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Cost-effectiveness analysis of pertussis vaccination during pregnancy in Japan

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ABSTRACT

Background: Both re-emergence of pertussis outbreak among adolescents/adults and recent approval of the extended use of DTaP vaccine for boosting adolescents/adults against pertussis in Japan, have raised the possibility of using aP-containing vaccine in pregnant women to protect neonates and unvaccinated infants. There is a need, therefore, to evaluate the value for money of such possibility.
Methods: We evaluated the cost-effectiveness of conducting antepartum maternal vaccination (AMV) strategy in Japan. Considering the duration of vaccine effectiveness for infant (single year) and for mother (multiple years), the decision tree model and Markov model was adapted for infant and mother, respectively. Incremental cost-effectiveness ratio (ICER) compared with current no AMV strategy from societal perspective were calculated. The transition probabilities, utility weights to estimate quality-adjusted life year (QALY), and disease treatment costs were either calculated or extracted from literature. Costs per vaccination was assumed at ¥6000/US$54.5. Markov model for mothers with one-year cycle runs up to year four after vaccination, based on the waning of vaccine effectiveness. Infant who survived from pertussis was assumed to live until to his/her life expectancy.
Results: AMV strategy reduces disease treatment costs, while the reduction cannot offset the vaccination cost. Incremental QALYs were at 0.0002802, among them 79.5% were from infants, and others from mothers. ICER was ¥9,149,317/US$83,176 per QALY gained. One-way sensitivity analyses identified that the incidence rate and costs per shot were the two main key variables to impact the ICER.
Conclusion: We found that vaccinating pregnant women with aP-containing vaccine to prevent neonatal and unvaccinated infants from pertussis-associated disease in Japan can be cost-effective from societal perspective, under the WHO-suggested "cost-effective" criteria (1 to 3 times of GDP). Pertussis is expected be designated as a notifiable disease in 2018, re-analysis should be conducted when straightforward incidence data is available.

1. Introduction

Pertussis is an acute respiratory disease caused by the bacterium *Bordetella pertussis*. It is a highly contagious disease transmitted through respiratory droplets and is usually difficult to be differentiated from similar pathological conditions such as prolonged cough or common cold [1]. These similar pathological manifestations lead to underdiagnoses, thus leaving a pool of patients harboring the infection, which can serve as a source of future infections [1,2]. Pertussis can affect people of all ages, but with particularly severe complications among neonates and unvaccinated infants, thus making the prevention of such infection among the said vulnerable population of prime importance [1,2]. Even after the introduction of vaccination programmes and the achievement of high vaccination coverage, pertussis, which is endemic to all countries, have epidemic cycles occurring every 2–5 years [1].

Strategies for preventing pertussis among young infants before they commence their vaccinations at 2 or 3 months of age include: (1) booster doses in adolescents or adults (though there is yet have a substantial evidence that these programmes have significant impact) [1]; (2) cocooning strategy, i.e., vaccinating the infant's close contacts (beneficial effects of this strategy are inconsistent) [1]; (3) antepartum maternal vaccination (AMV) strategy, i.e., giving aP-containing vaccine in the third trimester in every pregnancy to prevent severe infant morbidity and mortality from pertussis during the narrow window before receiving their first dose of

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vaccine. Though AMV is relatively new [3], convincing and robust evidences have consistently indicated that it will not only reduce the infection among mothers, but also protect infants through the transfer of maternal antibody [1,4,5]. High-income countries, such as United States, the United Kingdom, Belgium, Ireland, Italy, Portugal, and New Zealand, where pertussis immunisation programmes have existed for a long time have already been implementing AMV [4,6].

In Japan, DTaP vaccine was introduced in 1981 and pertussis has been controlled by means of a vaccination schedule of three primary doses (at 3, 4, 5 months) and a single booster dose (18–23 months). Vaccine coverage of three primary doses of DPT-IPV in 2014 were at 99.2%, 99.1%, and 99.1%, in the first, second and third doses, respectively [7]. Similar to other countries, there is a re-emergence of pertussis outbreak in adolescents and adults, raising topics about pertussis control through various strategies. Currently, national initiatives have paved way in addressing pertussis control. In February 2016, the Ministry of Health, Labour and Welfare (MHLW) approved the extended use of DTaP as a booster for both adolescents and adults. This has then led to the possibility of using DTaP in pregnant women [8]. Taking into account the current progress in pertussis control, our study aims to estimate the value for money of AMV strategy by using aP-containing vaccine in Japan, assuming that in the future, there may be a need to consider its implementation.

2. Method

We conducted a cost-effectiveness analysis to evaluate the cost-effectiveness of the vaccination programme. The model was constructed by using TreeAge Pro, 2017, TreeAge Software.

2.1. Literature search

We searched the various databases for the parameters which were included in the modeling. Studies pertaining to epidemiology and prognosis of pertussis-relevant disease in Japan's setting were accessed from Medline database, Igaku Chuo Zasshi database (a Japanese medical bibliographic database which contains over 10 million citations originating from Japan), MHLW Grant System, and annual statistical reports published by the government. Due to insufficient evidences from Japan, overseas' reports from Medline, The Cochrane Database of Systematic Reviews, Health Technology Assessment database, and National Health Service, Economic Evaluation Database regarding vaccine effectiveness and utility weights to estimate QALY were used instead. Though we didn't limit the literature search to recently published journal articles, we selected, as much as possible, the robust ones suitable to our model, particularly data relevant to the epidemiology and prognosis of the disease, together with the vaccine effectiveness and the related utilities.

2.2. Programme

Our study estimated the value for money of AMV strategy in Japan by comparing AMV strategy with current no AMV strategy.

2.3. Models and variables

Two cohorts were followed via a decision tree and Markov model; one for the pregnant women and the other for their new born babies (given that maternal pertussis antibodies protect the newborn in the first 3 months of life). The decision tree model describing the courses for individuals started from a decision node, which were consequently followed by chance nodes with regard to the following circumstances (Fig. 1): (1) vaccinated/not vaccinated, (2) perinatal mortality/live birth, (3) pertussis contraction/no pertussis contraction, and (4) clinical courses after the contraction. Adverse effects of vaccination were not incorporated based on reports from large clinical trials and from post-marketing surveys [9,10].

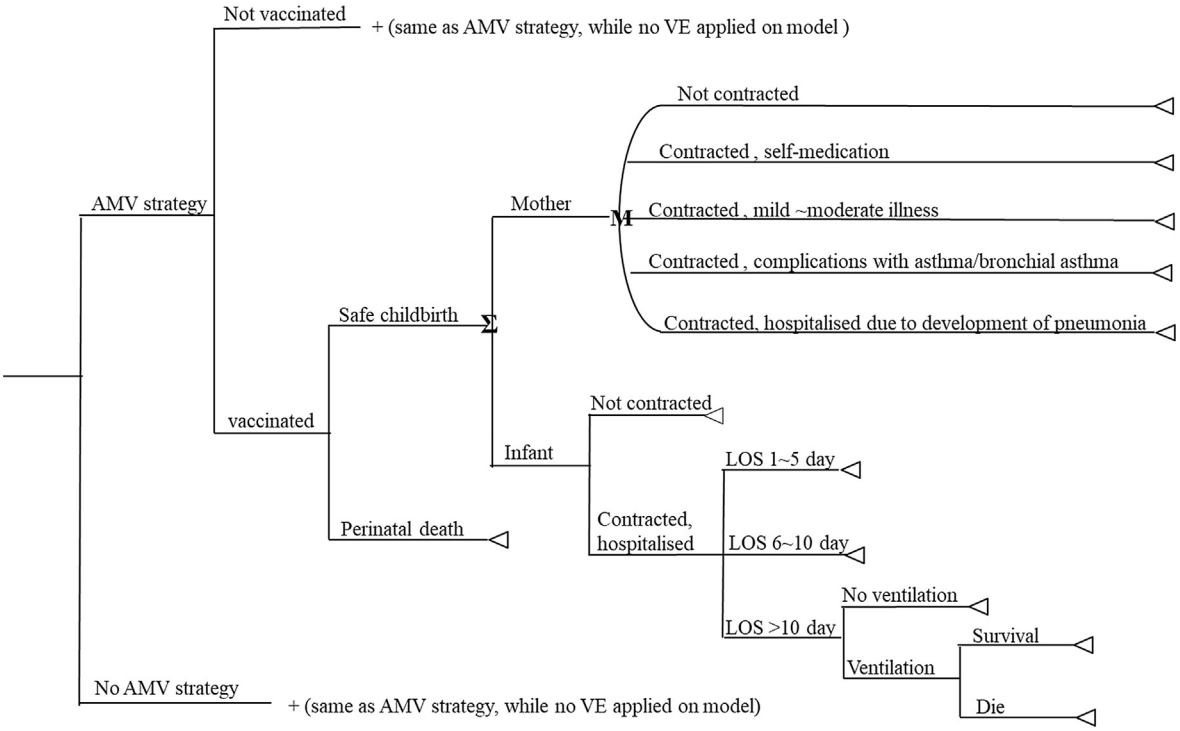

Fig. 1. Model. M: Markov model; Σ: Sum of both mother's and infant's results; LOS: Length of stay (in hospital).

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