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MODELLING THE PUBLIC HEALTH IMPACT OF ALTERNATIVE VACCINE STRATEGIES FOLLOWING THE DISCONTINUATION OF MENITORIX (HIB/MENC) IN ENGLAND

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INTRODUCTION

- Immunisation is the best strategy to protect individuals from Invasive Meningococcal Disease (IMD).
- IMD is a particularly devastating disease as it has a high case fatality rate (CFR) and can lead to devastating lifelong sequelae in survivors.
- Infants and toddlers contribute to the highest proportion of IMD cases, with the majority of cases being caused by B, C, W and Y serogroups[1, 2]
- The planned discontinuation of GlaxoSmithKline's (GSK) Hib/MenC vaccine (approximately around 2023) will create a gap in the vaccination schedule at 12 months in the UK National Immunisation Programme (NIP).

OBJECTIVES

- An incidence-based static population model was developed to examine the introduction of a quadrivalent MenACWY vaccine into the UK National Immunisation Programme in toddlers compared to the current Hib/MenC product.
- The model compares alternative MenACWY vaccination strategies to the current situation in the UK in which direct protection against serogroup C is given to toddlers .This allows the public health impact of any changes to be assessed compared to what is observed currently.

METHODS

- The model was run to simulate IMD incidence for each year of a 30-year timeframe. This timeframe corresponds to progressive introduction of the vaccine as opposed to considering a steady state.
- Compared to the use of MenC/Hib#, the impact on public health was examined when a MenACWY vaccine is introduced into the schedule (base-case) or when no vaccination is given at 12 months of age (scenario analysis) (Table 1).
- Ten types of physical, neurological and psychological sequelae were included in the model with their associated disutilities and health spill-over effects.[3, 4, 5, 6] (Table 2).
- A 1.5% discount rate was applied for the health outcomes and 3.5% for the costs.
- The model allows IMD cases, IMD-related sequelae, IMD-related deaths. and quality-adjusted life-years (QALYs) gained to be predicted.
- Vaccine efficacy was assumed to be 90% for MenC vaccine (against serogroup C) and 90% for MenACWY vaccine (against serogroups A, C, W, Y) based on Delea et al., 2017 [7] and assumptions made by the Haut Conseil de la Sante Publique (HCSP) in 2009 [8] for the evaluation of MenC vaccine. Average duration of protection was 6.67 years.
- Estimates for the incidence of IMD used in the model were based on the incidence rates observed under the currently existing vaccination strategy. Annual incidence rates were calculated from Public Health England data by serogroup and age group in 2018-2019[2] taking into account the size of the population.
- Mortality rates were calculated based on Edge et al., 2016[9], considering mortality by serogroup as the priority, then adjusted according to distribution by age group.
- The model was equipped with functionality to adjust the QALY losses associated with severe long-term sequalae in order to reflect social preferences (Quality Adjustment Factor of 3) and incorporate spill-over effects on the family and network (1.33).
- To account for the impact of premature death in the base case, a family bereavement factor of 1.09 was applied to the QALYs lost in fatal cases.

Table 1: Strategies compared in the base-case and scenario analysis

	Base-case	Scenario analysis
Strategy 1	MenC at 12 months*	MenC at 12 months*
Strategy 2	MenACWY at 12 months*	No vaccination at 12 months*

***MenACWY is given at 14 years of age according to the routine immunisation schedule**

Table 2: Frequency of sequelae considered in the model

Age: Start	Age: End	Amputation	Hearing loss	Renal disfunction	Motor deficit	Epilepsy: seizures of any type	Substantial communication disability	Skin scarring	Anxiety	Separation anxiety	Attention deficit hyperactivity disorder
0	0	1.26%	6.47%	0.49%	4.06%	2.09%	3.77%	3.93%	2.68%	6.85%	11.41%
1	4	1.26%	6.47%	0.49%	4.06%	2.09%	3.77%	3.93%	2.68%	6.85%	11.41%
5	14	1.26%	6.47%	0.49%	4.06%	2.09%	3.77%	3.93%	2.68%	6.85%	11.41%
15	24	3.00%	5.30%	0.49%	0.89%	2.09%	3.77%	2.45%	2.68%	6.85%	11.41%
25	64	3.00%	3.34%	0.49%	0.89%	2.09%	3.77%	2.45%	2.68%	6.85%	11.41%
65	99	3.00%	3.34%	0.49%	0.89%	2.09%	3.77%	2.45%	2.68%	6.85%	11.41%

Table 3: Number of IMD cases, IMD death and IMD cases with sequelae considered in the model over 30 years – undiscounted results

Health outcomes	Strategy 1	Strategy 2	Incremental
Base-case results			
Number of IMD cases	15,345	15,090	-255
Number of IMD death	559	541	-18
Number of IMD cases with sequelae	5,845	5,742	-103
Scenario analysis			
Number of IMD cases	15,345	15,519	+174
Number of IMD death	560	564	+4
Number of IMD cases with sequelae	5,844	5,915	+71

Table 4: Discounted QALYs lost over the model timeframe (30 years)

QALYs lost	Strategy 1	Strategy 2	Incremental
Base-case	81,501	79,046	-2,455
Scenario analysis	81,501	82,900	+1,398

DECLARATIONS

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RESULTS

- The base-case analysis indicated that introducing vaccination with a quadrivalent MenACWY at 12 months of age was associated with improved health outcomes (see Table 3 and 4).
- Protection against IMD caused by serogroup C would be maintained.
- An additional 255 cases of IMD could be avoided over a 30-year duration with the introduction of a quadrivalent vaccine due to the additional protection against serogroups W and Y.
- 18 deaths, and 103 IMD cases with sequelae would be avoided along with an additional 2,455 QALYs gained over 30 years.
- In contrast, no replacement at 12 months of age (scenario analysis) would result in 4 deaths and 174 additional serogroup C IMD cases over the 30-year timeframe.

DISCUSSION

- It is crucial that after the withdrawal of Menitorix® infants/toddlers are not left unvaccinated against IMD as they are the group with the highest IMD incidence and risk of mortality with devastating, potentially lifelong sequelae following infection[2,10,11].
- A routine immunisation programme with a quadrivalent MenACWY vaccine for toddlers would ensure that this high-risk population has broad, direct protection against IMD caused by multiple serogroups.
- In our model the base-case analysis indicated that introducing vaccination with a quadrivalent MenACWY at 12 months was associated with improved health outcomes.

CONCLUSIONS

- **It is thus important that the imminent change in the meningococcal infant vaccination schedule is promptly addressed to ensure continuity of protection.**
- **Quadrivalent meningococcal vaccination offers broad protection against IMD caused by serogroups A, C, W and Y.**
- **Given the withdrawal of Menitorix® from the UK NIP, there is now an opportunity to consider a quadrivalent IMD vaccine at 12 months of age.**
- **Routine immunisation with MenACWY at 12 months of age is the best strategy for direct protection to reduce the incidence of IMD and avoid the burden of IMD on patients, the healthcare system and the society.**

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CONFLICT OF INTEREST & ACKNOWLEDGMENTS

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