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Potential dengue vaccine demand in disease endemic and non-endemic countries

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Abstract

A dengue vaccine is likely to be available within the next 3-5 years and we estimated vaccine doses needed for dengue endemic countries (public and private markets) and non-endemic countries (travelers market) in the first 5 years after initial licensure. Calculations were based on 2015-2020 population projections for Asian and Americas endemic countries, and expected country-specific vaccination coverage in public, private, and travelers' sectors. Fifty-four countries were considered dengue-endemic with a population of 2.8 billion, including an annual cohort of 54 million 12-23 month old children. During the 5-year period an estimated 645 million vaccine doses would be required for early childhood immunization and up to 2 billion doses for catch-up immunization, with 80% in endemic countries being in the public sector. An estimated 59-89 million doses would be needed for the travelers market. These should be considered upper-limit estimates, with actual demand dependent on country-specific introduction strategies, price and final [1]vaccine product profile

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1. Background

Dengue is most prevalent in tropical and subtropical countries of Asia, the Pacific and the Americas [1,2]. Several vaccine candidates are under development and four have entered clinical trials, including one in a large-scale efficacy trial [3,4]. A dengue vaccine might be available within the next 3-5 years based on the present progress of large-scale clinical trials. For most routine childhood vaccines delivered in countries where dengue is endemic, purchase and delivery occurs through public sector government channels and to a smaller extent through private sector markets outside National Immunization Programs (NIPs). In dengue non-endemic countries, the potential market for a dengue vaccine is expected mainly to be composed of travelers.

The existing high level of concern about dengue fever among policymakers and the public in disease endemic countries indicates a large potential for a dengue vaccine both in the public and private sectors [5]. From a vaccine manufacturer's perspective this means that a potential market for a dengue vaccine probably already exists. Our objective was to provide a preliminary description of the potential markets for dengue vaccines in endemic and non-endemic countries. We expect this will help policy makers, program mangers, vaccine manufactures and other stakeholders to better understand the potential demand of a dengue vaccine and inform the decision making process during their early introduction process both disease endemic and non-endemic countries.

Estimation of markets for a vaccine under development is complex because of several unknowns including the product profile (e.g., vaccination schedule, number of doses, duration of protection), indicated age-groups for vaccination (e.g., routine early childhood, catch-up immunization), country-specific introduction strategies (e.g., incremental, universal) and vaccine price. Our estimates were made for a tetravalent, live attenuated dengue vaccine, the type of dengue vaccine most commonly in clinical trials. The projections provided in this paper are based on a number of assumptions and should be considered preliminary.

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Preliminary estimates of vaccine doses for public sector in dengue-endemic countries

Estimates of dengue vaccine doses required for the first five years of introduction (2015-2020) were developed for disease endemic countries of Asia and the Americas; African countries were not included because of the unknown public health impact of dengue. Included were 54 dengue-endemic countries with population >100 000 (21 GAVI eligible and 33 non-GAVI eligible countries) with a total projected population of almost 2.8 billion in 2015. The estimated annual birth cohort is approximately 53 million and the estimated 1-14 age group is 674 million. Estimates of the target population for this time period are based on projections available from the US Census Bureau [6], except for India, China and north Queensland, Australia, where we used country projections [7-9]. For China and India, we only included states that have reported dengue.

The public market for the first five years after commencement of dengue vaccine introduction was estimated for two programs: (i) routine early childhood vaccination within the NIP for children 12-23 months of age, which is probably the optimum time for administration of live attenuated vaccines due to interference from maternal antibodies in younger children, and (ii) catch-up vaccination for some or all of the 2-14 year-old age cohort. We assumed that routine early childhood vaccination is feasible and that catch-up vaccination for some or all of the older age-group will be essential to achieve dengue control in the early years after vaccine introduction. Three age-groups were considered for catch–up vaccination: 2-4, 2-9, and 2-14 year-olds.

No multiple dose vaccine is administered during the second year of life from which to benchmark dengue vaccine coverage as part of routine early childhood immunization, so we used country-specific measles vaccine coverage as a surrogate. Sixty percent of 2007 measles coverage was used to estimate the baseline for first year of dengue vaccination [10], rising stepwise to 100% of the 2007 measles coverage by the end of the fifth year after dengue vaccine introduction. Estimates were derived for both a 2-dose and 3-dose schedule and country-specific DTP vaccine dropout rates were used to estimate dropout from the first to the third dose of dengue vaccine.

We set the desired coverage for catch-up immunization at 80-90%, to make it effective as a public health intervention. However, experience from measles catch-up programs indicates that achieving high coverage is difficult, particularly with older age groups. Therefore, we estimated catch-up immunization coverage for each age cohort separately and assumed a 20% coverage decline from the first to third dose, which was applied to an expected optimum first dose coverage for each age group: 90% to 70% in 2-4 year-olds, 85% to 65% in 5-9 year-olds and 80% to 60% in 10-14 year-olds. We did not modify coverage rates based on approaches to catch-up immunization (e.g., single, compressed efforts or a staggered program over the 5-year period). We assumed that vaccine will be available both in single and multi-dose vials, and 10% to 25% wastage would be expected in the immunization strategies expected for dengue - routine early childhood and catch-up campaigns.

Our estimates show the potential vaccine demand in the 54 dengue-endemic countries would be nearly 440 million doses for routine vaccination of 12-23 month-old children over the first five years with a 2-dose schedule, and over 645 million doses for a 3-dose schedule. Depending on the age-group included for catch-up vaccination, the number of required doses could exceed 2 billion over the five year period.

Table 1: Estimated public sector demand for dengue vaccine (doses in millions) by different schedules and strategies with 25% vaccine wastage

	GAVI Eligible Countries		Non GAVI Countries		Total
	Early Childhood* (12-23 months)	Catch-up (2-14 yrs)**	Early Childhood* (12-23 months)	Catch-up (2-14 yrs)**	
2-dose schedule	276.7	1,037.3	164.1	485.2	1,963.3
3-dose schedule	400.7	1,464.5	244.7	685.0	2,794.9

GAVI = Global Alliance for Vaccines and Immunization
* Assumes integration into national immunization program and Expanded Program on Immunization.
**Catch-up includes only the 2-14 year cohort;

2. Preliminary estimates of vaccine doses for private sector in dengue-endemic countries

Literature on the size and impact of private vaccine markets in low to middle income countries is sparse and makes it difficult to estimate the size of the private sector market for a dengue vaccine. The private market share is usually < 10% of the total demand / market and is higher in urban areas (e.g. In India 27% in an urban versus 15% in a rural setting; in Thailand 33% in urban versus 10% in entire country), and higher among adults than children (e.g. In India, 36% in women compared to 17% in children) [11-13].

We estimated demand for dengue vaccine doses in the private market using assumptions specific for age-groups, urban versus rural residency, and country income level [14]. We assumed that in the 1-14 year old age-group the private market share would not exceed 10% of the total population as this age-group will be covered by public sector immunization programs, that in rural areas the private market would only be half that in urban areas for this age group, and in upper middle and high income countries the private market would be twice that in low and low middle income countries. We estimated the private market share for adults (age 15-49) to be threefold that of children in the same residential region and country income-level group. Using these assumptions, the maximum private market share would be 10-30% of the total population in urban areas of upper-middle and high income dengue-endemic countries. Our estimates show that the highest dengue vaccine demand would occur in private markets in upper middle income countries in the Americas and low middle income countries in the Asia-Pacific region. Over the first five years after vaccine introduction, the potential private sector demand under a 2-dose schedule would be 321 million and 121 million doses for Asia and the Americas, respectively, while 3-dose schedule would require 481 million and 183 million doses, respectively for the two regions. (Table 2)

Table 2: Summary of potential demand for a dengue vaccine (million of doses) over the first five years after introduction, public and private sectors.

	Public sector*	Private sector in endemic countries		Travelers	Total
		Asia	Americas		
2-dose schedule	1,897	321	121	59	2,398
3-dose schedule	2,695	481	183	89	3,448

Note: Vaccine wastage is 25% for public sector and zero for both private in endemic countries and travelers
*Includes routine vaccination of the 12-23 month age group, and catch-up vaccination of the 2-14 year cohort in 55 countries. Excludes private sector estimates and numbers deviates therefore from those presented in Table 1

3. Potential dengue vaccine demand in non-endemic countries: the travelers' market

Dengue fever is an important arboviral infection in travelers [15]. There are currently about 60 million international tourist arrivals annually to dengue-endemic countries in Asia and 51 million in the Americas [16]. The World Travel Organization predicts a continuous increase in these numbers over the next 15 years [16]. Therefore, it is reasonable to conclude that the demand for a dengue vaccine among travelers could be considerable if the vaccine has a favorable product profile (i.e. 1-3 doses administered over a maximum 4 week period).

We estimated the potential demand for a dengue travelers' vaccine assuming a favorable product profile for the 21 most popular dengue-endemic tourist destinations as determined by number of international arrivals. The estimated number of doses was based on the following assumptions: (i) all first-time and 50% of repeat visitors would require dengue vaccination (ii), vaccination coverage in this population was comparable to coverage of hepatitis A vaccination in travelers. Under these assumptions we estimated that within the first 5 years after licensure of a dengue vaccine 59 to 89 million doses would be required depending on either a 2- or 3-dose schedule, respectively. (Table 2)

4. Conclusions

This initial attempt to estimate the size of the various markets for a dengue vaccine showed that in the first five years following commencement of vaccination programs the demand could exceed 3 billion doses, with highest demand in the public sector of dengue-endemic countries. These estimates required several assumptions regarding the product profile, vaccination strategies and coverage rates. We anticipate that the product profile will strongly influence the vaccine's introduction, uptake and coverage and therefore demand within each population. Our estimates of vaccine coverage were based on an imperfect model, namely implementation of measles vaccination. Although we attempted to modify multi dose measles vaccine coverage in NIP, using drop-out rates for other vaccines the true rate of dengue vaccine coverage will not be known until large-scale demonstration projects are implemented in some dengue-endemic countries. In addition, further advances in vaccine development may be able to better adapt the product profile to facilitate vaccine coverage rates.

These estimates provide a basis to begin to determine the resources required for procurement and distribution of dengue vaccines. The degree to which public and private sector markets in dengue-endemic countries will interact in first years of vaccine introduction is unknown, so following the evolution of the private market would be important. Large-scale studies in adults will be necessary before there is a demand for this vaccine through travel medicine clinics, including studies on simultaneous vaccinations with other vaccines and alternative dosage schedules that would improve vaccine coverage. However, the greatest public health impact of dengue vaccine will be in disease endemic countries and policymakers should develop the decision making process for dengue vaccine introduction, which would include demand forecasting.

5. Acknowledgement

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