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Economic evaluation of vaccination programme of mumps vaccine to the birth cohort in Japan

Shu-ling Hoshi*, Masahide Kondo, Ichiro Okubo

Department of Health Care Policy and Health Economics, Faculty of Medicine, University of Tsukuba, 1-1-1, Tennoudai, Tsukuba, Ibaraki 3058577, Japan

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ABSTRACT

The most common preventative measure against mumps is vaccination with mumps vaccine. In most parts of the world, mumps vaccine is routinely delivered through live attenuated Measles-Mumps-Rubella (MMR) vaccine. In Japan, receiving mumps vaccine is voluntary and vaccine uptake rate is less than 30%. The introduction of mumps vaccine into routine vaccination schedule has become one of the current topics in health policy and has raised the need to evaluate efficient ways in protecting children from mumps-related diseases in Japan.

We conducted a cost-effectiveness analysis with Markov model and calculated incremental cost effectiveness ratios (ICERs) of 11 different programmes; a single-dose programme at 12–16 months and 10 two-dose programmes with second dose uptakes at ages 2, 3, 4, 5, 6, 7, 8, 9, 10 and 11. Our base-case analyse set the cost per shot at ¥6951 (US$72; 1US$ = 96.8).

Results: show that single-dose programme dominates status quo. On the other hand, ICERs of all 10 two-dose programmes are under ¥6,300,000 (US$65,082) per QALY from payer's perspective while it ranged from cost-saving to <¥7,000,000 (US$72,314) per QALY from societal perspective.

By adopting WHO's classification that an intervention is cost-effective if ICER (in QALY) is between one and three times of GDP as a criterion, either of the vaccination programme is concluded as cost-effective from payer's or societal perspectives. Likewise, to uptake second dose at 3–5 years old is more favourable than an uptake at any other age because of lower incremental cost-effectiveness ratios.

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1. Introduction

Mumps is a viral infection of humans, primarily affecting the salivary glands. Serious complications of mumps include meningitis, encephalitis, orchitis, and hearing loss. There is no specific therapy for mumps. In most countries, live attenuated Measles-Mumps-Rubella (MMR) immunisation is delivered against mumps which dropped the incidence of mumps dramatically [1,2]. By December 2005, two-dose schedules were implemented in more than 80% of 110 countries where mumps vaccine is on routine immunisation schedule [1].

In Japan a voluntary mumps vaccination begun in 1981. From 1989, MMR vaccination has been allowed as an alternative to monovalent mumps vaccine for routine immunisation. However, because of unexpected high incidence of aseptic meningitis caused by mumps vaccine (Urabe Am9 strain), MMR vaccination was discontinued in 1993. Since then, measles and rubella vaccines have been in routine vaccination schedule, while mumps monovalent vaccine has been optional as it was before 1989 [3]. Currently, two kinds of mumps vaccine are available in Japan, each containing different strains, namely, Torii and Hoshino [4]. Despite some municipalities giving subsidies to vaccines to encourage the uptake of mumps vaccine, the estimated vaccine uptake rate is less than 30% [4]. Consequently, Japan has experienced annual outbreaks of mumps estimated from 430,000 to more than one million cases [5], and thus an increase in hearing loss caused by mumps was also observed [6]. The introduction of mumps vaccine into routine vaccination schedule has become one of the current topics in health policy [7] and has raised the need to evaluate efficient ways in protecting children from mumps-related diseases in Japan.

The efficiency of mumps vaccination has been reported overseas since 1970s. Either single-dose strategy or two-dose strategy was shown to be cost-beneficial [8–12]. In Japan, only one peer-reviewed article [13] reported a benefit-cost ratio of 5.1 for single-dose mumps vaccination programme from societal perspective with an unrealistic assumption of 100% non-vaccine infection.

* Corresponding author. Tel.: +81 29 853 3255; fax: +81 29 853 3255.
E-mail addresses: hoshi@hcs.tsukuba.ac.jp, shulingst@hotmail.com (S.-l. Hoshi).

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The same study also assumed that there is no waning of vaccine-derived immunity, which contradicts the findings of several studies where waning of vaccine-derived immunity is observed [14–21].

This study aims to appraise the value for money of expanding the current voluntary mumps vaccination to routine single-dose or two-dose vaccination programmes, and also to explore the potential impacts of schedule changes, i.e., the appropriate age to uptake the second dose, because of the variety of ages being recommended to uptake the second dose among countries where two-dose MMR is recommended [22,23].

2. Method

We conducted a cost-effectiveness analysis with Markov modelling from both payer's and societal perspectives. In defining vaccination programmes and constructing the model, we conducted a literature survey to find out the available evidence. Studies pertaining to epidemiology and prognosis of mumps-relevant disease in Japan's setting were accessed from PubMed database, Igaku Chuo Zasshi database, MHLW (Ministry of Health, Labour and Welfare) Grant System, and annual statistic reports published by the government. Igaku Chuo Zasshi (Japana Centra Revuo Medicina) is a Japanese medical bibliographic database which contains 7.5 million citations originating in Japan, which comprehensively covers articles published in Japanese-language medical journals. Due to insufficient evidences from Japan, overseas' reports from PubMed, Medline, The Cochrane Database of Systematic Reviews, HTA (Health Technology Assessment database), and NHS EED (The NHS Economic Evaluation Database) regarding vaccine effectiveness, utility weight to estimate QALY and economic evaluation related to mumps vaccine were used instead.

2.1. Programmes

The 11 routine vaccination programmes were composed of one single-dose programme and 10 two-dose programmes. All programmes schedule the first dose at 12–18 months. Each of the 10 two-dose programmes will have the second dose at ages 2, 3, 4, 5, 6, 7, 8, 9, 10 and 11. All these programmes were compared to status quo. We also compared two-dose programmes with single-dose programme to explore the efficiency of the second dose. The vaccine uptake rates are assumed at 30% for status quo [4] and 76% for single-dose programme and for first dose of two-dose programme based on the willingness-to-pay reported by Muta et al. [24], and 72.7% (76% × 0.957) for second dose of two-dose programme; where 0.957 is the proportion of second dose to first dose of vaccine coverage of measles over the last 5 years in Japan [25]. Vaccination with MMR2 was not considered as an alternative because it is not yet approved in Japan [4,26].

2.2. Markov model

A Markov model of courses followed by the birth cohort under consideration was constructed based on epidemiological data, vaccine effectiveness and models from previous studies. Eleven mutually-exclusive health states were modelled (Fig. 1). A Markov cycle for each stage was set at 1 year with a cohort time frame of 40 years. After turning 40 years old, those without sequelae were assumed to have a life expectancy of Japanese population [27], while those with neurological sequelae will have an average life expectancy of 53.9 years old [28]. Natural infection is thought to confer lifelong protection [1]. Considering that all state transitions do not occur simultaneously at the end of each cycle, we implemented a half-cycle correction in estimating the incremental cost effectiveness ratios (ICERs) of the programmes. We did not consider herd immunity in our model because: (1) the reported basic reproduction number of mumps is largely varied from 4 to 12 [29,30]. (2) Even when the assumption of vaccine effectiveness is as high as 95% for two doses of vaccine, vaccine coverage of 78.9%, 87.7%, 92.1%, 94.7% are needed to reach herd immunity if the corresponding reproductive values were four, six, eight, and 10; respectively [17]. (3) The experience of unexpected high incidence of aseptic meningitis caused by mumps vaccine in MMR during 1989–1993 in Japan [3] became a barrier to raise vaccine coverage in reaching herd immunity [31].

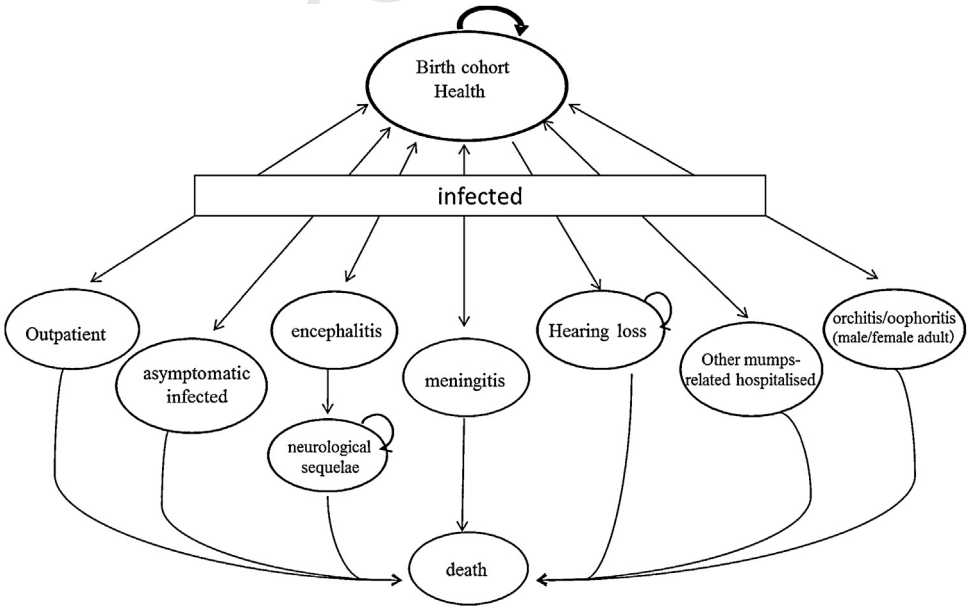

Fig. 1. Markov model. Eleven mutually-exclusive health states were modelled: health, asymptomatic infected, symptomatic infected (outpatient), hospitalised due to meningitis, encephalitis, neurological sequelae due to encephalitis, hearing loss, other mumps-related hospitalisation (including pancreatitis, myocarditis, severe mumps without complication), hospitalised due to orchitis/oophoritis (male/female adult patient only), and death of or other than the related diseases.

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