Introduction of a New Dengue Vaccine (TAK-003) in Brazil's Public Health System: Impact on Public Health and Cost-Effectiveness Across Different Age Groups

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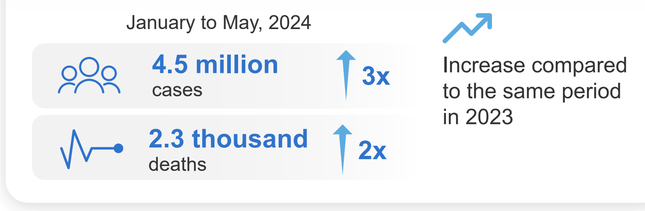
Background

The incidence of dengue has grown substantially over the last century, and it is estimated that the observed growth will continue in the coming years, with over 1 billion new people at risk of dengue by 2080.[1,2] The increase in cases is driven by climate change, urbanization, and increased human migration.[3,4] Dengue fever represents a significant burden for the Brazilian population. Between January and May 2024, more than 4.5 million cases and 2300 deaths related to dengue had been reported, three and two times increase respectively, compared to the same period in 2023[5] (**Figure 1**). Given that there is no specific treatment for dengue and prevention programs based on vector control and individual care are insufficient on their own, there is a significant unmet public health need for a safe and effective vaccine, applicable regardless of the population's prior serological status, capable of substantially reducing the burden of this disease in the country and worldwide. TAK-003, a new dengue vaccine, has demonstrated efficacy in a robust clinical development program, and currently there is a need to understand its utility in a real-world public health setting. In the pivotal phase-3 trial (DEN-301), TAK-003 demonstrated efficacy against virologically confirmed dengue (VCD) and hospitalized cases up to 4.5 years.[6]

Figure 1. Dengue cases and deaths in the Brazilian population[5]



Objectives

This study evaluates the public health impact and cost-effectiveness of vaccination strategies across different age groups, compared to no vaccination.

Methods

A **cost-effectiveness analysis** using a static model with a dynamic component was **performed** to assess the impact of vaccination with TAK-003 on epidemiologic, economic and quality of life outcomes in Brazil, capturing both direct and indirect protections[3,4]. The indirect protection was captured by the dynamic component of the model, which allowed varying the probability of infection at each model cycle based on the number of infections predicted at the previous cycle, unlike in a conventional static model where the probability of infection is constant over time. Model inputs were derived from Brazil's official databases and the model was fitted to the country's dengue epidemiology and an expansion factor of 1.8 was considered for both incidence and mortality to account for underreporting.[7] Vaccine efficacy was derived from DEN-301 study and extrapolated over 20 years to assess the impact over this period. Vaccination strategies were analyzed within each five-year age group across the age indication locally approved (**Figure 4**), assuming 90% coverage each year, which means that every year 90% of previously unvaccinated subjects would be vaccinated, and an illustrative cost of US$ 25 per dose. Benefits were measured by quality-adjusted life years (QALY). Both the payer's and society's perspectives were covered, in accordance with the World Health Organization (WHO) Guide to Standardizing Economic Evaluations of Immunization Programs[8]

Results

Model calibration was conducted by fitting the model to the average age-specific incidence based on data from 2014 to 2022, excluding the COVID pandemic years and Zika outbreaks that resulted in significant underreporting, and minimizing the difference between the predicted and observed incidence rates of symptomatic dengue in each specific age band, as per **Figure 2**. Furthermore, in the model the percentage of seropositivity at the age of 9 years was 19.5%, consistent with what is expected for this age group, taking into account the variations in disease incidence across the country (**Figure 3**).[9]

Figure 2. Model calibration according to the incidence curve: observed vs predicted values

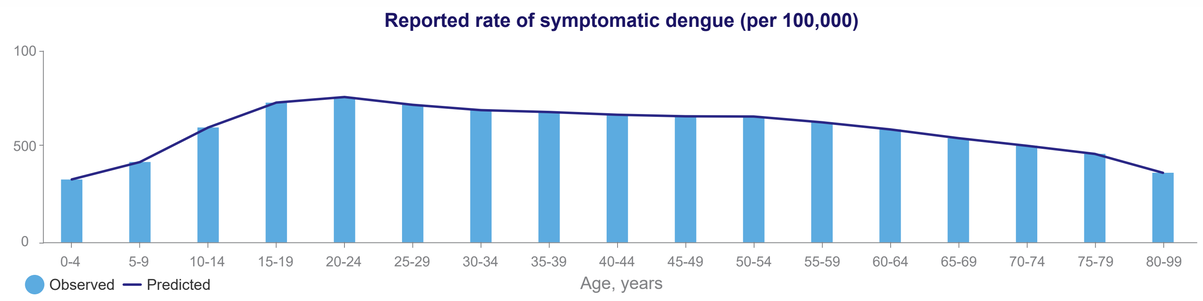
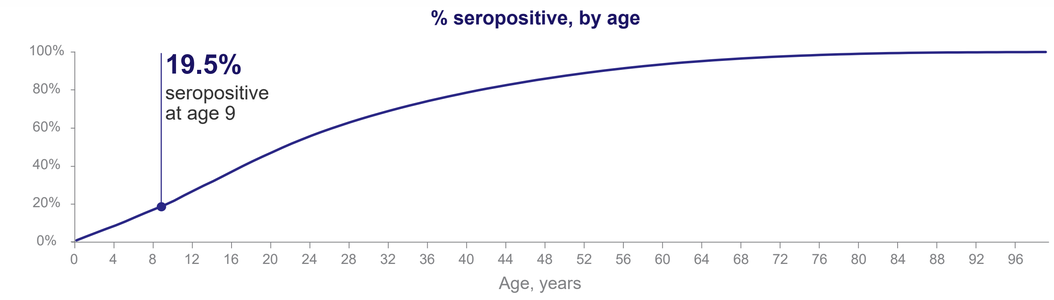
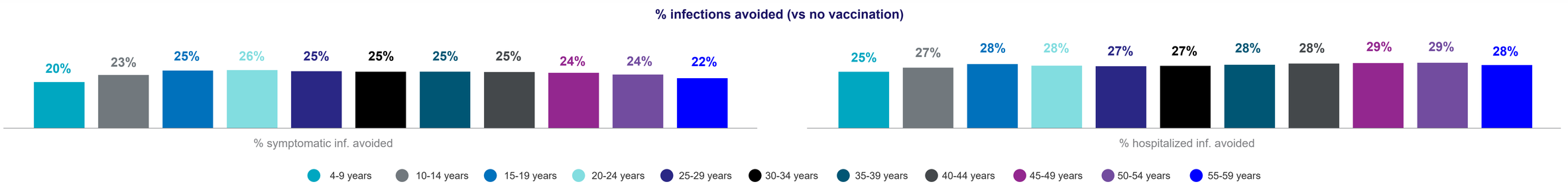


Figure 3. Seroprevalence by age predicted by the model



Modeling results revealed that implementing vaccination strategies with TAK-003 holds the potential to decrease by up to 26% and 29% symptomatic cases[10] and hospitalizations[11,12] respectively, compared to no vaccination, depending on the age strategy assessed, **even when vaccinating narrow five-year groups** (**Figure 4**).

Figure 4. Proportion of symptomatic and hospitalized cases avoided vs no vaccination per routine 5 years age-group simulated over a 20 year time horizon



The modeling results show that TAK-003 significantly reduces the costs associated with dengue management (**Figure 5**). This is important because the direct and indirect costs associated with dengue create significant financial strain, making the reduction of its economic burden a top priority for the WHO.[13]

Figure 5. Predicted cost savings among the simulated 5 years age-group vaccination scenarios over 20 year time horizon (versus no vaccination)

TAK-003 vaccination was dominant in most scenarios from a societal perspective, with up to **353,748 QALYs** gained and savings of up to US$ 260 million (**Figure 6**). From a payer's perspective, TAK-003 was cost-effective across all evaluated scenarios, considering the **US$ 8,264/QALY** threshold set by the Brazilian Health Technology Assessment (HTA) agency (**Figure 7**)[14].

Figure 6. Cost-effectiveness plane (societal perspective)

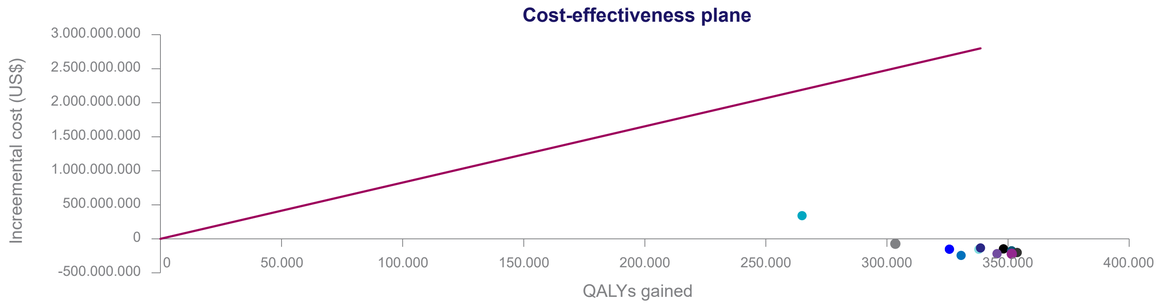
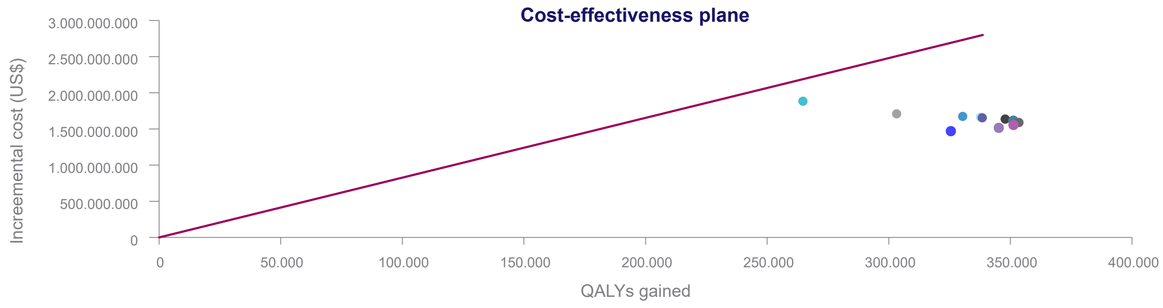


Figure 7. Cost-effectiveness plane (payer perspective)



The budgetary impact of its inclusion in the national immunization schedule is largely offset when considering the broader social perspective, including the macroeconomic cost context, and has even greater potential considering that the benefits of a vaccination program grow exponentially in the long term.

Conclusions

TAK-003 represents a major advancement in dengue prevention and offers a sustainable long-term solution to address the growing dengue burden in the Brazilian population. The modelling shows that TAK-003 vaccination program lead to a significant reduction in disease burden and costs, regardless of the age group evaluated, and serve as an additional effective dengue control measure for the study population. Through this analysis, which considered the vaccination of narrow groups composed of five individual ages, it is plausible to expect that vaccinating larger groups has the potential to prevent even more infections and generate greater savings, both directly and indirectly, related to disease management.

HTA: Health Technology Assessment; **CP:** cross-protection; **DALY:** disability-adjusted life-year; **DEN:** Dengue; **DSA:** deterministic sensitivity analysis; **PSA:** probabilistic sensitivity analysis; **QALY:** quality-adjusted life-year; **TAK:** Takeda; **VCD:** virologically confirmed dengue, **WHO:** World Health Organization.

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