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Optimising the introduction of multiple childhood vaccines in Japan: A model proposing the introduction sequence achieving the highest health gains

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ABSTRACT

Background: Many countries struggle with the prioritisation of introducing new vaccines because of budget limitations and lack of focus on public health goals. A model has been developed that defines how specific health goals can be optimised through immunisation within vaccination budget constraints.
Methods: Japan, as a country example, could introduce 4 new pediatric vaccines targeting influenza, rotavirus, pneumococcal disease and mumps with known burden of disease, vaccine efficacies and maximum achievable coverages. Operating under budget constraints, the Portfolio-model for the Management of Vaccines (PMV) identifies the optimal vaccine ranking and combination for achieving the maximum QALY gain over a period of 10 calendar years in children <5 years old. This vaccine strategy, of interest and helpful for a healthcare decision maker, is compared with an unranked vaccine selection process.
Results: Results indicate that the maximum QALY gain with a fixed annual vaccination budget of 500 billion Japanese Yen over a 10-year period is 72,288 QALYs using the optimal sequence of vaccine introduction (mumps [1st], followed by influenza [2nd], rotavirus [3rd], and pneumococcal [4th]). With exactly the same budget but without vaccine ranking, the total QALY gain can be 20% lower.
Conclusion: The PMV model could be a helpful tool for decision makers in those environments with limited budget where vaccines have to be selected for trying to optimise specific health goals.

1. Introduction

Quite a high number of new vaccines have been introduced into the global healthcare programme during the past 15 years. Among them vaccines against *Streptococcus pneumonia*, *rotavirus*, *human papillomavirus, Neisseria meningitides*, varicella zoster virus (responsible for *herpes zoster*), dengue, and new ones against *influenza viruses* [1], are now in the market, but others against malaria and Ebola are coming soon [2].

The shift from therapeutic intervention to active-prevention should normally lead to a less cumbersome and a financially more attractive healthcare service [3,4]. However, the introduction of a new vaccine takes time before full implementation is reached [5]. Starting budgets for the new vaccine need to be found, integration into existing vaccination calendars must be arranged, and hesitancy needs to be overcome among decision makers regarding promised benefits to be supported with real-world evidence data that are not there at launch. Since healthcare authorities need a way to reach specific health goals over time while taking budget constraints, time frame, and country-specific characteristics into account, many of them are therefore struggling with questions about the new vaccines regarding the one that should be given priority for maximising the health gains when the budget is limited [6]. That particular question has been raised several times by local authorities, such as Italy, where the central government proposed an additional budget for improving the immunisation planning in the regions, and those regions need to decide which vaccine to select first with that extra budget.

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At this moment, there is no tool available that can help making that decision when many different vaccines can be introduced at the same time in the market. In addition, healthcare decision makers would like to know all the benefits to be achieved by their selected vaccines (e.g. potential overall reduction in hospital bed occupancy or in medical visits) related to their financial investment in vaccination. Typically, they require information about safety, vaccine efficacy (VE), and the calculated full value-for-money of the vaccine [7]. But they often do not receive a helicopter view regarding which vaccines should be given priority among all possible combinations.

Reasons for this lack of information are manifold, but performing an overall economic analysis with different vaccines as a measure of priority setting might be hard using currently available tools. Other evaluation techniques should be selected that help identify the optimal order of introducing new vaccines, enabling the overall investment-minimisation and the benefit-maximisation to be reached [8]. That new model should take into account the vaccination budget available as well as the new vaccines that could be introduced during a pre-defined time frame: cost, impact, uptake scenario, and maximally-achievable coverage rates. It should present as well an overall view of what the vaccination programmes can achieve in avoiding number of hospitalisations and medical visits and associated cost offsets. Supplemented with budget planning, this information is often requested by ministries of finance where the money for funding generally comes from [9].

Including all those different aspects into one analysis could be a most useful tool as it integrates one overall objective linked to specific constraints [10]. We developed that approach with optimisation modelling using linear programming, focusing on pediatric vaccines and children under the age of 5 years old. We applied it to one specific country situation as an example. In the next paragraphs we explain the working of the model called the Portfolio-model for the Management of Vaccines (PMV) and the necessary conditions for its application.

2. Methods and data

The country example for the evaluation of the PMV-model is Japan using data from their extended pediatric vaccination programme. Many of the new vaccines have not been introduced yet in the country [11], while the necessary budget is available and data about the burden of the various diseases under study and their management processes are accessible. The overall objective of this exercise is to develop an optimisation tool capable of evaluating the introduction of pediatric vaccines recommended by the World Health Organization (WHO), with an impact in children aged 0–5 years [12]. From that list of vaccines one should select those of interest to a particular country and assess their ranking in order to determine an optimal introduction scheme that achieves the greatest possible benefit while complying with constraints such as a multi-year vaccination budget plan. The model delivers then a justifiable economic argument as it compares the optimised results with those generated from a process where no programmed vaccine ranking is made (i.e., an "unranked" selection process). The perspective considered for this analysis is that of the healthcare decision maker, often in the ministry responsible for health in a country.

2.1. Model construction and running

The model introduces the selected vaccines in a sequential order. It uses a static, multi-cohort Markov model that follows birth cohorts over time in annual time cycles [13]. It has been developed

Table 1
Summary of model input: epidemiology, costs, and VE.

Parameter	Pneumococcus meningitis [30,31]	Pneumococcus bacteraemia [30,31]	All-cause pneumonia [31,32]	All-cause AOM, excl. myringotomy [31,33]	AOM myringotomy [31,33][a]	Rotavirus [34]	Mumps [35][b]	Influenza [36]
Age-dependent incidence estimates per age group (%)[c]								
0–1 years	0.0070%	0.0143%	1.760%	20.55%	1.44%	9.13%	0.86%	16.90%
1–2 years	0.0037%	0.0445%	1.760%	50.45%	3.55%	27.07%	6.77%	20.60%
2–3 years	0.0011%	0.0122%	1.760%	31.76%	2.23%	10.98%	13.34%	17.60%
3–4 years	0.0010%	0.0061%	1.760%	19.62%	1.38%	10.98%	21.05%	20.00%
4–5 years	0.0003%	0.0042%	1.760%	13.08%	0.92%	4.67%	26.73%	21.20%
GP visits (proportion)	0.00	0.00	0.21	1.00	0.00	1.00 [37]	0.65[e]	1.00
Hospitalisation (proportion)	1.00	1.00	1.00	0.00	1.00	0.07 [37]	0.01 [38]	0.02
Hospitalisation: length (days)	13.78	7.17	6.07	0.00	1.00	5.00 [37]	5.00 [39]	6.08 [31][e]
Hospitalisation: adjusted length	13.79	7.17	6.08	0.00	1.00	0.37	0.06	0.11
Death rate (%)	0.021	0.004	0.00091	0.00	0.00	0.00 [40]	0.00	0.00002 [41]
Cost/GP visit (JPY)	0	0	16,998	18,185	0	14,295[42]	10,477[38]	10,000[e]
Cost/hospitalisation (JPY)	767,447	340,905	286,209	0	45,853	136,000[43]	129,608[38]	286,209[31][e]
Disutility/event[d]	0.023 [44]	0.008 [44]	0.006 [44]	0.005 [45]	0.005 [45]	0.006 [46]	0.005 [47][e]	0.005 [47]
Maximum VE	100.0% [48]	100.0% [48]	23.4% [48]	18.0% [44][f]	40.4% [44][f]	87.1% [49]	69.6% [39]	52.0%
Age at which VE starts (in months)	2.0	2.0	2.0	2.0	2.0	1.5	12.0	NA

[a] 7% of AOM.
[b] Data of vaccine exist as voluntary vaccination.
[c] Cohort size reference [14].
[d] Adjusted for duration of illness.
[e] Assumption.
[f] AOM is not included in vaccine indication in Japan; AOM, acute otitis media; excl., excluding; GP, general practitioner; JPY, Japanese Yen; VE, vaccine efficacy; NA, not applicable.

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