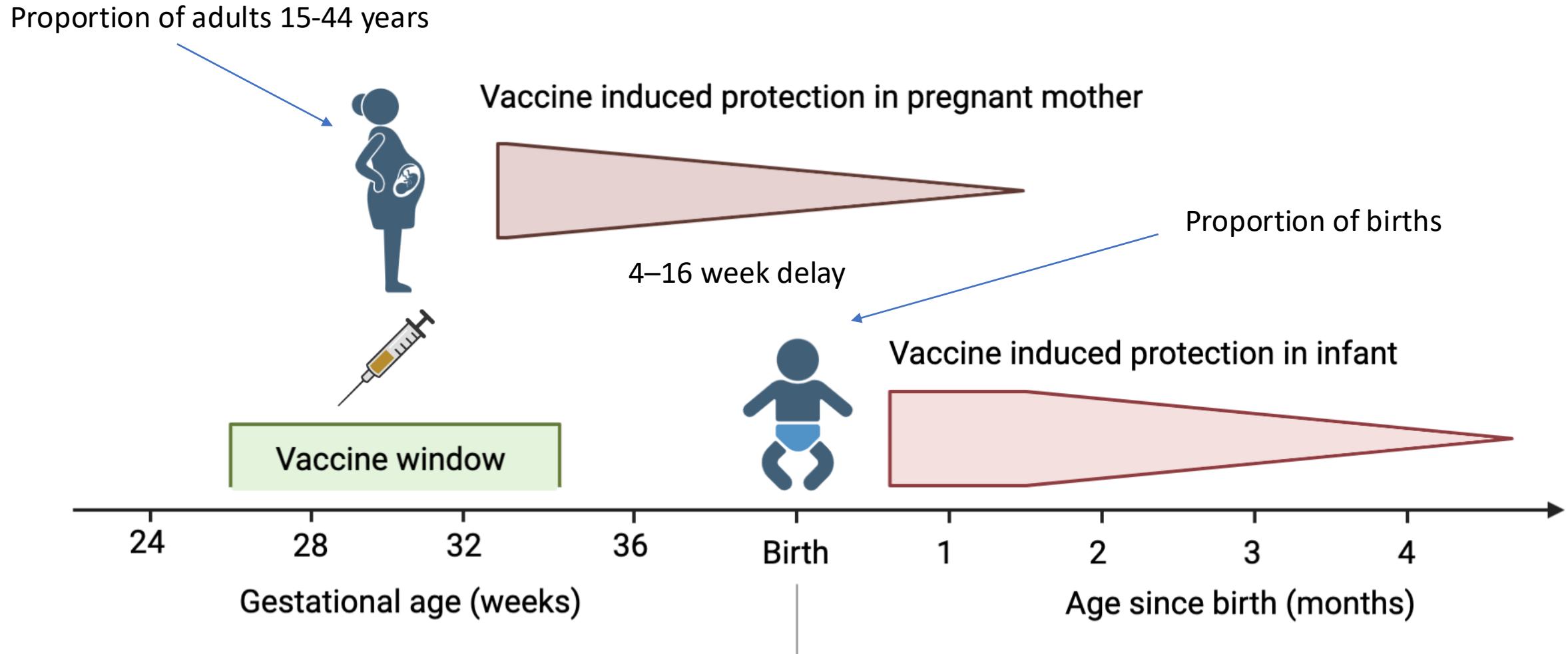
\* Paediatric Critical Care, Advanced Critical Care 1–5 (XB01Z–XB07Z). *National schedule of NHS costs*

\*Adult Critical Care, 0–6+ Organs Supported (XC01Z–XC07Z).



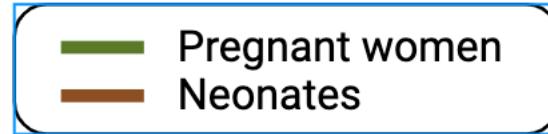
# Intervention programmes

# Modelling maternal vaccination (conceptually)

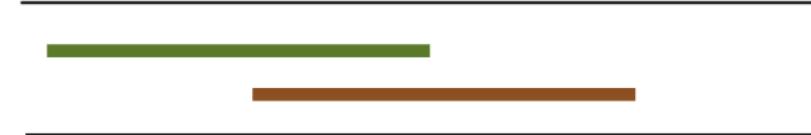


# Modelling maternal vaccination (implementation)

## Calendars



Seasonal



Year-round



July

Jan

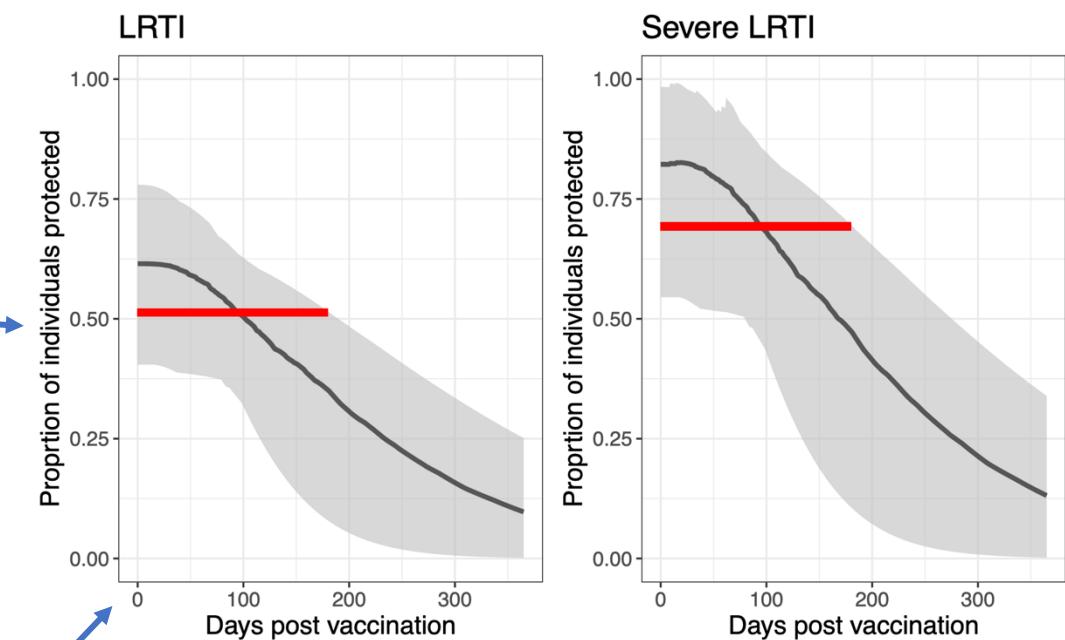
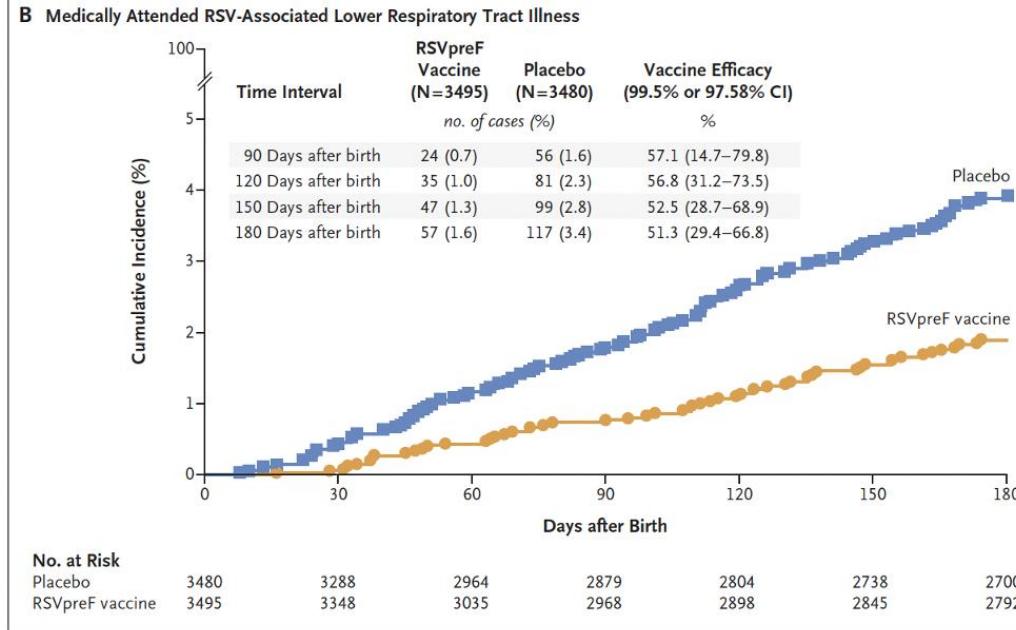
Jun

## Coverage in pregnant women (%)

	Flu	Pertussis
2022/23	35.0	—
2021/22	37.9	60.0
2020/21	43.7	65.0
2019/20	43.6	73

Base assumption: **60% (50-90)**

# Modelling maternal vaccination (implementation)



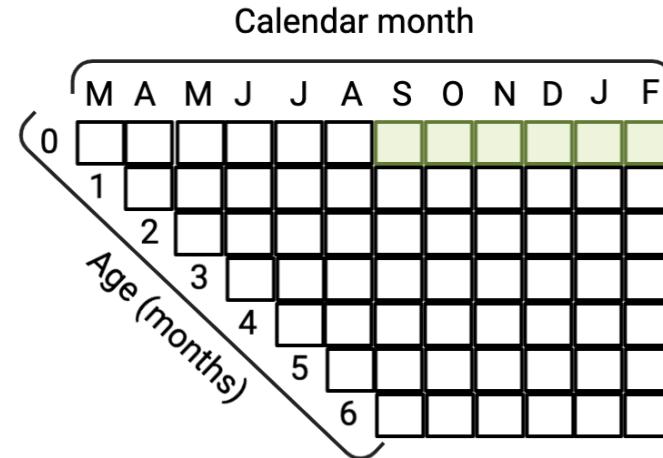
**Figure 4.** Figure 1b, taken from [Kampmann2023]. The Kaplan-Meier plots show the efficacy of RSVPreF3 vaccine in preventing Medically Attended RSV-Associated Lower Respiratory Tract Illness in infants.

0.093 (95% 0.001–0.237) of infants still have protection 365 days after vaccination.

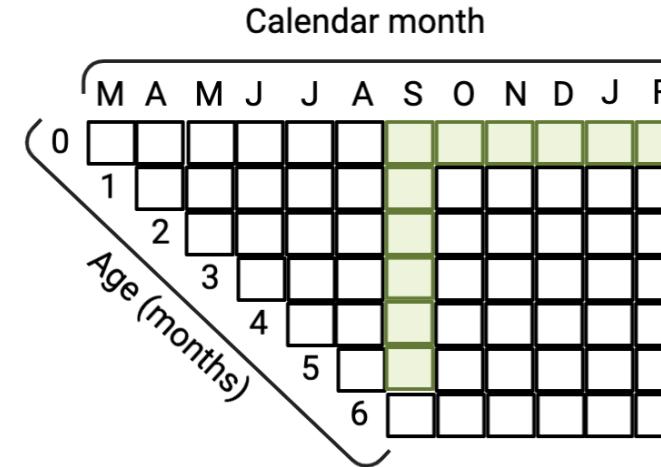
Health outcome	Efficacy $e_d$ (point-estimate, 180 days)	Disease protection proportion ( $f_d$ )
Infection	51.3%	0
Symptomatic	51.3%	0
GP consultations	51.3%	0
A + E attendances	69.4%	0.35
Hospital admission	69.4%	0.35
ICU admissions	69.4%	0.35
Death	69.4%	0.35

# Modelling monoclonal antibodies (implementation)

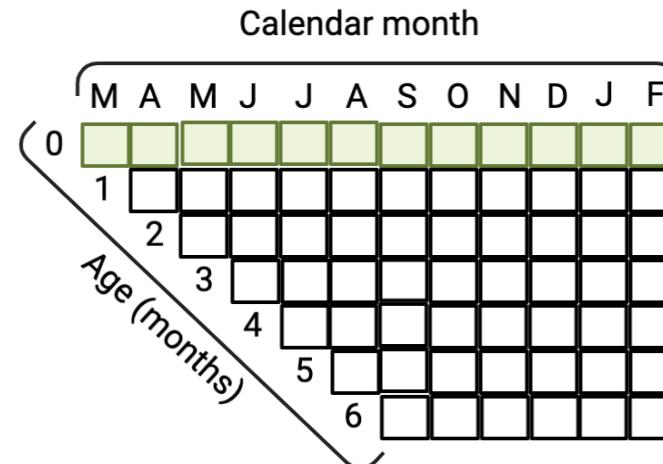
SEASONAL



SEASONAL + ANNUAL CATCH-UP

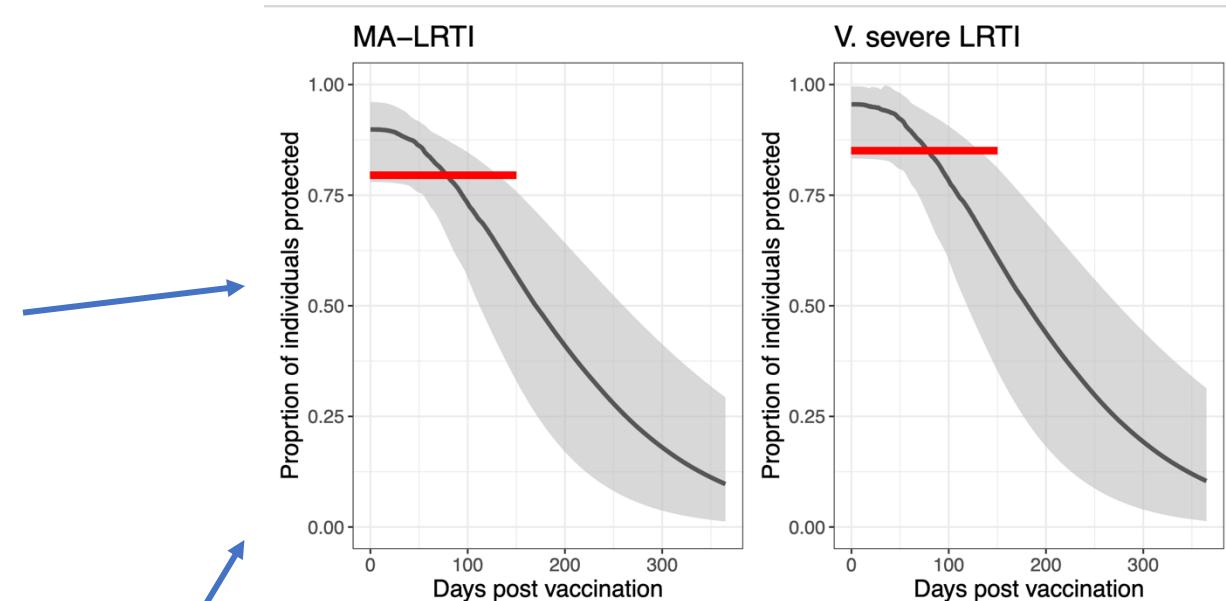
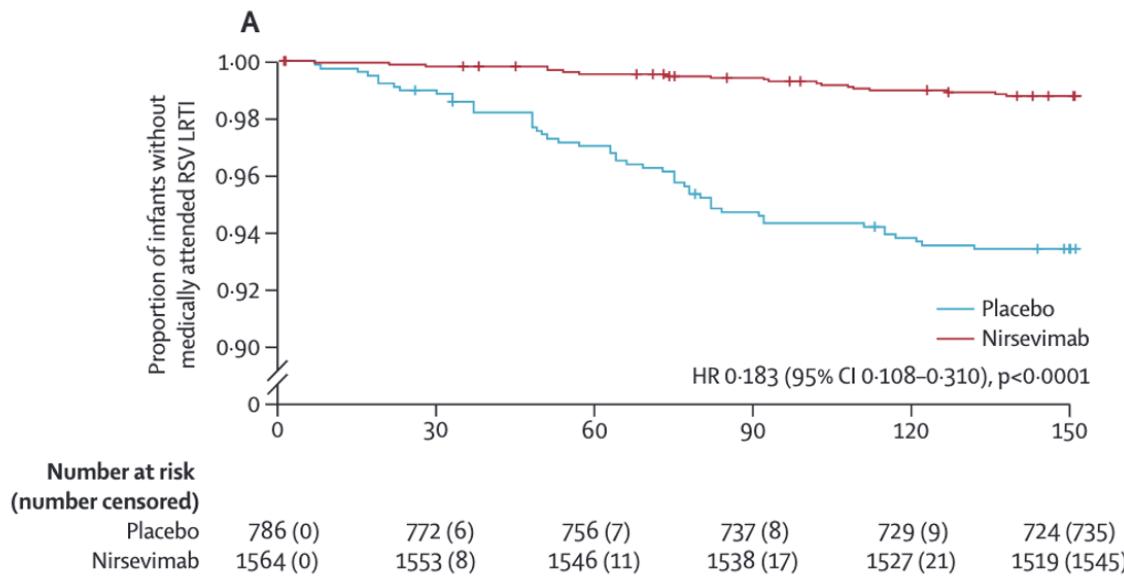


YEAR ROUND



**Coverage: 90% (as Vitamin K) (range: 70–90)**

# Modelling Ia-mAB (implementation)

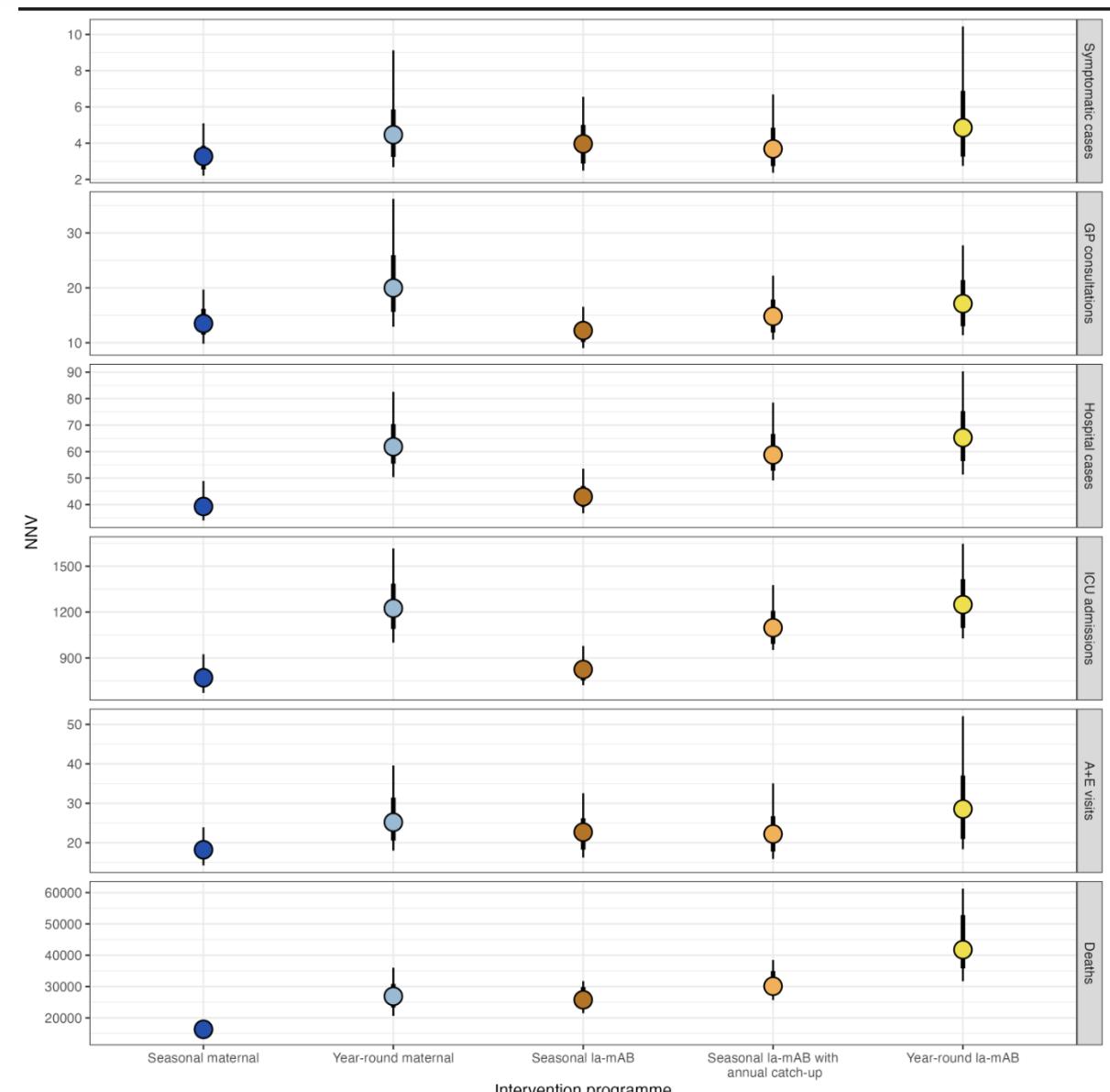
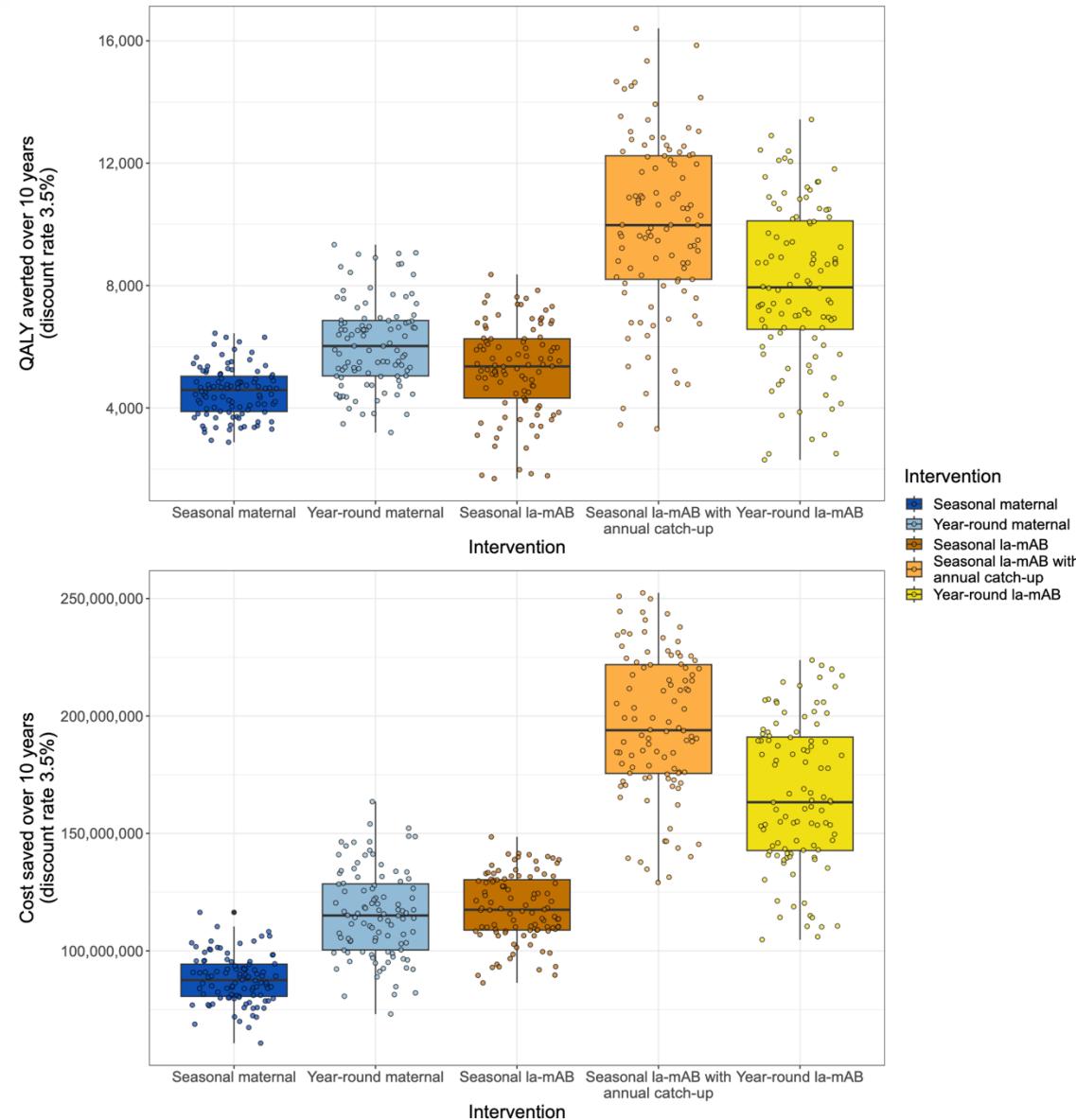


**Figure 7.** Figure 1A, taken from [Simoes2023]. The Kaplan-Meier plots show the efficacy of Nirsevimab in preventing Medically Attended RSV-Associated Lower Respiratory Tract Illness in infants.

0.148 (95% 0.015–0.338) of infants still have protection 365 days after vaccination.

Health outcome	Efficacy $e_d$ (point-estimate, 180 days)	Disease protection proportion ( $f_d$ )
Infection	79.5%	0
Symptomatic	79.5%	0
GP consultations	79.5%	0
A + E attendances	79.5%	0
Hospital admission	79.5%	0
ICU admissions	86.0%	0.08
Death	86.0%	0.08

# Comparison of impact



# Cost-effectiveness analysis

Cost-effectiveness analysis conducted according to NICE guidelines:

- Cost from perspective of NHS only (GBP)
- Health burden in QALYs
- 3.5% annual discount rate, 10-year time horizon
- ICER threshold at £20,000/QALY

Algorithm to determine most cost-effective programme (for a MC sample)

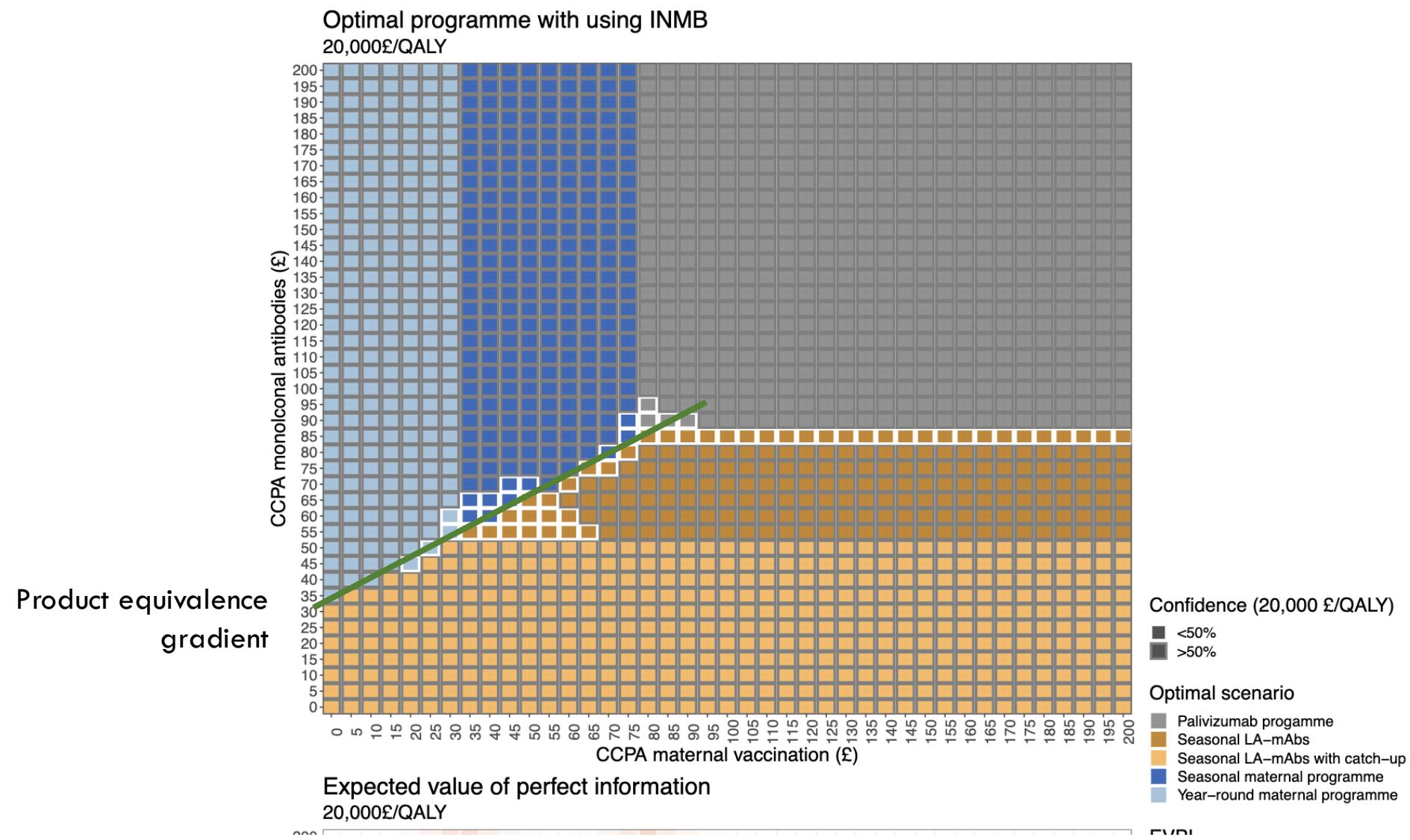
- A CCPA is picked for maternal vaccination (£0–200) + monoclonal antibodies (£0–200)
- Calculate costs (implementation + healthcare costs) for all five intervention programmes
- Calculate the INMB of each programme compared to Palivizumab only
- The programme with the greatest INMB is the most cost-effective programme

Blicke, Beutels 2022, *Med Decis Making*

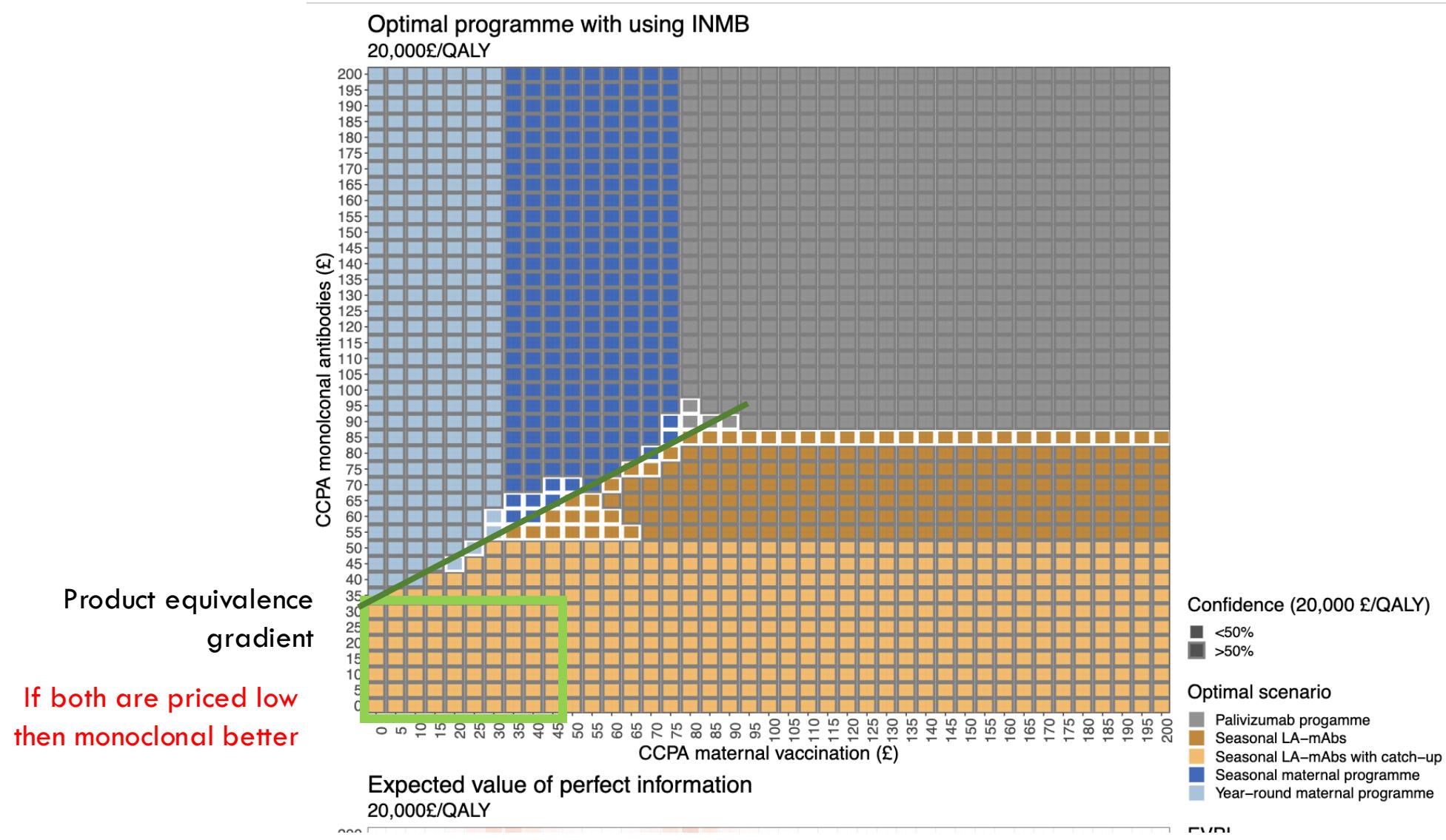
CCPA = cost of buying and administration of product per dose

NMB = (Incremental health gain) \* 20000 – (Incremental cost gain)

# Cost-effectiveness analysis



# Cost-effectiveness analysis

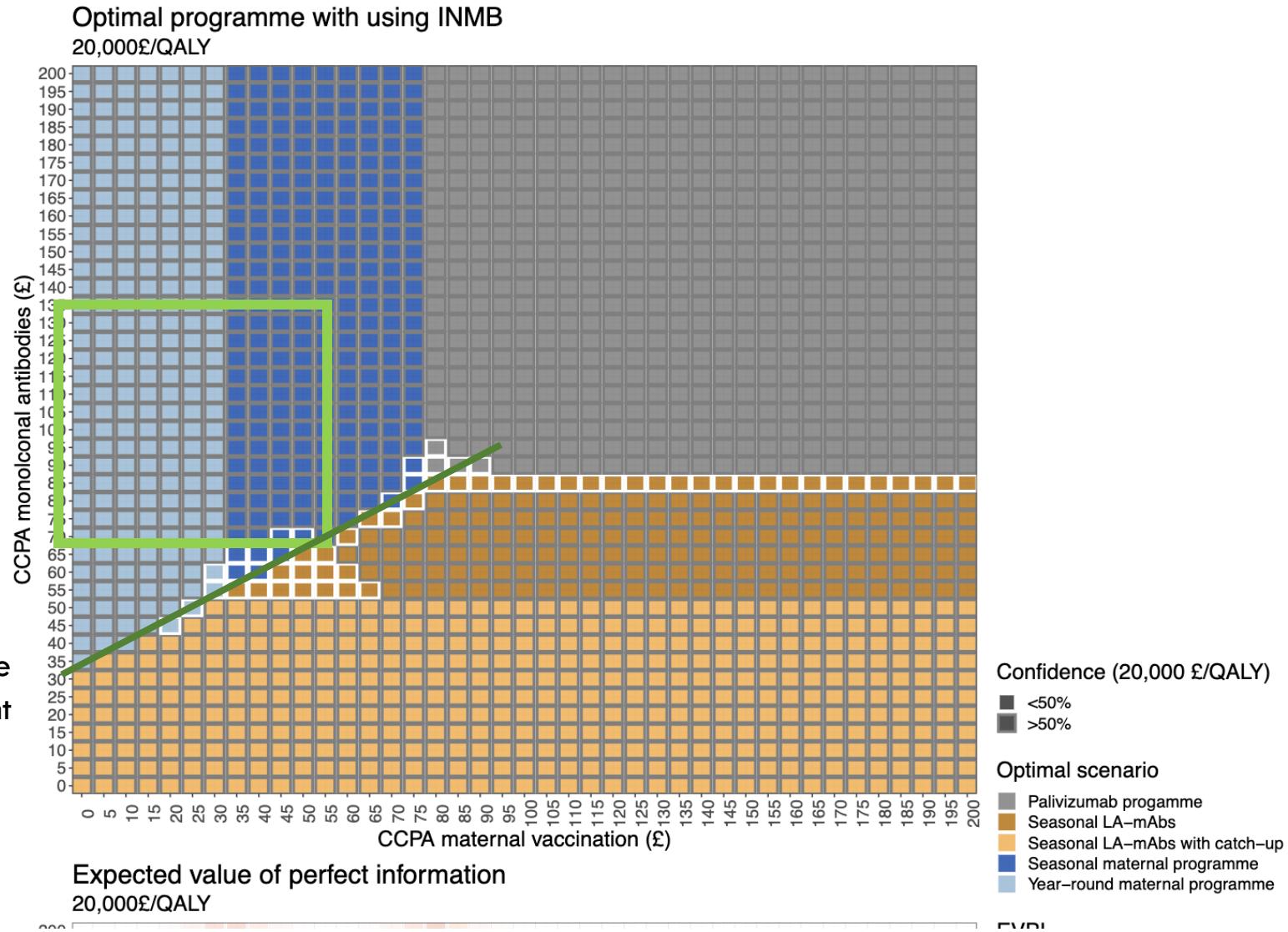


# Cost-effectiveness analysis

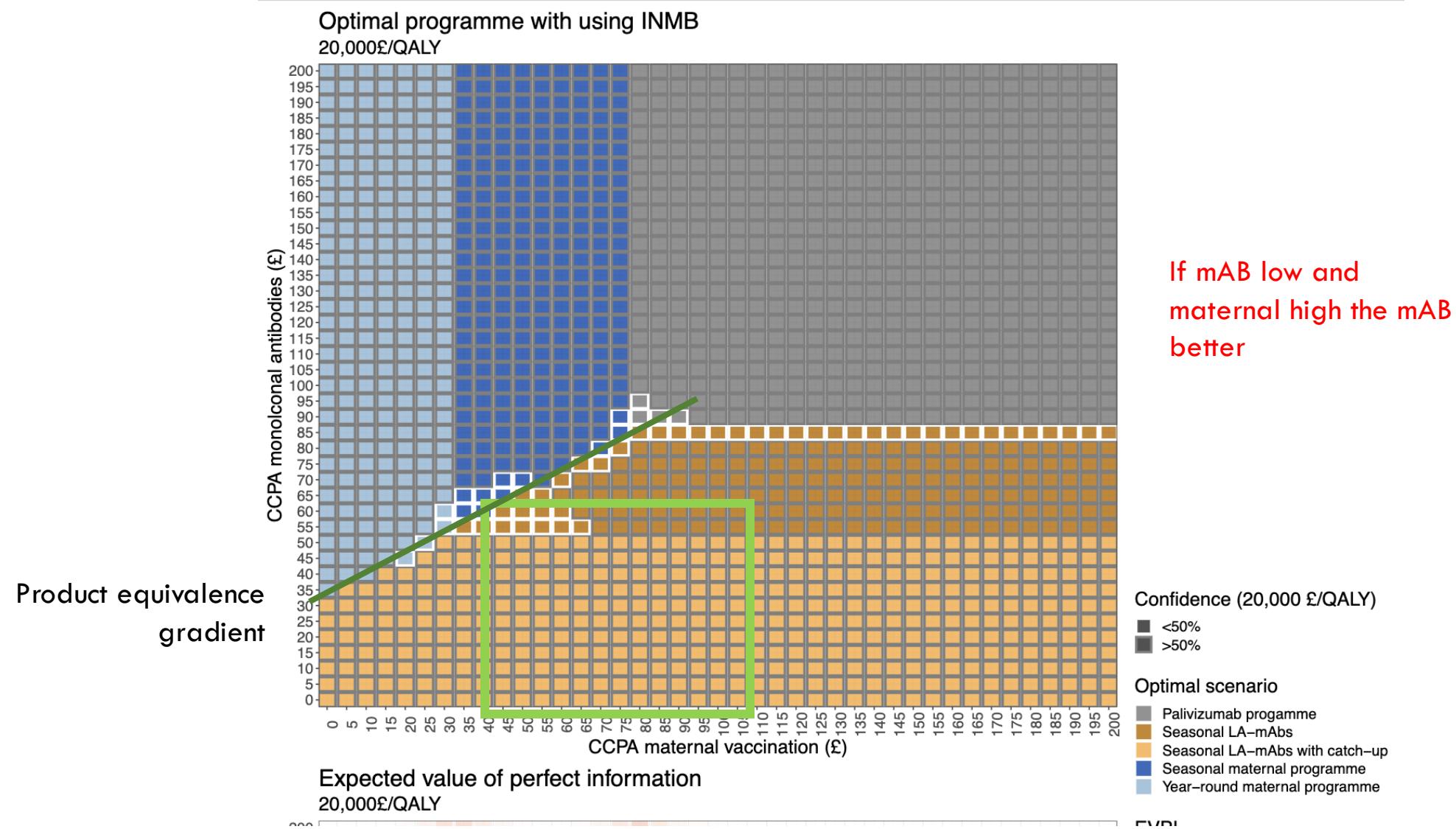


If mAB high and  
maternal low the  
maternal better

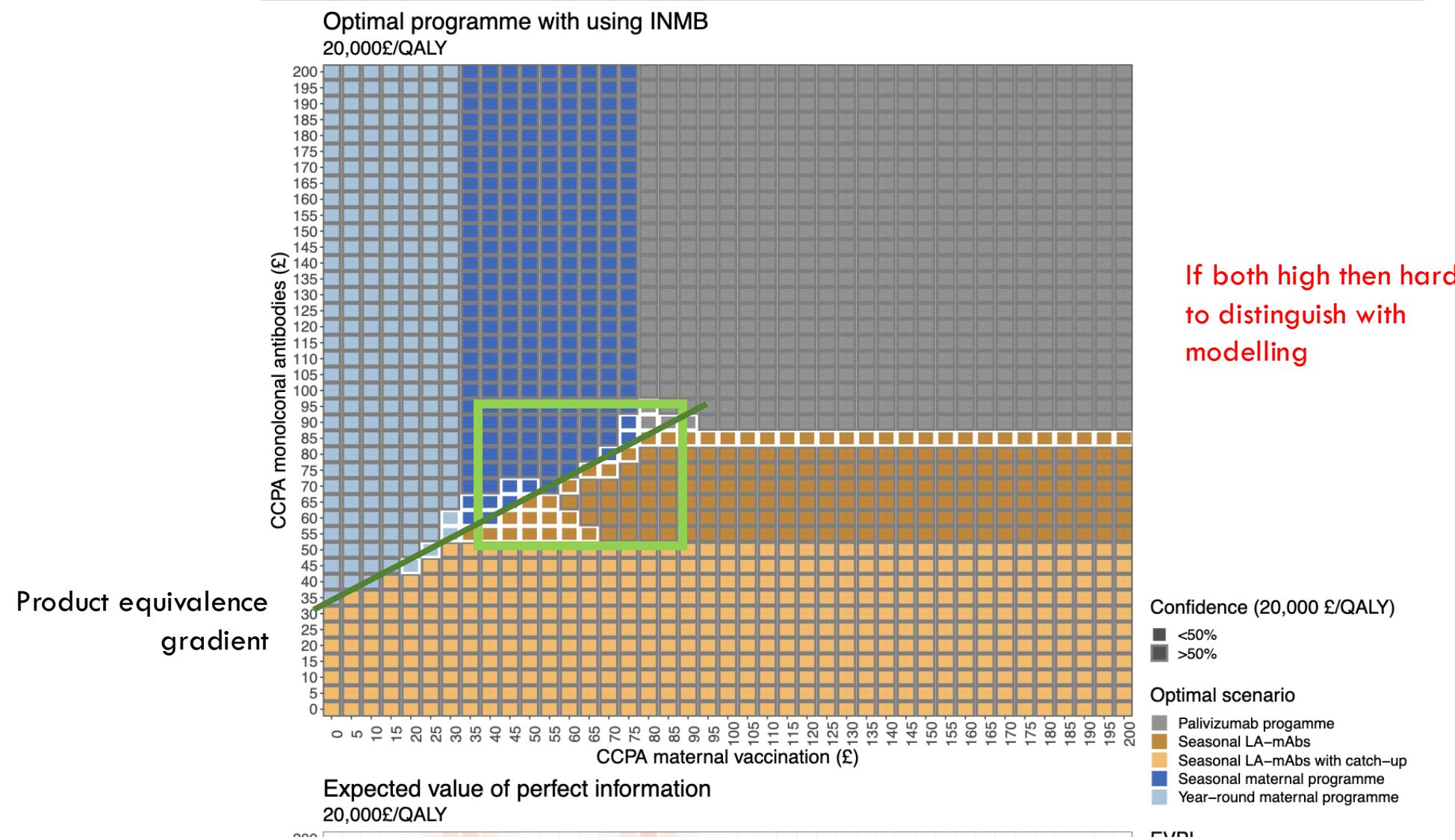
Product equivalence  
gradient



# Cost-effectiveness analysis



# Cost-effectiveness analysis



## **Maternal vaccine programme**

- Year-round cost-effective up until £30–35 (to pregnant women, 60% cov)
- Seasonal cost-effective up until £75–80 (July until December pregnant women, 60% cov)

## **Nirsevimab**

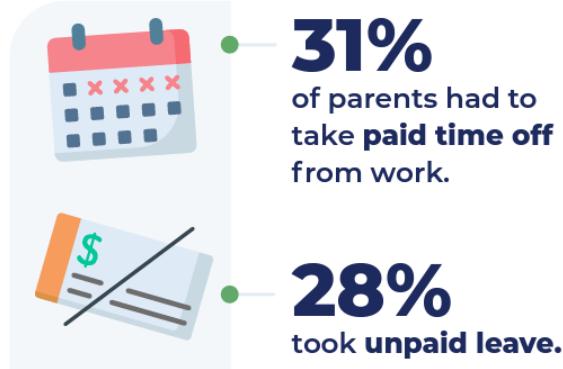
- Seasonal + catch-up cost-effective up until £50–55 (to birth, 90% cov)
- Seasonal cost-effective up until £85–90 (September until February to birth, 90% cov)

If priced similarly then difficult to differentiate between the two using CEA

# Limitations

Priced according to NICE's guidelines

- Healthcare-payers perspective only
  - no societal costs



Potential impacts on other respiratory diseases, particularly IPD

- HARMONIE IIIB study shows 54% reductions in ALL LRTD-respiratory disease

<https://www.globenewswire.com/news-release/2023/05/12/2667568/0/en/Press-Release-Nirsevimab-delivers-83-reduction-in-RSV-infant-hospitalizations-in-a-real-world-clinical-trial-setting.html>

[https://admin.allianceforpatientaccess.org/wp-content/uploads/2023/01/AfPA-and-NCfIH\\_The-Indirect-Impact-of-RSV\\_Survey-Report\\_Jan-2023.pdf](https://admin.allianceforpatientaccess.org/wp-content/uploads/2023/01/AfPA-and-NCfIH_The-Indirect-Impact-of-RSV_Survey-Report_Jan-2023.pdf)

Acceptability between products

Monoclonal never given at birth before, is 90% too high?

Maternal vaccination coverage varies (40–80%)

Looked at many different coverage assumptions when informing policy

# Acknowledgements

## Model development

Dr. Katie Atkins

Dr. Richard Pebody

Dr. Marc Baguelin

Dr. Jasmina Panovska-Griffiths

Prof Mark Jit

Prof Stefan Flasche



LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



## Further guidance on policy

Dr. Conall Watson

Dr. Edwin van Leeuwen

Dr. Neil Wilkins

Dr. Jonathon Crofts

+ Members of the JCVI

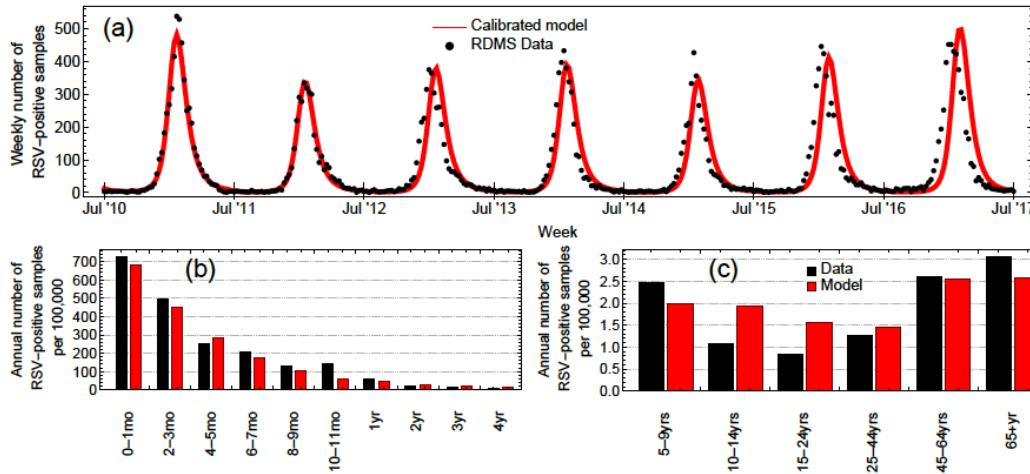




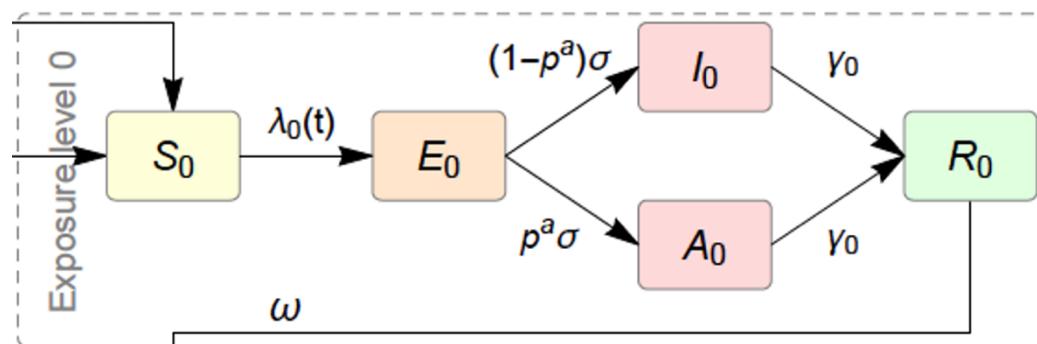
# Extra slides

# Modelling RSV transmission

## SEIRS model fitted to RDMS (RSV positive samples)



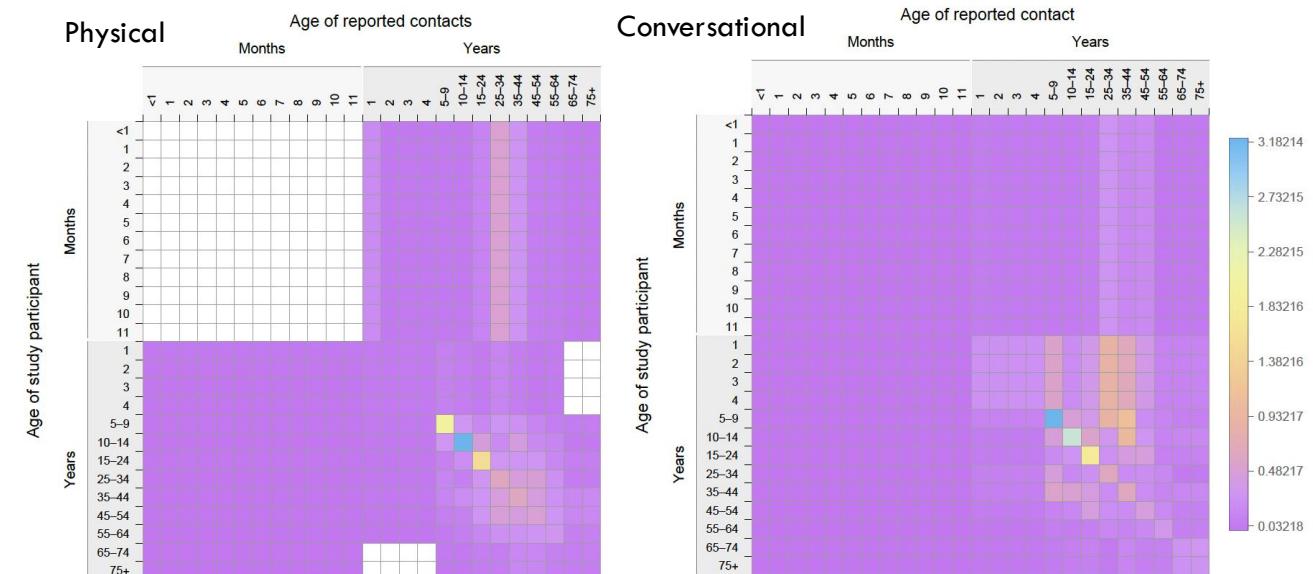
## SEIRS model per age group



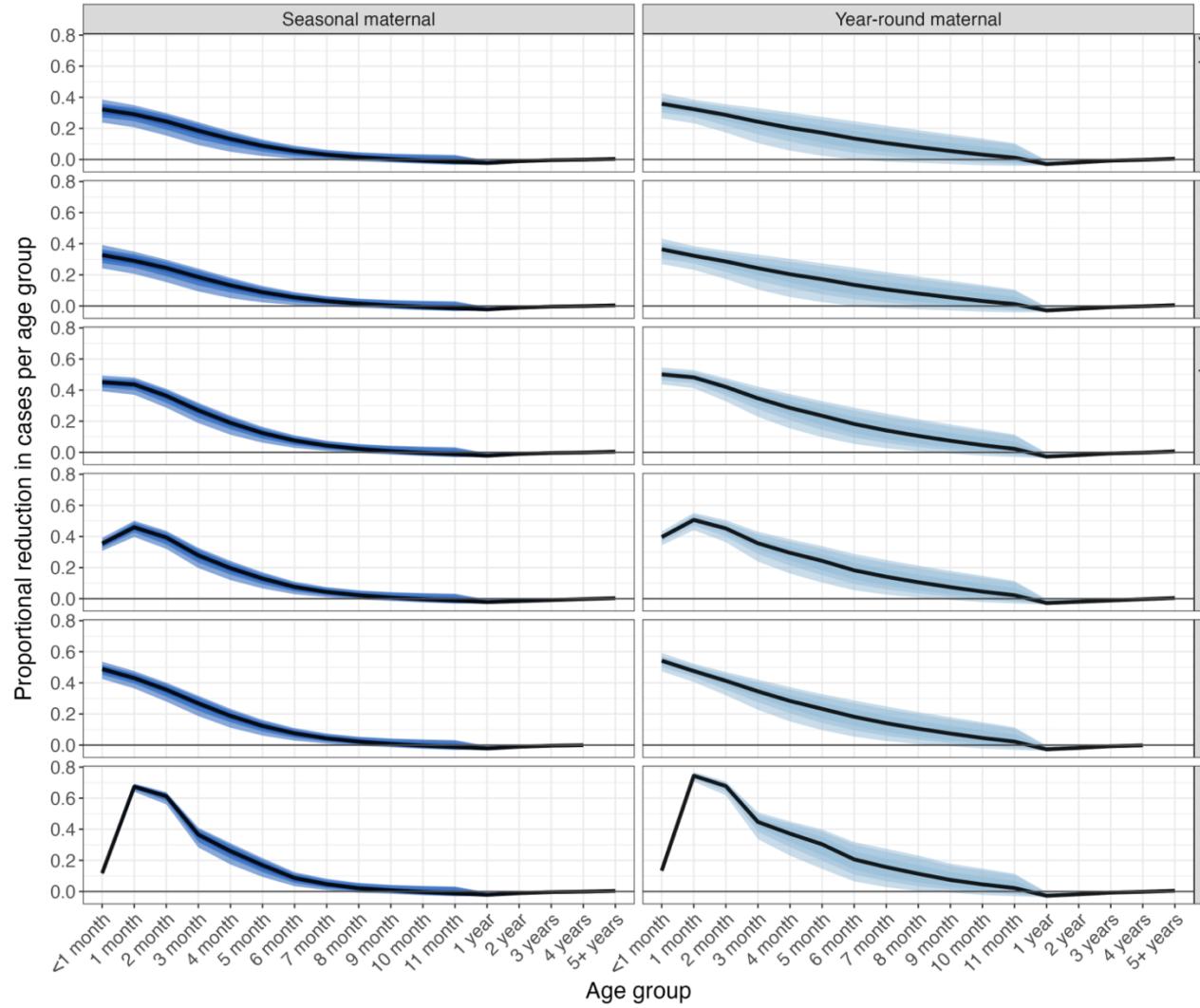
## 25 age groups:

Monthly up to 11 months, 1, 2, 3, 4, 5-9, 10-14, 15-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75+ years

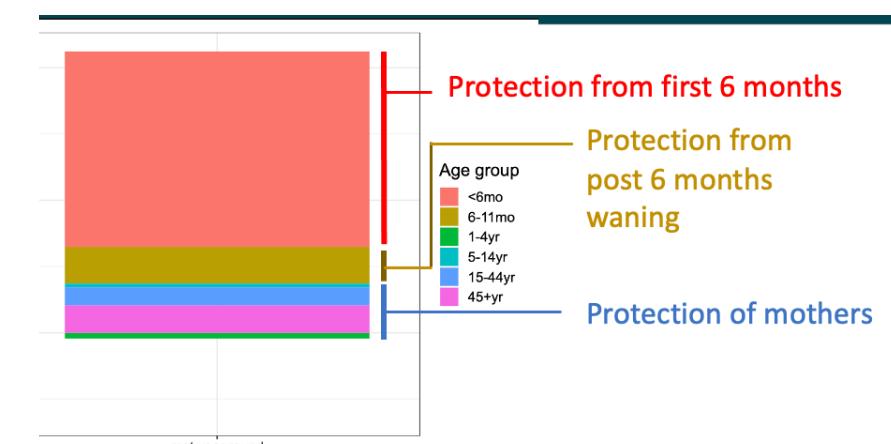
## Contact matrix from POLYMOD



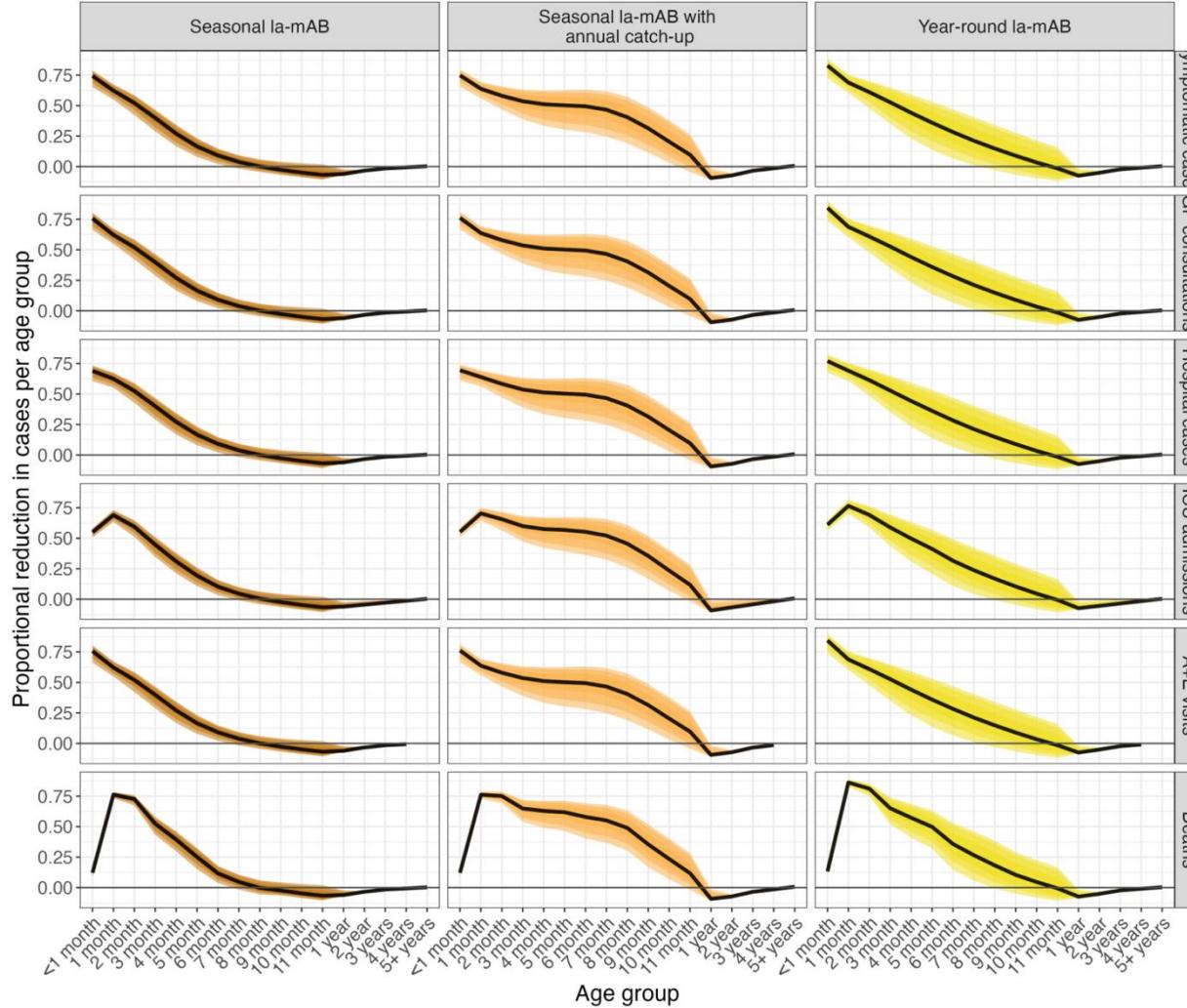
# Impact of MV programmes



Metric	Annual number of cases averted seasonal (mean, 95% CrI)	Annual number of cases averted year-round (mean, 95% CrI)
Symptomatic	64,079 (39,999-91,887)	94,754 (44,705-152,103)
GP cons.	15,225 (10,324-20,700)	20,705 (11,261-31,570)
A + E visit	11,307 (8,508-14,257)	16,284 (10,300-22,663)
Hospital cases	5,162 (4,154-5,979)	6,587 (4,939-8,092)
ICU admissions	264 (220-303)	333 (252-408)
Deaths	13 (11-15)	15 (11-20)



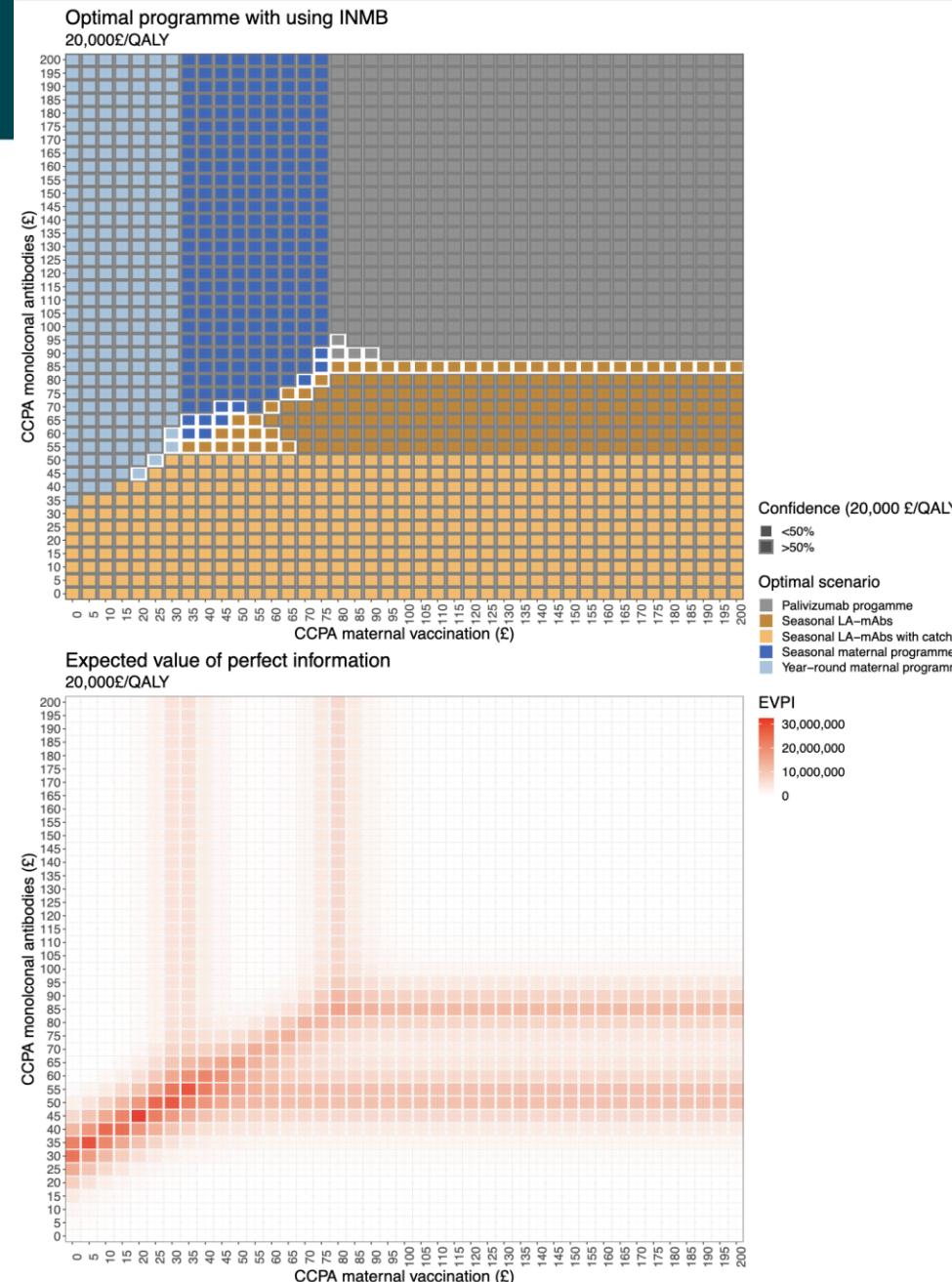
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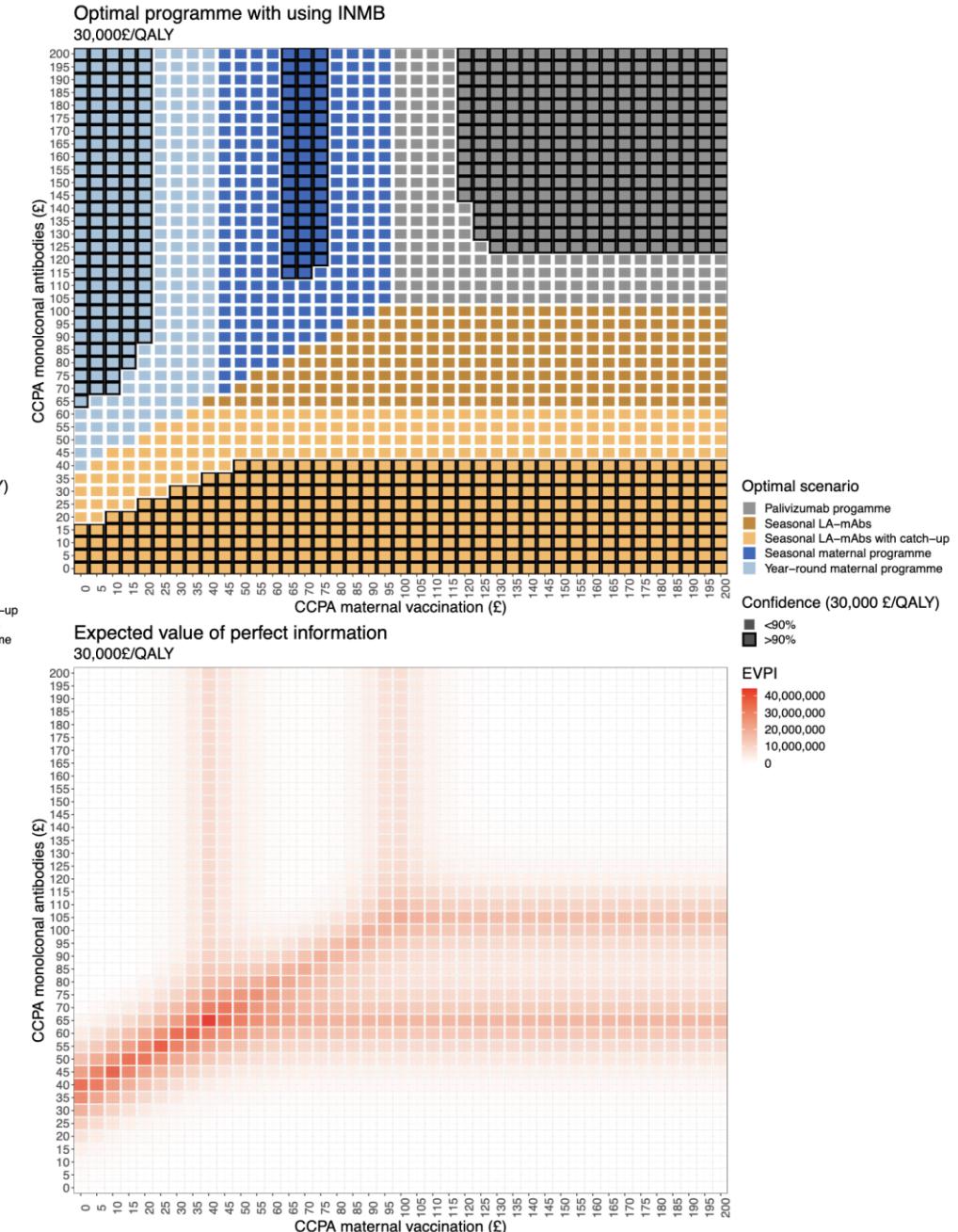
Metric	Annual number of cases averted seasonal (Ia-mAB) (mean, 95% CrI)	Annual number of cases averted seasonal (Ia-mAB) + annual catch-up (mean, 95% CrI)	Annual number of cases averted year-round (Ia-mAB) (mean, 95% CrI)
Symp.	82660 (47095-124161)	176110 (93511-263758)	136835 (59448-225610)
GP cons.	26102 (18677-34211)	43283 (28118-59113)	37606 (22342-54421)
A + E visit	14137 (9494-19032)	28881 (17837-39319)	22631 (11904-33786)
Hospital cases	7171 (5771-8414)	10549 (7958-12720)	9562 (6864-12066)
ICU admissions	377 (316-428)	570 (454-656)	499 (376-603)
Deaths	12 (10-14)	20 (16-24)	15 (10-20)

## Short-stay costs

Max £75–80 a dose of maternal vaccine (20k ICER)

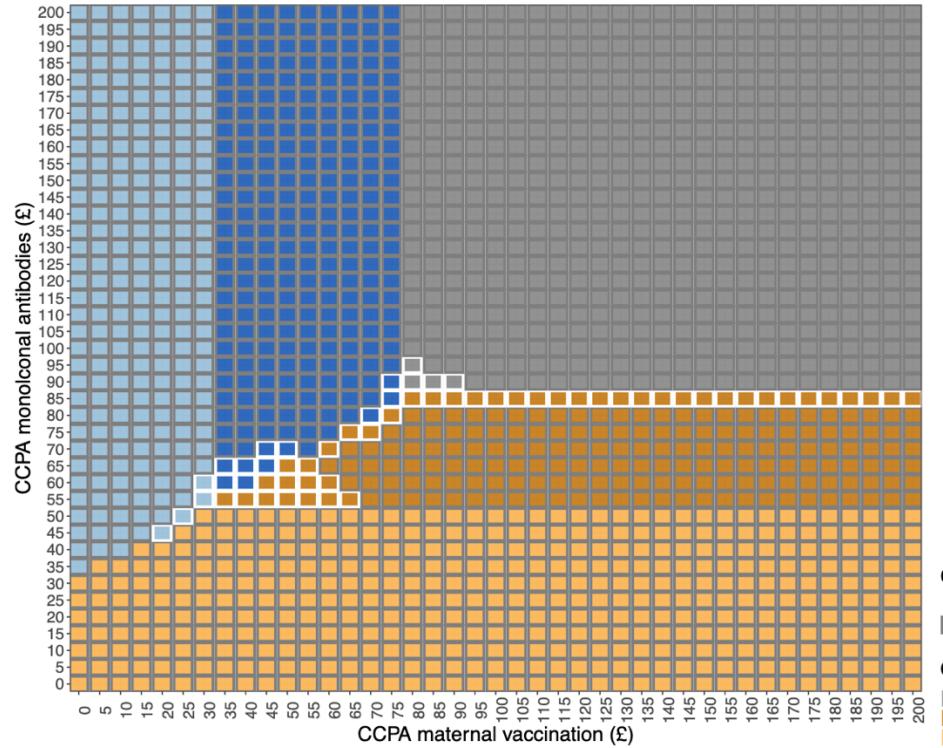


Max £85–90 a dose for LA-mAbs (20k ICER)



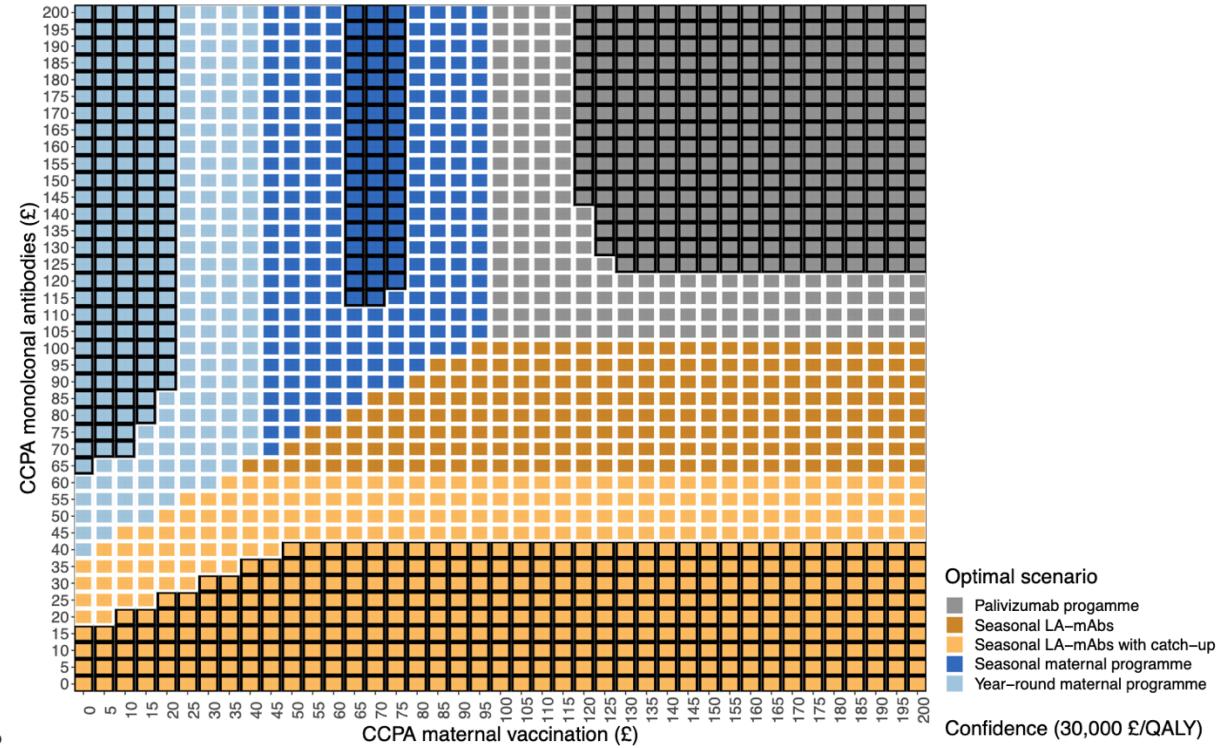
More uncertainty

Optimal programme with using INMB  
20,000£/QALY



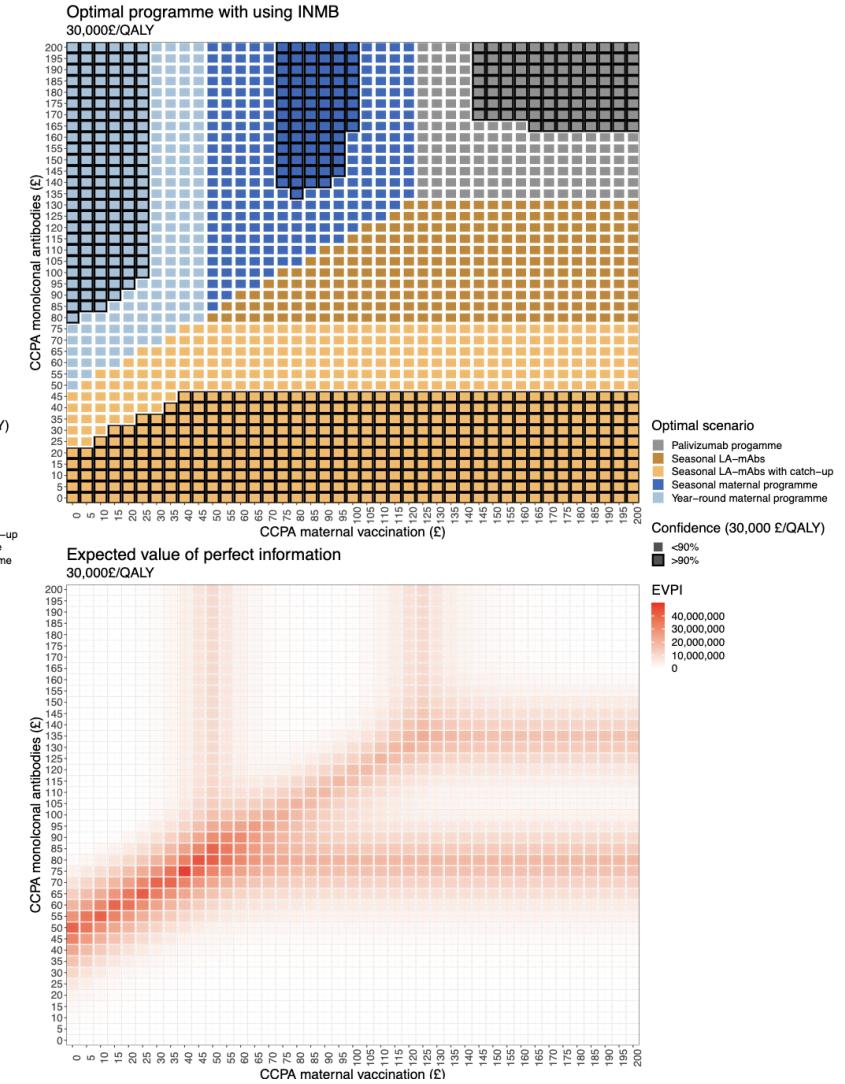
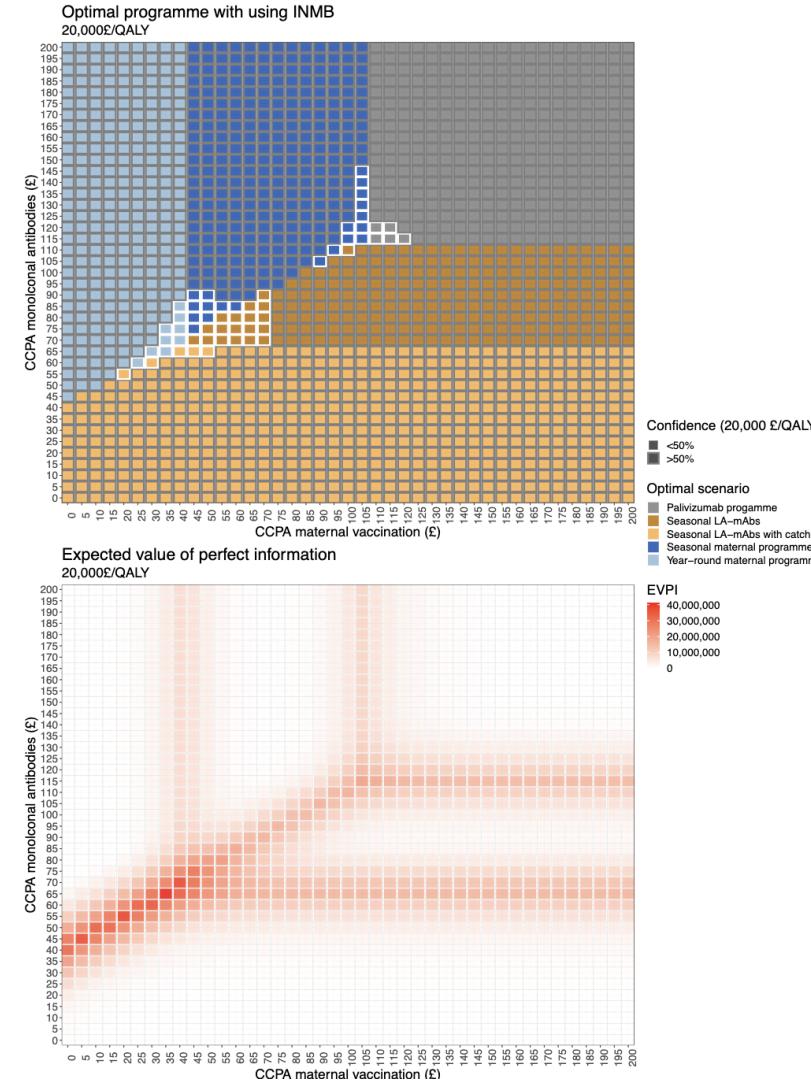
Expected value of perfect information  
20.000£/QALY

Optimal programme with using INMB  
30,000£/QALY

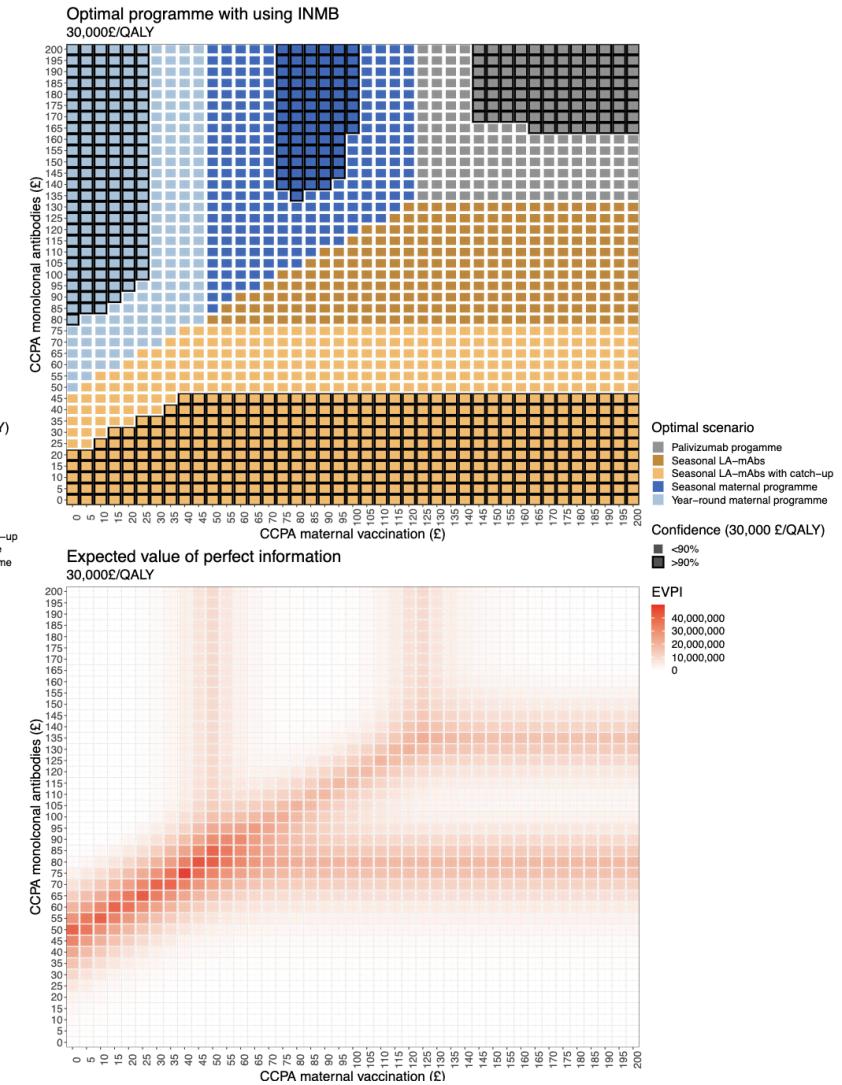
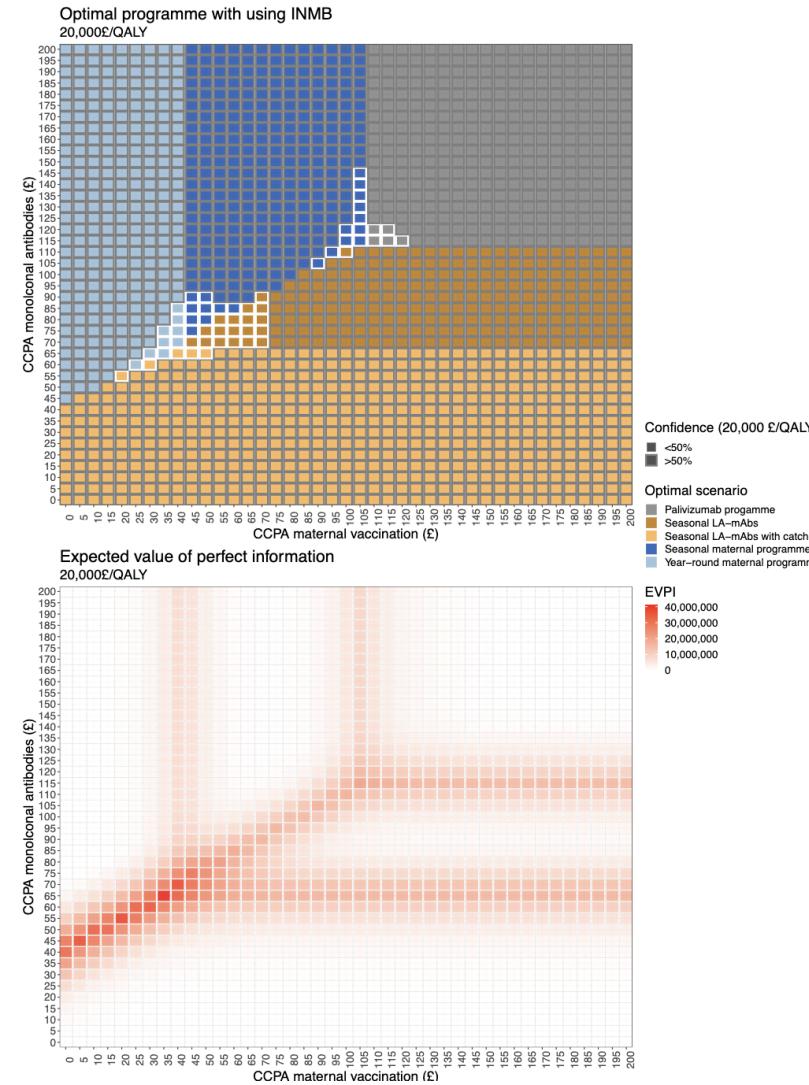


Expected value of perfect information  
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## No catch-up for LA-mAbs

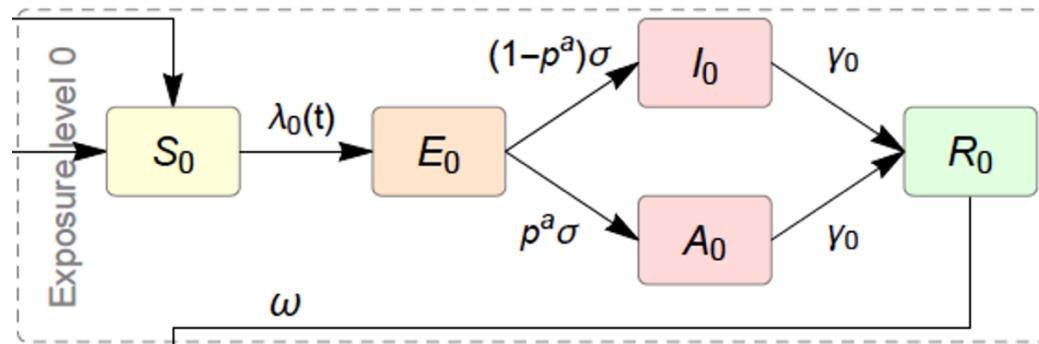


## Long + short-stay costs



# Modelling RSV transmission

SEIRS model fitted to RDMS (RSV positive samples)



S: susceptible

E: exposure but not yet infectious

A: Infected but asymptomatic

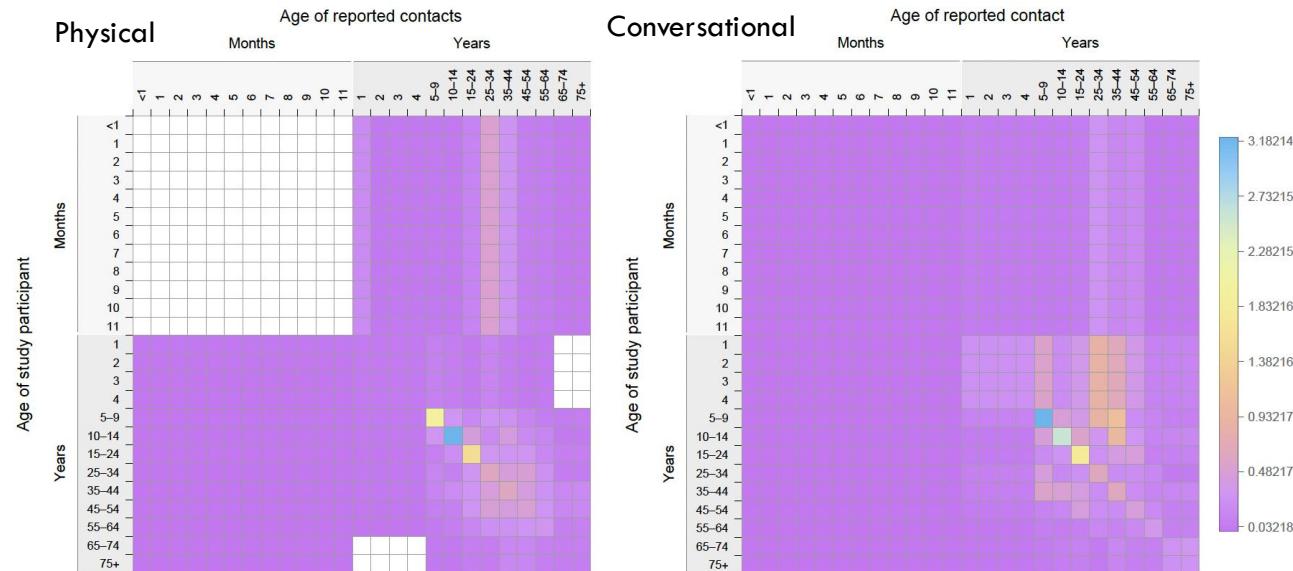
I: Infected but symptomatic

R: Post-infection immunity (temp)

25 age groups:

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Contact matrix from POLYMOD



# Update risks



## Symptomatic cases

- Taken from model



## GP consultations

- Cromer et al. 2017 *Lancet Public Health*
- Taylor et al. 2016 *BMJ*
- Fleming et al. 2015 *BMC Inf Dis*



## A+E

- Ajayi-Obe et al. 2008 *Epidemiol Infect*



## Hospital cases

- Reeves et al. 2017 *Influenza Other Respir Viruses*
- Reeves et al. 2019 *J Infect*
- Taylor et al. 2016 *BMJ*
- Sharp et al. 2022 *Influenza Other Respir Viruses*



## ICU

- Thwaites et al. 2020 *Eur J Pediatr*
- Walsh et al. 2022 *Health Sci Rep*

Annual burden health outcomes of RSV in England and Wales



Estimated risk of health outcome per infection

## Deaths

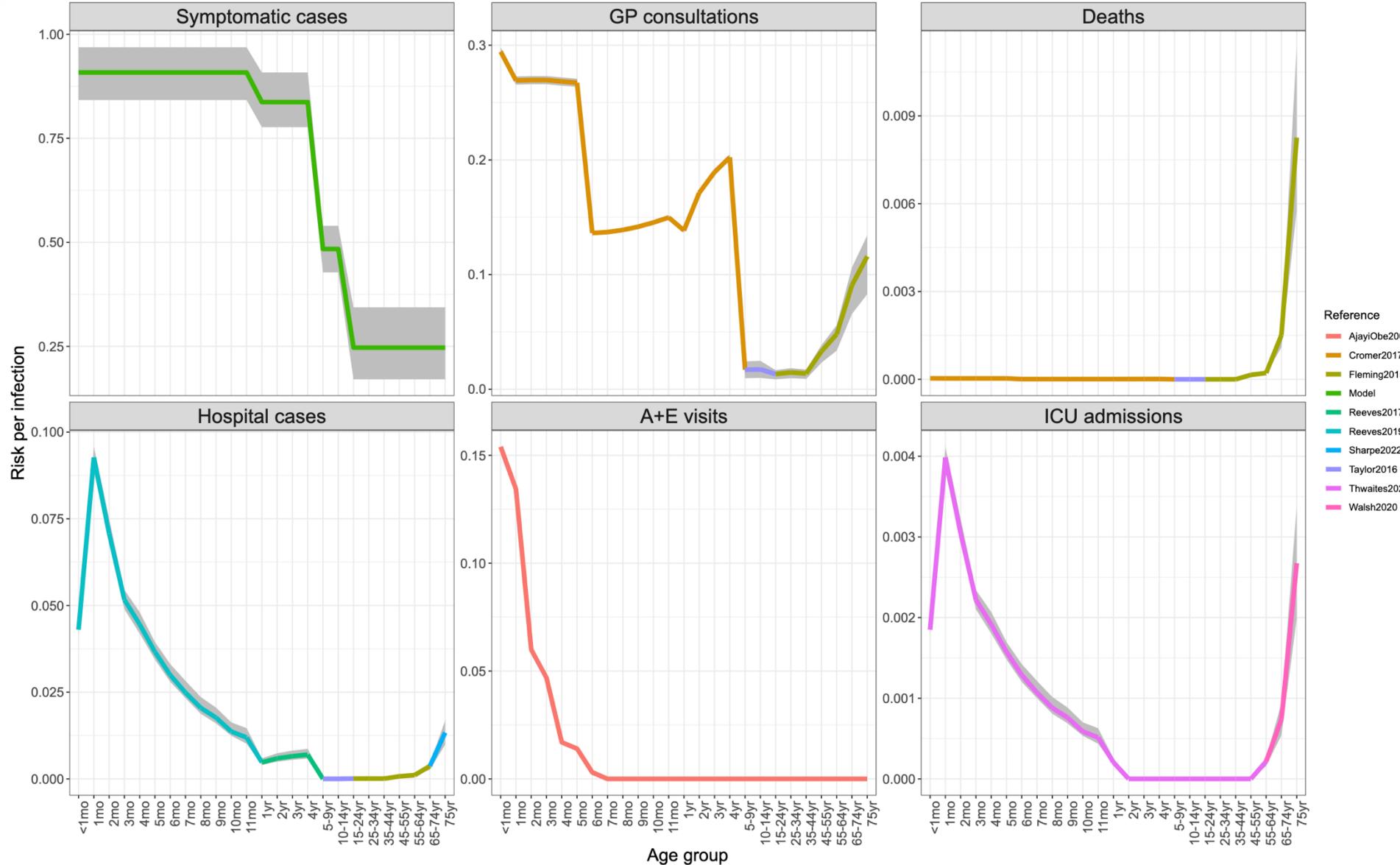
- Cromer et al. 2017 *Lancet Public Health*
- Li et al. 2023 *Infect Dis Ther*



# Update risks



**Risk per infection:**  
outcome incidence/  
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# Updated Economic parameters

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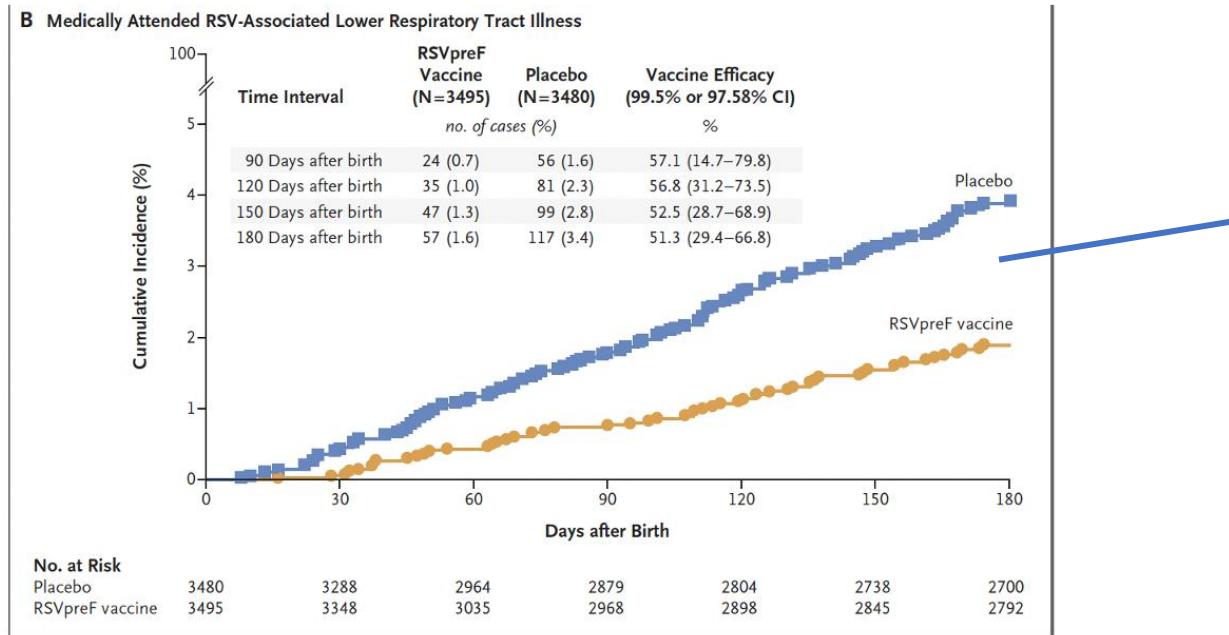
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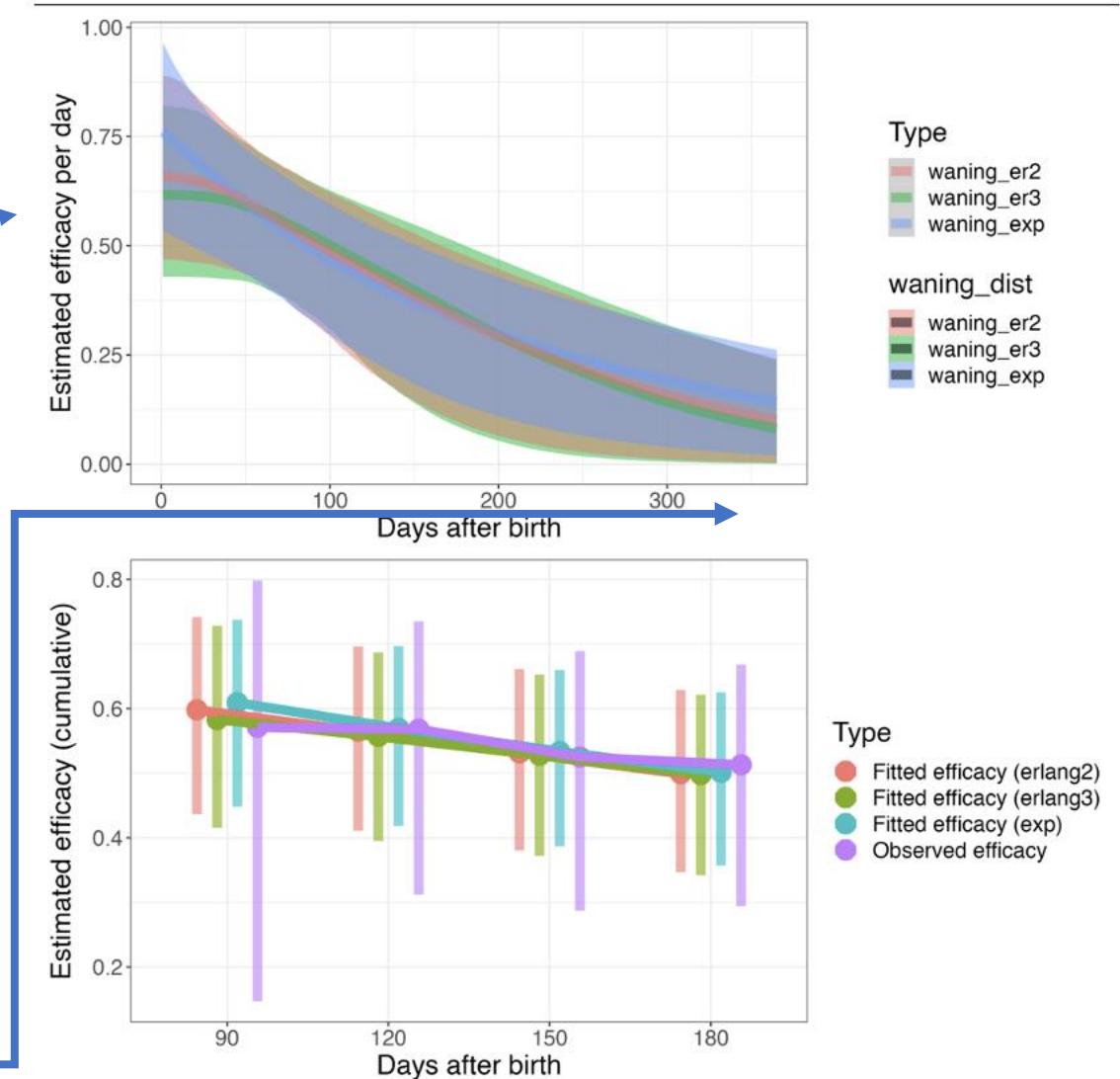
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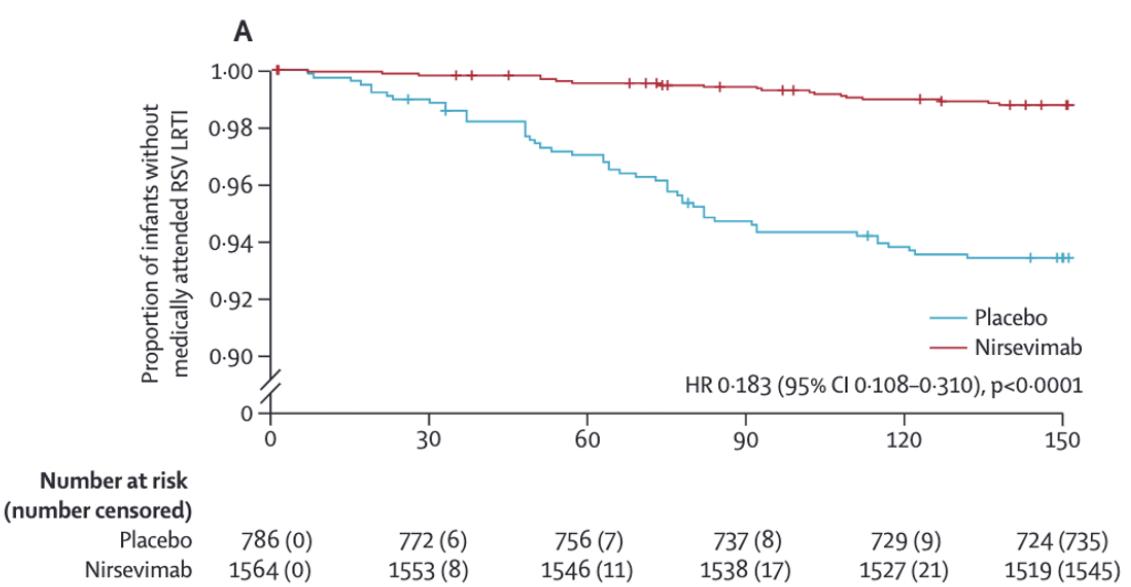
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A + E attendances	69.4%	0.35
Hospital admission	69.4%	0.35
ICU admissions	69.4%	0.35
Death	69.4%	0.35

0.093 (95% 0.001–0.237)  
of infants still have  
protection 365 days after  
vaccination.



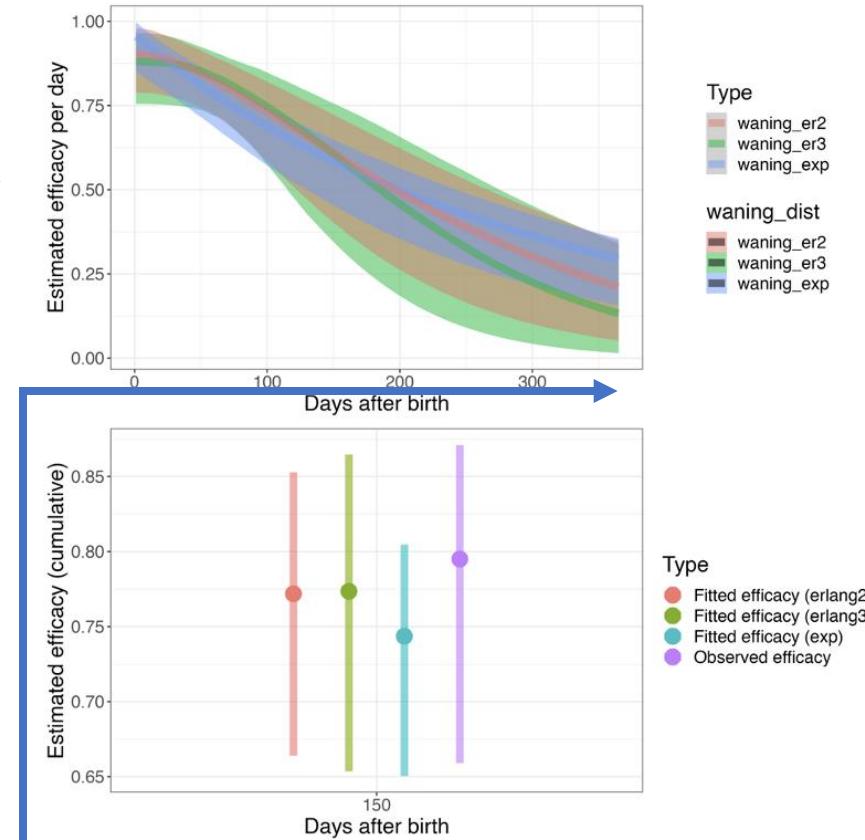
# Modelling Ig-mAB (implementation)



**Figure 7.** Figure 1A, taken from [Simoes2023]. The Kaplan-Meier plots show the efficacy of Nirsevimab in preventing Medically Attended RSV-Associated Lower Respiratory Tract Illness in infants.

Health outcome	Efficacy $e_d$ (point-estimate, 180 days)	Disease protection proportion ( $f_d$ )
Infection	79.5%	0
Symptomatic	79.5%	0
GP consultations	79.5%	0
A + E attendances	79.5%	0
Hospital admission	79.5%	0
ICU admissions	86.0%	0.08
Death	86.0%	0.08

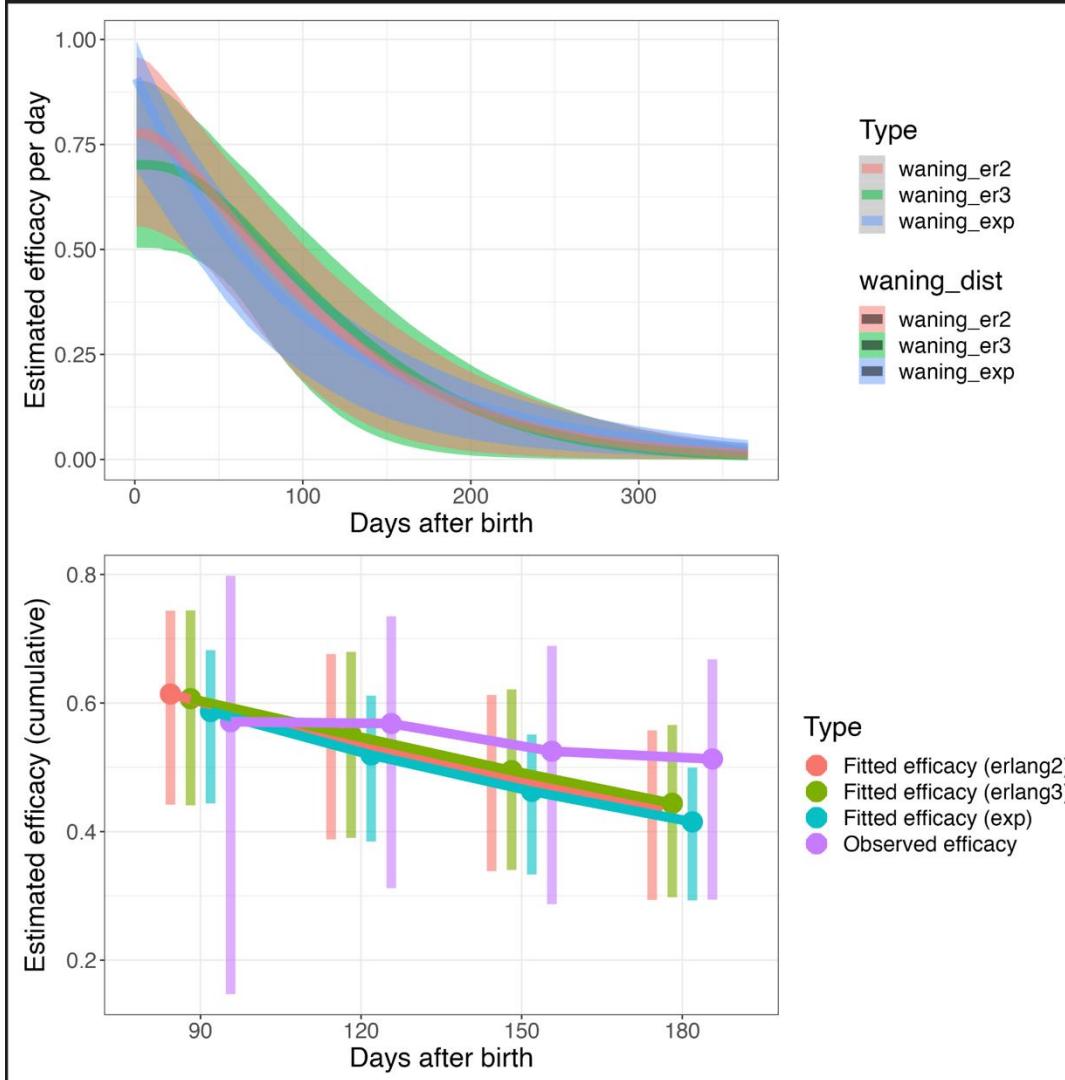
0.148 (95% 0.015–0.338) of infants still have protection 365 days after vaccination.



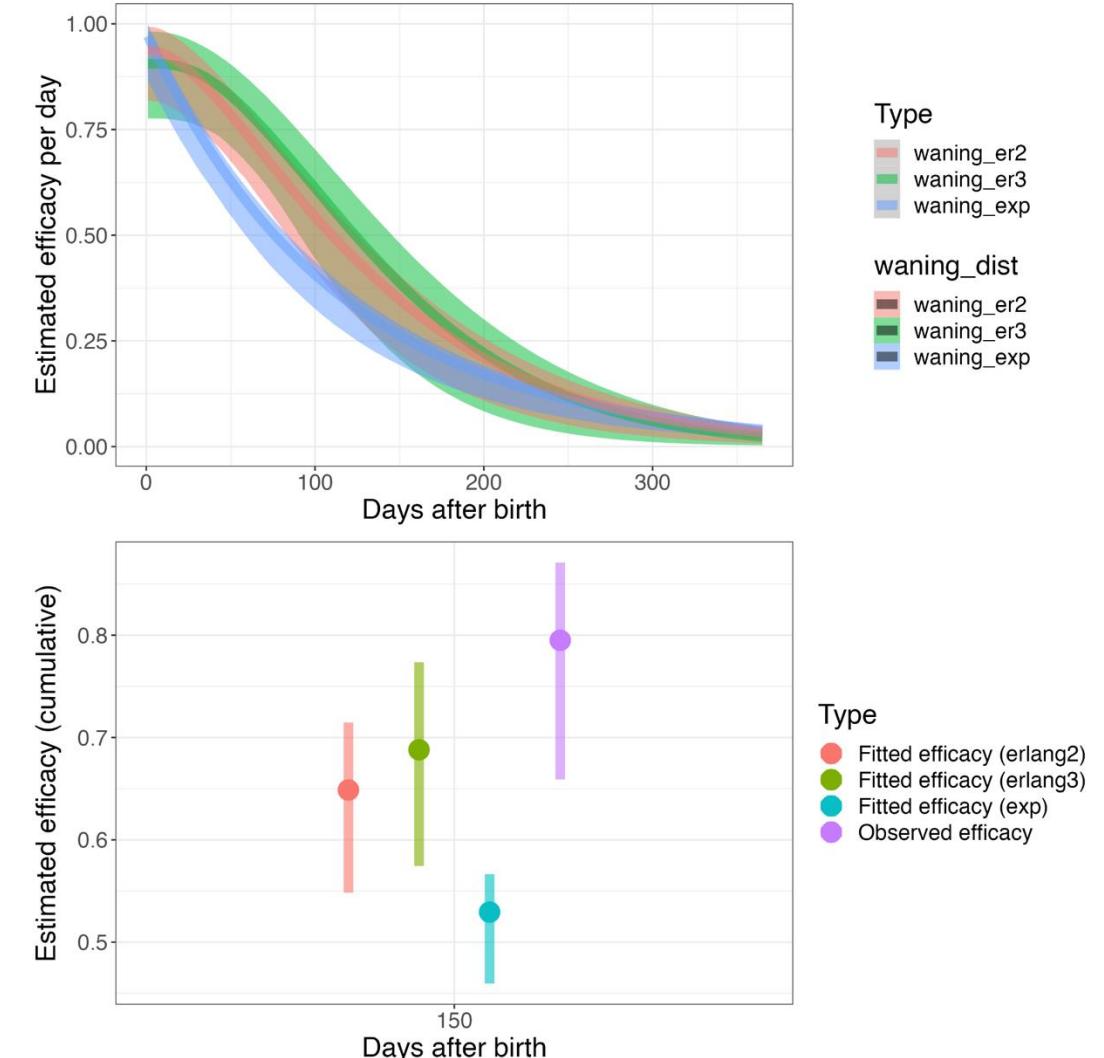
**Figure 9.** The posterior distributions and comparison to the quoted  $e$

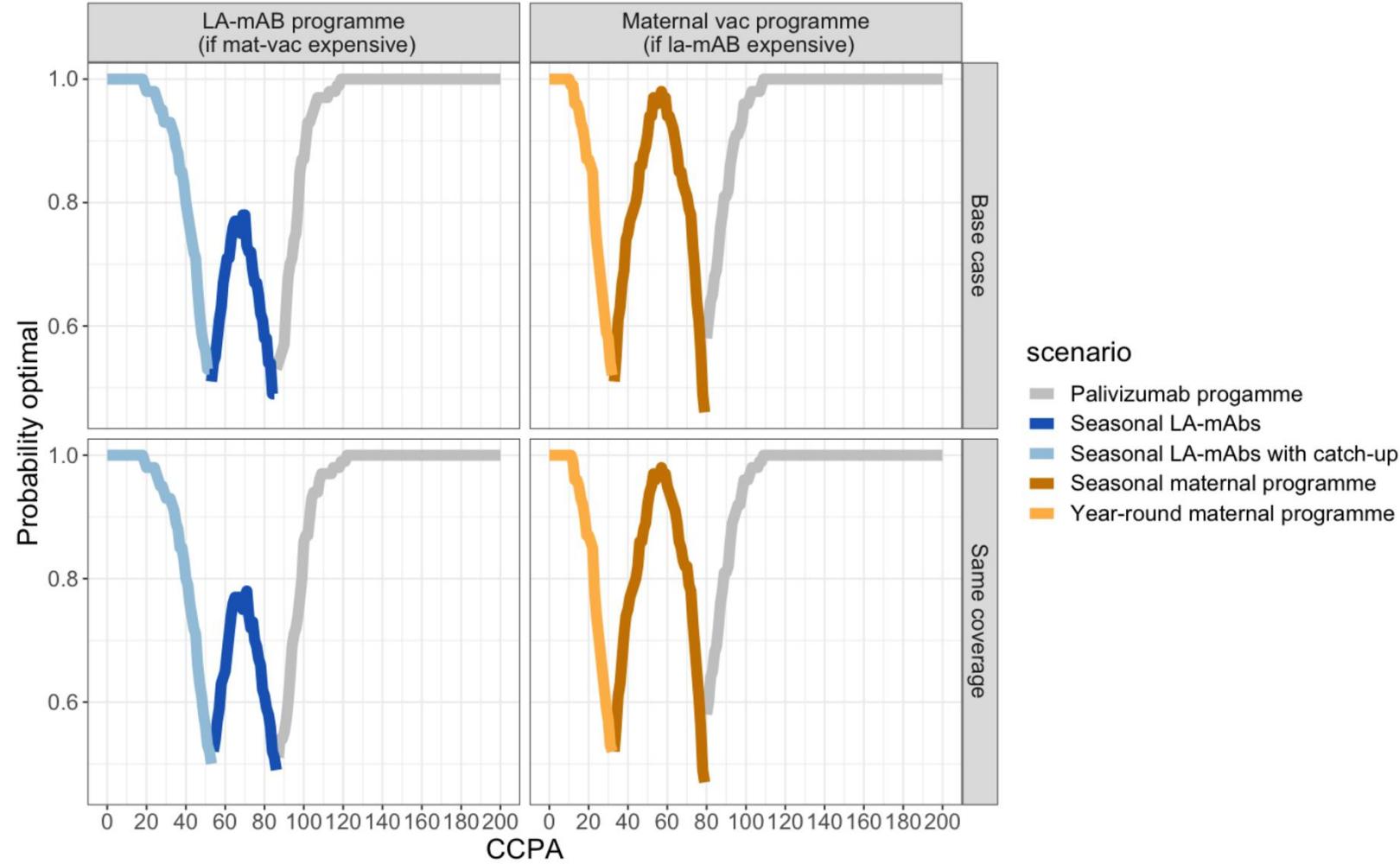
# Bounded efficacy (single year)

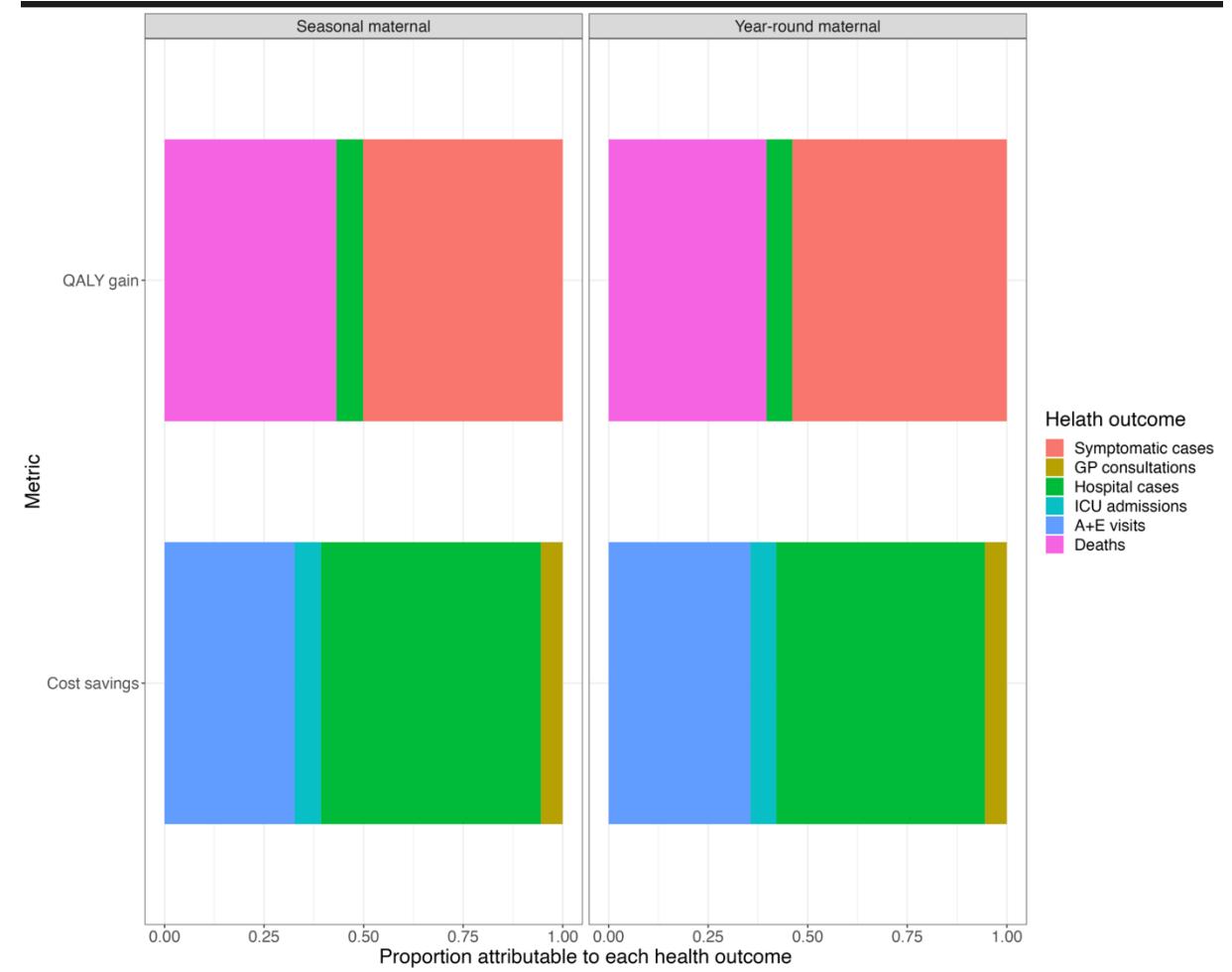
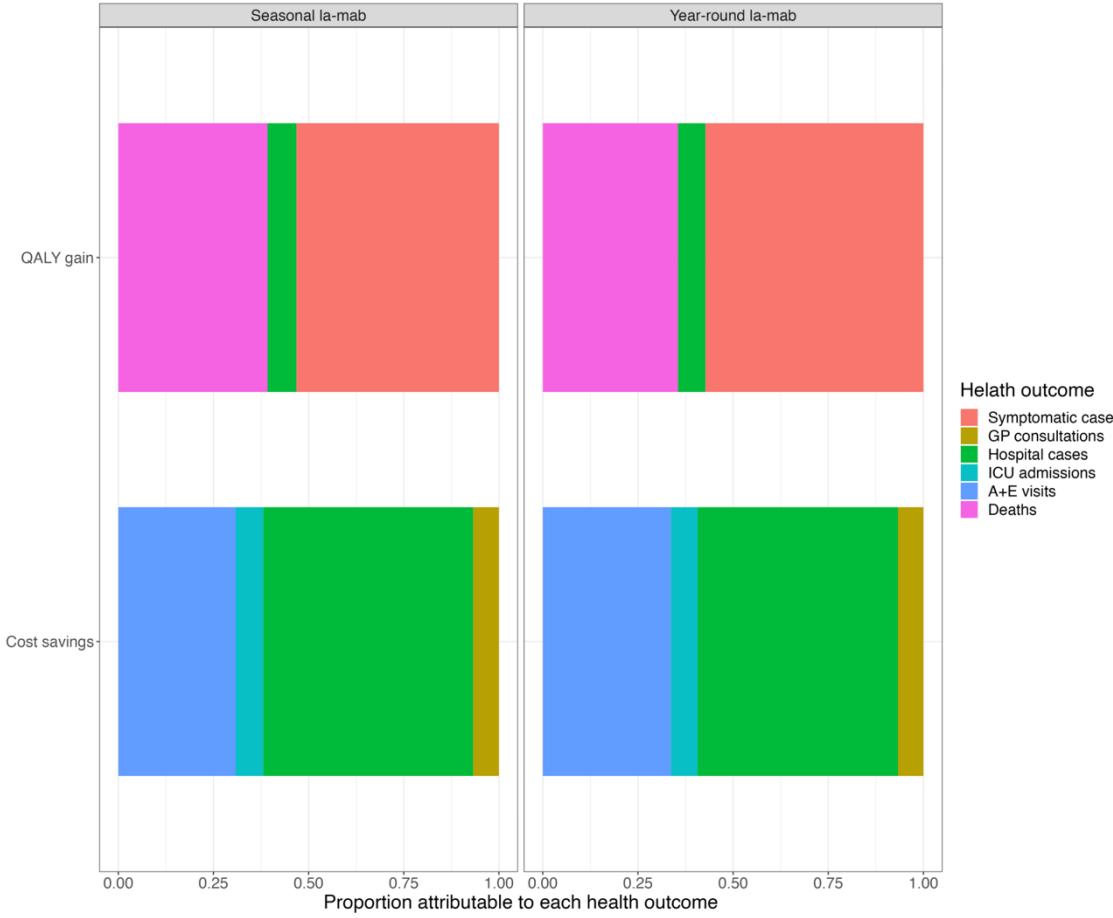
## Maternal vaccination

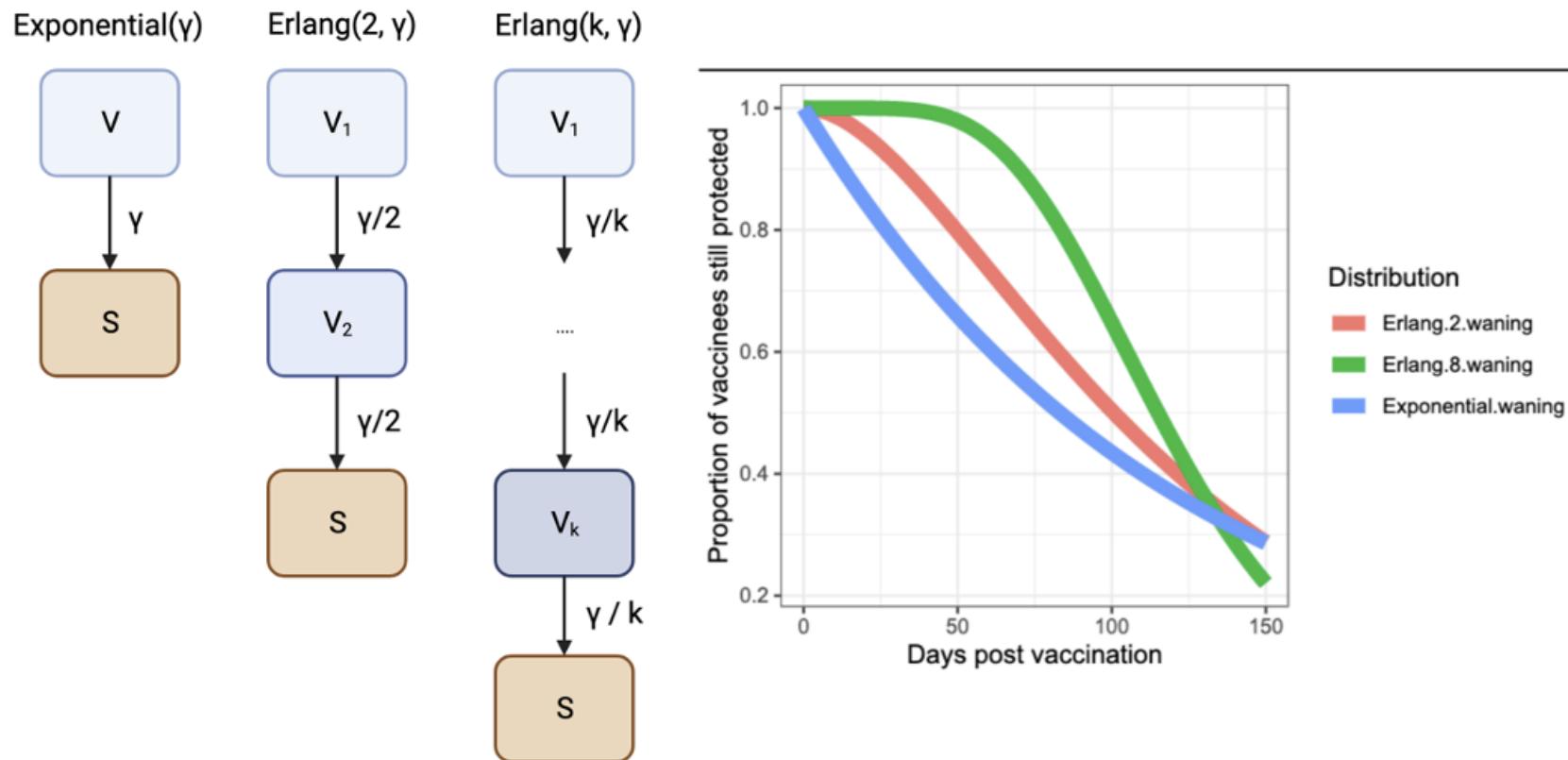


## Monoclonal antibodies

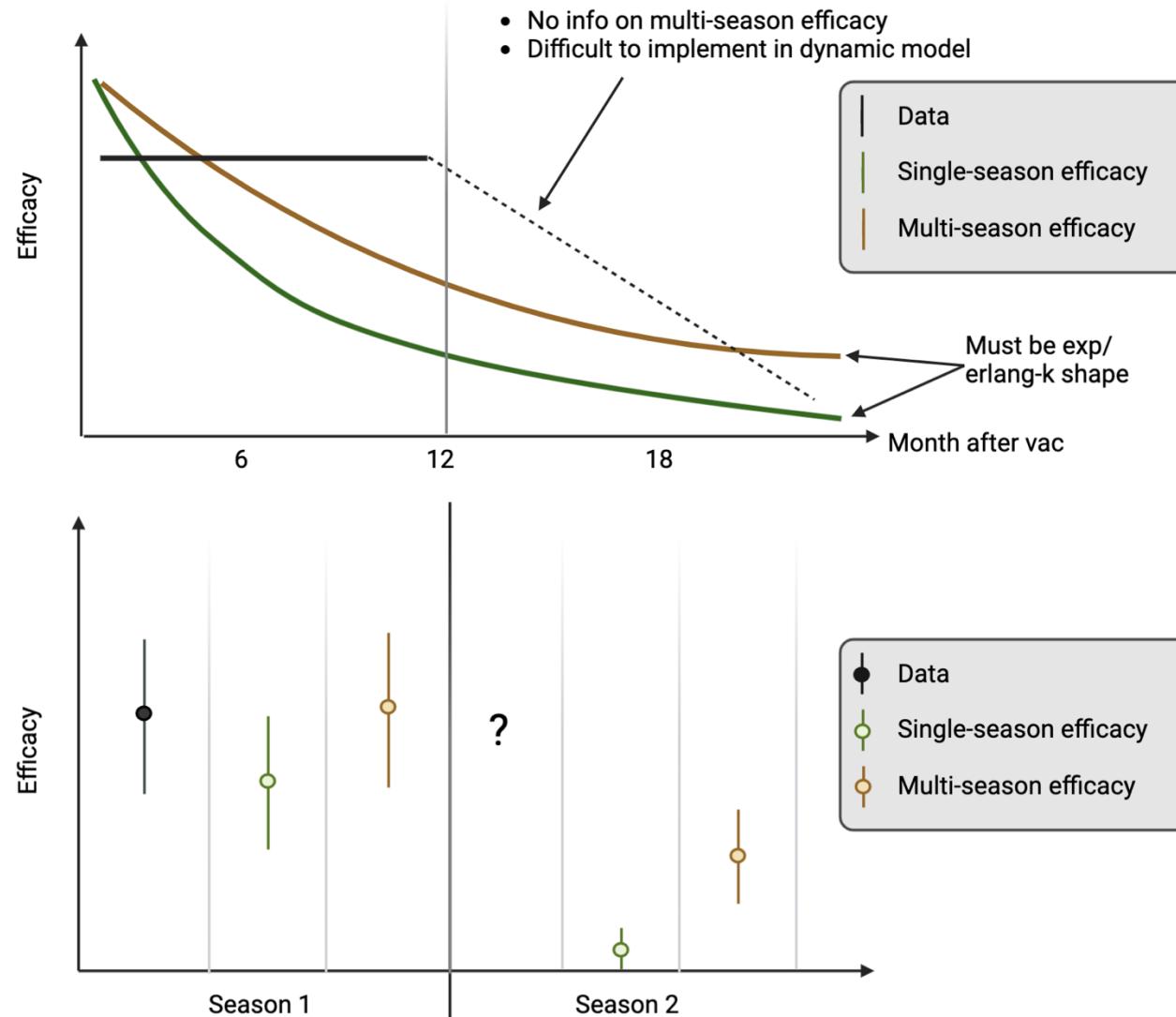








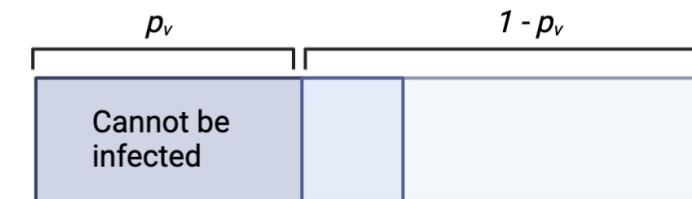
**Figure 2.** Schematic showing the relationship between exponential and erlang-k distributions in the context of dynamic transmission modelling. By chaining k compartments, the waning following an Erlang-k distribution which has more flexibility in waning structure in comparison to an Exponential distribution.



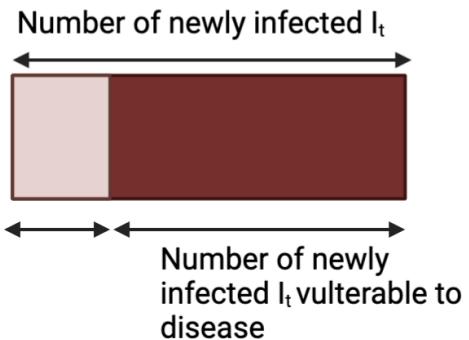
## Disease-specific efficacy

At time  $t$ , for age group  $a$  and risk group  $v$ :

Proportion of population



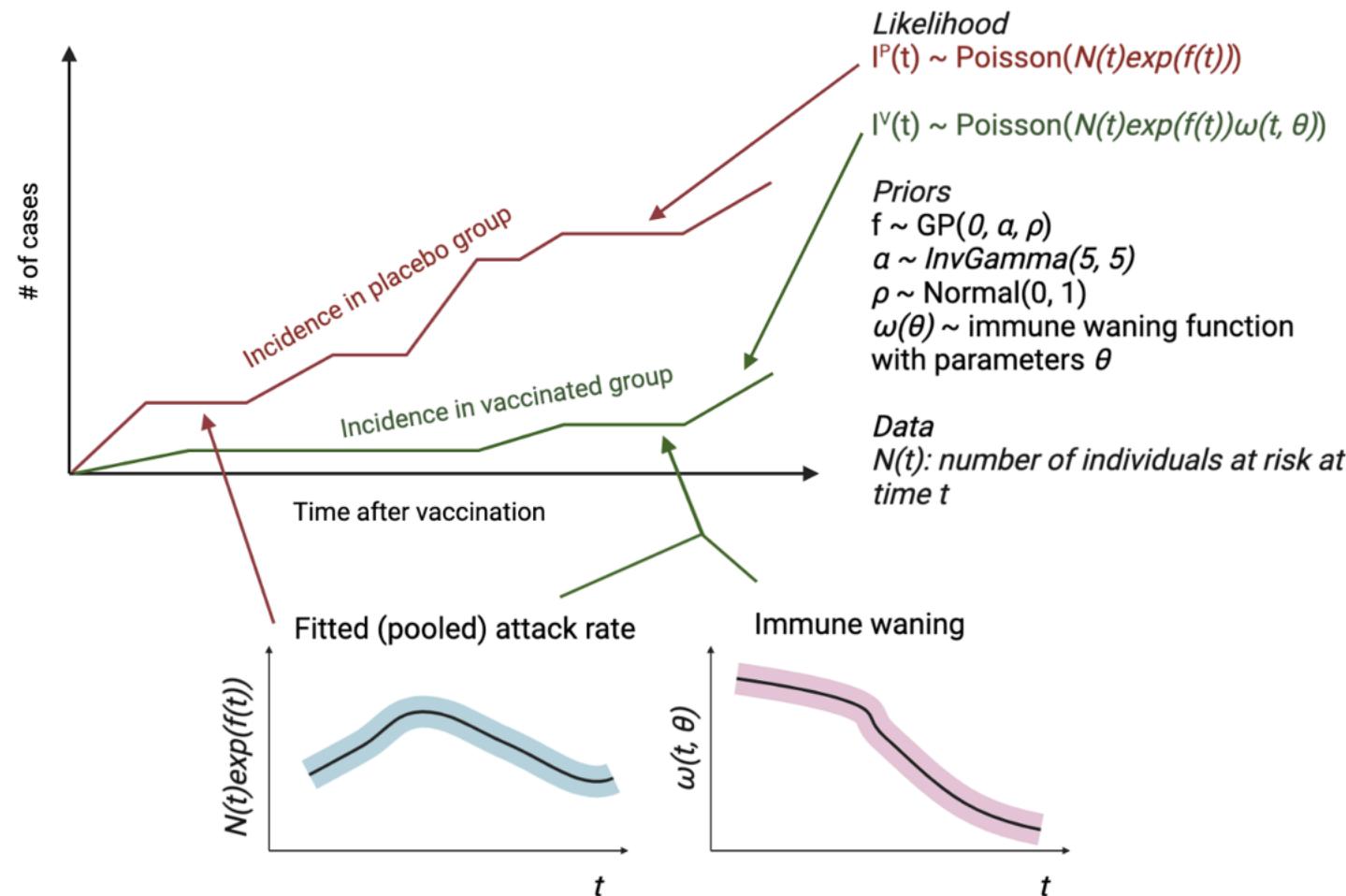
$$f_d = (e_d/e - 1)$$



$e_d$  efficacy against disease  
 $e$  efficacy against infection  
 $f_d$  disease protection proportion

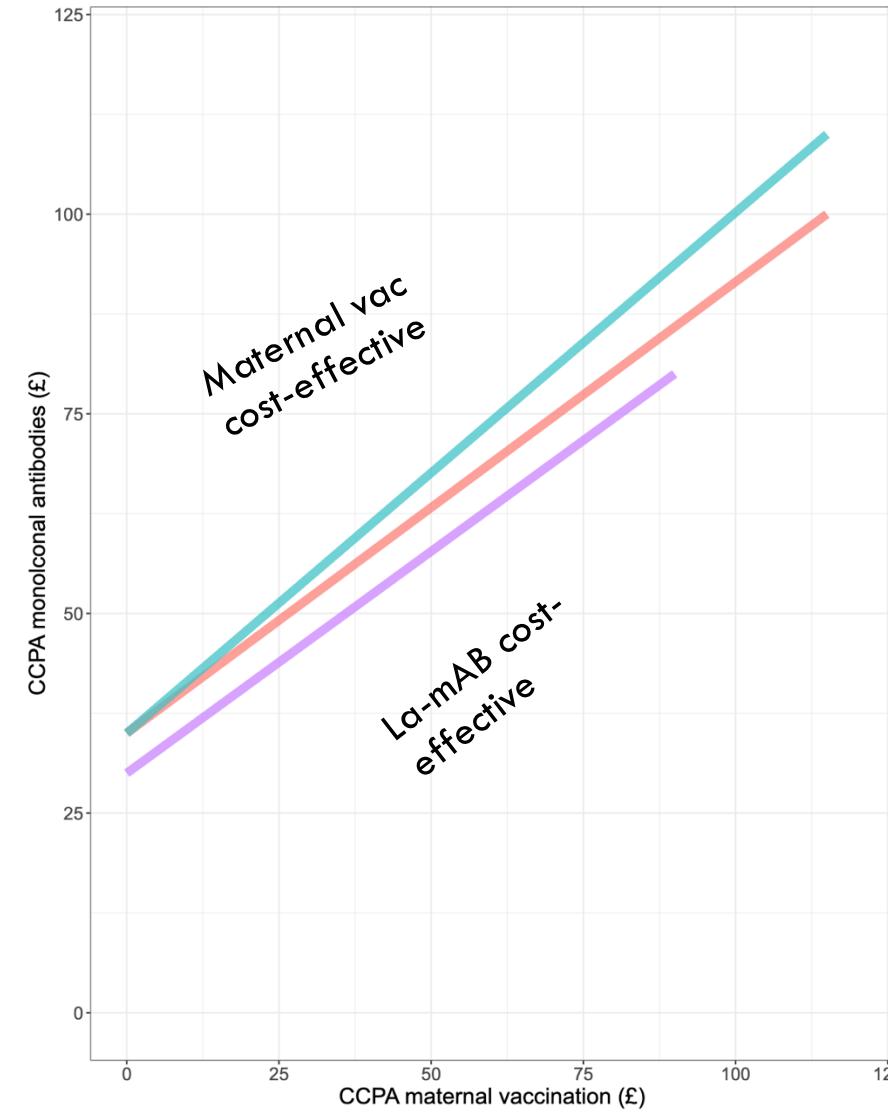
Number of newly infected protected to disease  
 $I_t p_v (f_d) / (1 - p_v)$

### A Kaplan Meier Plot



**Figure 1.** Schematic showing the hierarchical Bayesian model to estimate the time-varying efficacy given a Kaplan Meier plot.

Product equivalence line for costs + efficacies



Product equivalence line for different coverages

