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LIFECYCLE-MODEL-BASED ECONOMIC EVALUATION OF INFANT MENINGITIS B VACCINATION IN THE UK

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BACKGROUND

- Although uncommon, invasive meningococcal disease (IMD) due to serogroup B ("MenB") can impose catastrophic health and economic burdens on patients and families.
- We estimated private and social willingness-to-pay (WTP) for infant Men B vaccination (Bexsero) in the UK using a health-augmented lifecycle model (HALM) within a societal-perspective cost-benefit analysis (CBA).
- Traditional vaccine evaluations use cost-utility analysis (CUA), with an attitude of simplifying assumption of multiplicative separability in lifetime health and economic variables which do not always capture key disability interactions.[1,2]
- A health-augmented lifecycle model (HALM) captures in a more flexible and comprehensive utility theoretic way than CUA or traditional CBA the full range of pertinent life course interactions: mortality and morbidity risk, productivity and labor, consumption, leisure, and financial risk protection.
- This approach provides a more comprehensive valuation of the benefits of infant MenB vaccination than traditional vaccine evaluations using cost-utility analysis, where the simplifying assumption of multiplicative separability in lifetime health and economic variables cannot always account such interactions.

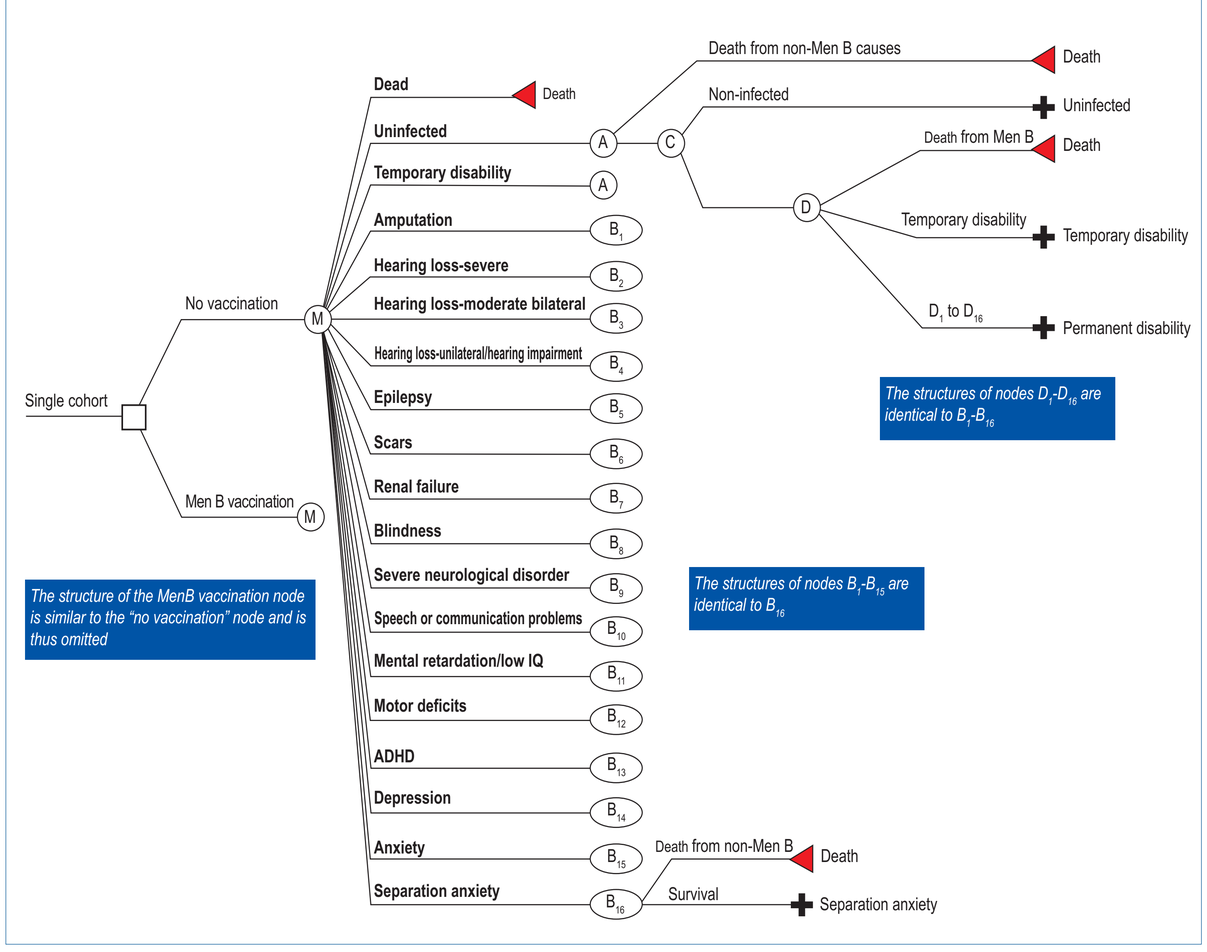
CONCLUSIONS

- **We show in the case of infant MenB vaccination that HALM-based CBA can integrate in a more comprehensive yet coherent utility-theoretic way than CUA the complex causal interactions over the lifecycle among mortality, morbidity, productivity and labor, consumption, leisure, and financial risk protection.**
- **Baseline private and social WTP/RoR to infant Bexsero vaccination are £395/55% and £969/281% respectively.**
  - **Baseline private and social RoRs compare very favorably with the long-run return to the UK stock market (5%)[33] providing strong justification for legislatures to transfer resources from households to the public sector health payer (e.g. through taxation) to finance MenB vaccination.**
  - **Baseline private and social RoRs also compare favorably with returns to non-health public expenditures such education and infrastructure (11-21%).[34-37] This provides strong justification for the Treasury to redirect public sector funds toward the health payer to finance MenB vaccination.**
  - **From a societal perspective, health payer budgets seem sub-optimally small, implying high opportunity costs for health payer funds. Given such high opportunity costs, it is an open question whether our RoRs justify redistribution of the health payer's budget to finance infant MenB vaccination.**

METHODS

- We used a single cohort static Markov disease model with 19 Markov states based on outcomes in vaccine recipients and unvaccinated individuals who either progress towards non-infection and death or infection with death or disability, including 16 permanent disability states (**Figure 1**). **Figure 2** shows all probabilities and associated utilities considered.[3-10]

Figure 1. Markov cycle graph



- In our HALM, lifetime utility is additively separable in period (i.e. yearly) utility, period utility is multiplicatively separable in survival probability, health utility, and utility from full consumption. Period utility from full consumption has a constant-relative risk aversion (CRRA) form. Full consumption is a constant elasticity of substitution (CES) function of consumption and non-market time. Non-market time is the sum of unpaid work (housework, childcare, and volunteering) and leisure.
- Survival and health utility have intrinsic value as natural complements to full consumption. Survival has instrumental value by promoting net savings. Preventing permanent disability has instrumental value by preventing the permanent disruption to productivity, earnings, and consumption that occur in the absence of disability insurance.[11-13]
- Parents of the permanently disabled face increased risk of the health utility and productivity consequences of depression.[14] The acute phase of infection involves severe decline in health utility[15] and parental productivity loss.[16]
- The model assumed MenB vaccination with a 2+1-dose schedule at 2, 4, and 12 months (m), relative to no vaccination

Figure 2. Sequelae and their health and economic profiles

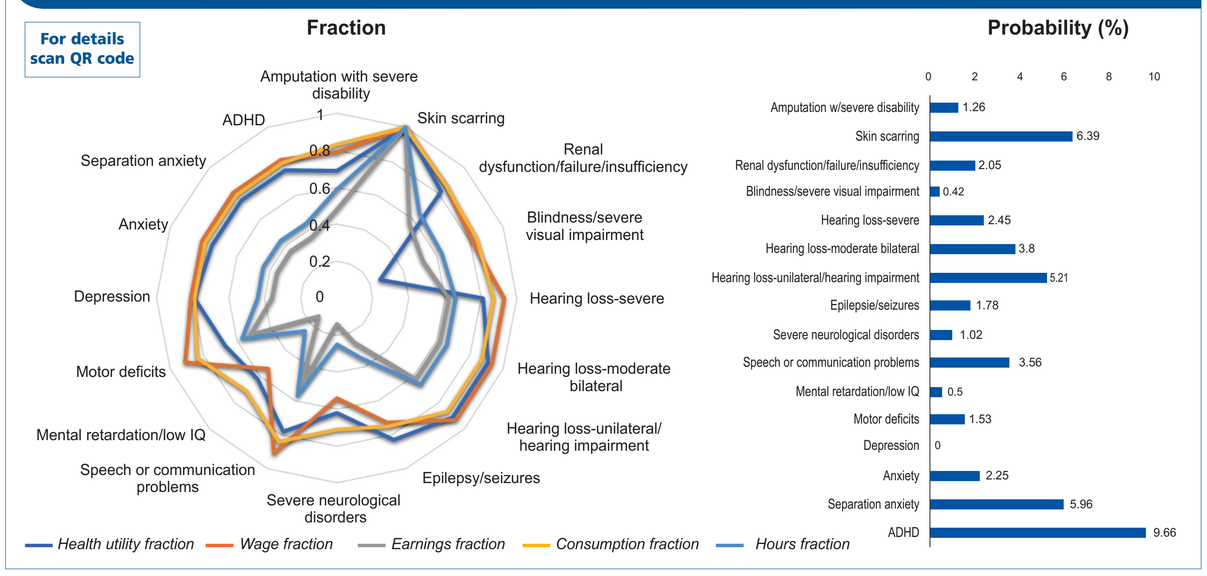


Table 1. Model inputs are based on UK real-world and relevant international health and economic data

Parameter	Base-case scenario	One-way sensitivity analysis (Scenarios A to E)
Incidence of MenB	Mean rate in England across 2000-2014[19]	Scenario C 2014 incidence[20]
Case fatality rate	2.7%-9.7%[21,22]	
Value of a Statistical Life (VSL)	£3.36M (2018)[23]	Scenario A £2.68M (2018)[24]
Subsistence consumption	50% of basic needs at poverty line[25]	Scenario B Conservative marginal utility of consumption
Life cycle per capita consumption	National Transfer Accounts Project[26]	Scenario E Earnings fraction drives consumption reduction from disability
Hourly earnings	UK Annual Survey of Hours of Earnings[27]	
Productivity/use of time	UK Harmonized European Time Use Survey[28]	
Vaccine effecacy[29-32] **Dose 1** **Dose 2** **Dose 3**	 0% 80.0% 82.8%	 Scenario D (D) 58.2% (D) 83.2% (D) 87.1%
Duration of Protection[29-32] **Dose 1** **Dose 2** **Booster**	 33 months 33 months 38 months	
Vaccine cost per-dose[20]	£84.80/dose (including £9.80 administration cost per dose)	
Discounting	3.5%	

- The model reports benefits of MenB infant vaccination private and social willingness-to-pay (PWTP and SWTP) and allied rates of return (PRoR and SRoR).
- PWTP equals the monetary compensation of vaccination-induced lifetime utility gain and is composed of four components: (i) disability insurance value, (ii) parental spillover benefits, (iii) acute phase benefits, and (iv) intrinsic and residual instrumental value of health.
- As SWTP reflects social preferences for preventing severe disease by giving greater weight to benefits accrued by patients with more severe outcomes, we accounted for this by multiplying long-term personal benefits to the vaccinated person (i.e. disability insurance value / intrinsic and residual instrumental value of health) by a factor of 3 in line with relevant literature.[17,18] then adding the parental spillover and acute phase benefits to generate an overall SWTP.
- Private Rate of Return (PRoR)= [(PWTP/vaccination cost)-1]*100.
- Social RoR (SRoR) = [(SWTP/vaccination cost)-1]*100.

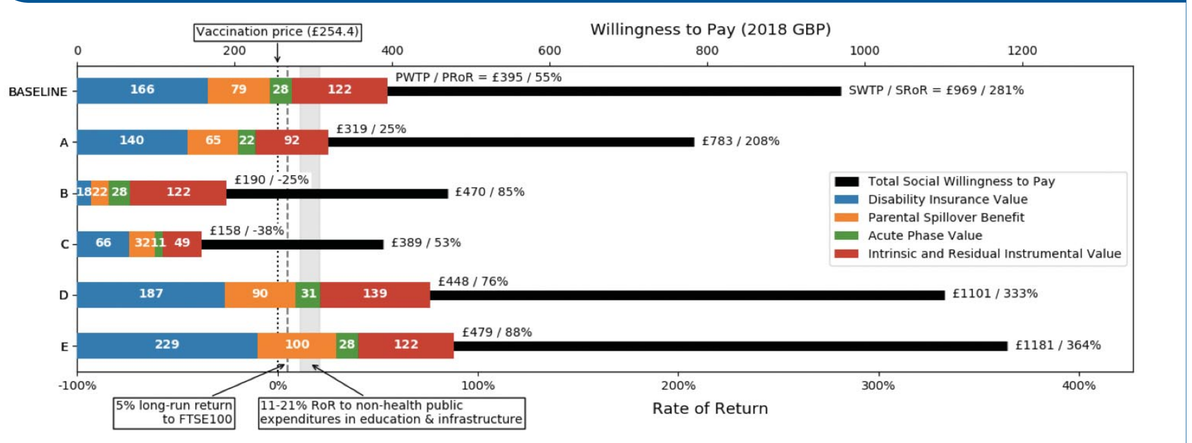
RESULTS

- PWTP is £395, comprising £166 of disability insurance value, £79 of parental spillover value, £28 in acute phase value, and £122 in intrinsic and residual instrumental value of health. This translates into a PRoR of 55% (**Figure 3**).
- SWTP and SRoR are £969 and 281% respectively.
- Vaccination produces an expected discounted health gain in a vaccinated infant (excluding parental spillovers) of 0.43 quality-adjusted days of life.
- One-way sensitivity analyses, using (A) a VSL of £2.68M GBP, (B) a conservative estimate of marginal utility of consumption, (C) conservative incidence rates from 2014, (D) higher vaccine effectiveness, and (E) larger effects of disability on consumption in the absence of disability insurance influenced outcomes (and had a greater impact on the private perspective) **Table 2** .

Table 2. Results of one-way sensitivity analysis

Scenario	Private		Social	
	PTWP	PRoR	PTWP	PRoR
A	£319	25%	£783	208%
B	£190	-25%	£470	85%
C	£158	-38%	£389	53%
D	£448	76%	£1,101	333%
E	£479	88%	£1,181	364%

Figure 3. Private and social WTP and RoR for infant MenB vaccination in the UK



The baseline scenario is described by the first horizontal bar and five one-way sensitivity analyses by subsequent bars (see legend for descriptions). The blue, orange, green, and red bars are four elements of PWTP that together sum to total PWTP. The thin black line shows the impact of severity preferences. The upper (lower) horizontal axes show PWTP and SWTP (PRoR and SRoR). PRoR and SRoR are measured relative to vaccination price represented by the leftmost vertical line.

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Sequelae	Probability (%)	Health utility fraction	Wage fraction	Earnings fraction	Consumption fraction	Hours fraction
Physical and neurological disorder						
Amputation w/ severe disability	1.26	0.69	0.79	0.48	0.83	0.59
Skin scarring	6.39	1	1	1	1	1
Renal dysfunction/failure/insufficiency	2.05	0.82	0.86	0.57	0.86	0.65
Blindness/severe visual impairment	0.42	0.26	0.81	0.52	0.84	0.63
Hearing loss-severe	2.45	0.81	0.93	0.62	0.87	0.66
Hearing loss-moderate bilateral	3.80	0.91	0.93	0.62	0.87	0.66
Hearing loss-unilateral/hearing impairment	5.21	0.91	0.93	0.62	0.87	0.66
Epilepsy/seizures	1.78	0.83	0.73	0.26	0.75	0.35
Severe neurological disorders	1.02	0.62	0.54	0.14	0.71	0.25
Speech or communication problems	3.56	0.78	0.91	0.52	0.84	0.57
Mental retardation/low IQ	0.50	0.62	0.54	0.14	0.71	0.25
Motor deficits	1.53	0.67	0.91	0.52	0.84	0.57
Psychological and behavioral						
Depression	0.00	0.789	0.81	0.36	0.79	0.44
Anxiety	2.25	0.75	0.81	0.36	0.79	0.44
Separation anxiety	5.96	0.75	0.81	0.36	0.79	0.44
ADHD	9.66	0.75	0.81	0.36	0.79	0.44

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