



## Commentary

## Informing pneumococcal conjugate vaccine policy in middle-income countries: The case of Malaysia



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Pneumonia is one of the leading infectious causes of death worldwide among all age groups, accounting for 15% of mortality in children aged under five years for an estimated 922,000 child deaths in 2015 [1]. *Streptococcus pneumoniae* is the major aetiological agent of the morbidity and mortality associated with paediatric bacterial pneumonia [1]. Since 2000, the widespread adoption of pneumococcal conjugate vaccines (PCVs) has seen a major advance in the prevention of pneumonia and will help prevent an estimated 1 million deaths among children by 2020, and 7 million by 2030 [2]. Two conjugate vaccines are currently marketed, the 10-valent (PCV10) and the 13-valent (PCV13), which include the serotypes responsible for  $\geq 70\%$  of the burden of pneumococcal disease in children under five. Despite widespread uptake of PCVs across many low and middle-income countries (MICs), Malaysia has not incorporated the vaccine into their national immunisation programme (NIP). Here we explore the evidence base surrounding PCV implementation and consider whether Malaysia should rethink current policy.

In 2012, the WHO renewed the worldwide recommendation for PCVs in NIPs for children under two [2]. According to the most recent WHO official estimates, in 2014, 117 countries had introduced the PCV compared with 103 countries in 2013, translating in an estimated global population coverage of 31% in 2014, up from 25% in 2013 [3]. After the licensure of the first PCV, high-income countries were the first to add PCVs to their NIPs. More recently, Gavi, the Vaccine Alliance, an international public-private partnership organisation that seeks to accelerate and expand access to life-saving childhood vaccines amongst the world's poorest nations, has supported the implementation of PCVs in more than 50 low-income countries (LICs) [4]. In contrast, only 27 of the 104 MICs have included PCVs in their NIP. Consequently, MICs are beginning to fall behind donor-supported LICs in terms of health improvements associated with widespread PCV immunisation [5]. In

2015, the WHO convened a Middle-Income Country Task Force that identified a lack of in-country evidence-based public health policy as one of the major barriers to immunisation in MICs [5]. Strengthened evidence-based decision-making on immunisation policy was recognised as an unmet need in the overall MIC strategy, as it underpins mobilisation of national political will and financing, contributes to an increased demand for vaccines by MICs, and supports efforts to reinforce immunisation systems and combat hesitancy [5].

Malaysia is an upper-MIC that is going through a period of rapid population growth and urbanisation, but has a national PCV policy that is likely failing to protect children from preventable pneumococcal infections. Importantly, there remains a paucity of carriage and disease epidemiology studies, particularly in relation to the burden of pneumonia and other acute respiratory tract infections. Until these are data available, it is not possible to measure the extent of preventable pneumococcal-associated morbidity and mortality at a national level [6]. Both local and international communities are aware of this weakness and some efforts have been made to fill the gaps. The Malaysian Paediatric Association and the Asian Strategic Alliance for Pneumococcal Prevention, for example, have an ongoing campaign in collaboration with a parent-led association to spread the voice of doctors and the public in urging the government to include PCV in the NIP. Alongside local initiatives, the broader scientific community has published data aiming to address the issue of PCV implementation in the WHO South East Asia and Western Pacific regions [7]. It is essential that infectious disease surveillance and both public and private initiatives are integrated to better inform national immunisation policy.

In 2015, a Health Technology Assessment Report (HTA) was published by the Medical Development Division of the Ministry of Health Malaysia (MoH) [8]. This states that, In 2011, the majority of Malaysian paediatricians from the public and private sectors came to an agreement that PCV immunisation should be added to the childhood NIP due to its high efficacy [8]. However, the Malaysian Committee for National Policy and Practice on Immunisation suggested that such an introduction required further consideration. This led to several aims of the HTA report which were to “review the evidence on the efficacy, safety, effectiveness,

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cost-effectiveness and organisational aspects of PCV10 and PCV13”, with the intention of seeking to determine “which PCV should be recommended into the National Childhood Immunisation programme for children below 5 years old” [8]. Yet this potentially important policy document failed in its aims in several ways. The MoH’s HTA did not provide guidance to Malaysian health practitioners on the use of PCVs nor did it satisfactorily inform and advance knowledge of PCV immunisation. It unhelpfully left the final choice between the two PCVs to the “preference of the decision-maker”, and does not provide an evidence-based recommendation for PCV to be added to the NIP. Importantly, the critical decision to not add PCV to the NIP was justified in the HTA on the grounds that the available formulations are too expensive given that Malaysia’s child mortality rate is lower than the threshold set to validate PCV implementation. However, the data on which this decision was partially based is flawed. Specifically, the under-five child mortality rate cited by the authors (0.6 per 1000 live births in 2006) was one order of magnitude lower than the MoH’s own statistics for the same year (7.2 per 1000 live births) [9], as well as those of the World Bank in 2015 (still 6 per 1000 live births) [10]. In fact, the HTA concedes a paucity of available data on which to base informed immunisation policy for Malaysia – either from direct disease surveillance or through indirect surveillance via pneumococcal carriage studies. We believe this lack of pneumococcal surveillance gets to the heart of the MoH’s inability to deliver an unequivocal recommendation for national PCV policy in Malaysia. It is impossible to assess the economic and health impact of widespread PCV immunisation when carriage data, serotype prevalence and antimicrobial resistance (AMR), from both urban and rural settings, are not available. A robust surveillance of invasive pneumococcal diseases at serotype level with relevant antibiotic sensitivity data is strongly required to model impact of a PCV programme and the appropriateness of one vaccine formulation over another.

Although the WHO recommends pneumococcal surveillance prior to PCV rollout, it should be stressed that such is the evidence in favour of widespread PCV immunisation, the WHO does not advise a delay in commencing such a programme if pneumococcal surveillance data is unavailable or of poor quality [2]. The overwhelming evidence in favour of the use of PCVs is what has persuaded organisations such as Gavi, the Vaccine Alliance to help facilitate PCV rollout in the most underprivileged countries, which has contributed to the rates of PCV immunisation improving in LICs around the globe [4]. Moreover, the seriousness of the threat to global health posed by pneumococcal AMR continues to grow, and requires international action across government sectors and society [11]. Instituting a policy of widespread immunisation can reduce pressures on the use of antibiotics and consequent selection pressures on AMR. Policymakers can also help tackle AMR by strengthening infection control practices and by improving monitoring of the emergence, extent, and causes of resistance. The value of conducting such pneumococcal surveillance studies in Malaysia to inform immunisation policy has been discussed previously [6].

Despite vaccine availability, pneumonia remains a disease which suffers from global underinvestment in terms of research funding and vaccine implementation. Compared with the global disease burdens of tuberculosis and influenza, pneumonia and pneumococcal research and development is poorly funded [12]. In 2011, only 2% of the US\$ 30.6 billion spent on development assistance targeted pneumonia, and the majority of this investment originated from Gavi, the Vaccine Alliance and the Bill & Melinda Gates Foundation, which primarily target LICs. Thus, well-informed national decision-making is all the more important in strengthening immunisation policy in MICs, with the reinforcement of domestic political will.

Aspiring to achieve developed nation status by 2020, it is recommended that Malaysia increases in-country investments in

health policy, by implementing surveillance programmes and research into diseases of national and global importance. Pneumococcal carriage studies and disease surveillance should therefore be introduced with some urgency, accompanied by a national PCV programme. Without actions in these priority areas, Malaysia will fail to capitalise on a likely substantial reduction of child mortality and morbidity associated with pneumonia and other pneumococcal diseases, meanwhile, the threat from AMR is ever increasing. The Malaysian government urgently needs to rigorously assess the burden of pneumococcal disease in the country, and properly utilise this information towards reducing a largely preventable disease burden for the benefit of all Malaysians and in the interests of wider international public health.

Similar issues are likely in other MICs, where Gavi, the Vaccine Alliance ineligibility and a lack of disease surveillance resources will result in the inability to make high quality vaccine policy decisions. These countries, assisted by the WHO and those with an interest in infectious diseases in such countries, should grasp the opportunity for improved disease and AMR surveillance. Evidence-based approaches will aid national and global public health and help reduce the burden of pneumonia and the spread of AMR.

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### Authors’ contributions

ST, HCM and SCC conducted the critical appraisal of the Malaysia Health Technology Report and wrote the main paper. MGH, DWC and SCC edited the manuscript. All authors and members of the Malaysia Pneumococcal Carriage Study Team gave their approval of the final version of the manuscript.

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### Appendix A. MYCarriage (The Malaysia Pneumococcal Carriage Study Collaboration)

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