Estimating the full public health value of vaccines

Optimal use of Dengue vaccines

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Les Pensières Fondation Mérieux Conference Center
Veyrier-du-Lac - France 5-7 December 2016
Current Dengue Control and Prevention Scenario

• Limited success in prevention activities despite efforts from countries at national or local level
• Focused on vector control and social mobilization (sometimes hard to achieve)
• Lack of new insecticides and increasing resistance for the existing ones

Source: World Health Organization
Number of Dengue Cases in the Americas by Decade, 1980 – 2016*

Kindly shared by J.L. San Martin / OPAS

Source: Programa Regional de Dengue de la OPS/OMS
* Hasta SE 35 del 2016
Dengue probable cases and hospitalizations, Brazil, 1986-2016*

* Preliminary data – November / 2016. Source: Sinan/SVS/MS e SIH/SAS/MS
Reported Cases by Week of Symptoms, Brazil, 2008-2016 *

*preliminary data for 2016
When I think of a dengue vaccine, what do I want?

What can I say? I want it all.

- Long term protection
- Affordable cost and millions of doses available
- High efficacy and effectiveness
- Balanced protective response against each serotype
- Safe
- Super Safe
- Easy to implement
Efficacy and Long-Term Safety of a Dengue Vaccine in Regions of Endemic Disease.


Efficacy of a tetravalent dengue vaccine in children in Latin America.


Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial.

Summary of efficacy results
25 months follow up*  Aggregated analysis†1

Efficacy for symptomatic dengue
65.6% (95% CI: 60.7–69.9)

Reduction of Hospitalizations
80.8% (95% CI: 70.1–87.7)

Reduction of severe dengue†
93.2% (95% CI: 77.3–98.0)

*Data come from the 2 pivotal, phase III, large-scale efficacy trials CYD14 and CYD15, which were designed to fully assess efficacy; postdose 1; †Full Analysis Set for Efficacy (FASE): all subjects who received at least one injection. †dengue hemorrhagic fever, World Health Organization 1997 criteria. CI=confidence interval; DENV=dengue virus.

Dengvaxia® First Dengue Vaccine Approved in Brazil

- Global introduction of the first Dengue Vaccine gains further momentum with this third approval in a row in an endemic country-

- With 1.4 million dengue cases reported this year, Brazil stands to gain tremendous value from this new dengue prevention tool -

Lyon, France - December 28, 2015 - Sanofi Pasteur, the vaccines division of Sanofi, announced today that Brazil has granted regulatory approval to Dengvaxia®, representing the third successful licensure of the dengue vaccine, which was also approved in Mexico and the Philippines earlier this month.

The Brazilian regulatory authorities ANVISA approved Dengvaxia®, tetravalent dengue vaccine, for the prevention of disease caused by all four dengue types in individuals from 9-45 years of age living in endemic areas.
Dengue Incidence by Age Group, Brazil, 2000 - 2015
Proportion of Dengue **Probable** Cases by Age Group, Brazil, 2000 – 2016*

*Preliminary data for 2016.

Source: Sinan/SVS/MS
Proportion of Dengue Probable Cases by Age Group, Brazil, 2000 – 2016*

*Preliminary data for 2016.
Source: Sinan/SVS/MS
Proportion of Dengue Hospitalized Cases by Age Group, Brazil, 2000 – 2016*

*Preliminary data for 2016.
Source: SIH/SAS/MS
Dengue Incidence by age group

Porcentaje de casos de dengue en Colombia por grupo etario

Colombia

Venezuela

Distribución de casos probables de Dengue, según grupos de edad, Tasa x 100.000 habitantes.

República Bolivariana de Venezuela año 2014. Semana epidemiológica N° 44.
WHO Position

- Countries should only consider introduction of dengue vaccine CYD-TDV in geographic settings (national or subnational) where epidemiological data indicate a high burden of disease.

- To maximize public health impact and cost effectiveness, age groups targeted for vaccination should have 70% or greater seroprevalence.

- Vaccine is not recommended when seroprevalence is below 50% in targeted age group.
How is the seroprevalence at 9 years of age?

• Baseline seropositivity rate in children 9 to 12 y old in the trial settings in Asia and Latin America was between 48% (Mexico) and 91% (Colombia).

• Other studies of dengue seroprevalence in endemic areas (Brazil; Thailand, Mexico, India) have found values of SP9 in the range of 40% to 81%

• Ongoing study for ~70 different cities in Brazil

Illustration of the assumed vaccine mode of action.


http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002181
The proportion of symptomatic and hospitalised DENV cases (rows) averted within 30 y after vaccine introduction in the reference scenario for the range of transmission intensities


http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002181
Fig 4. The number of symptomatic and hospitalized DENV cases averted per 100,000 population in the first vaccinated cohort within 30 y after vaccination.


http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002181
All models predicted that in settings with moderate to high dengue endemicity (SP9 > 50%), the default vaccination policy would reduce the burden of dengue disease for the population by 6%–25% (all simulations: –3%–34%) and in high-transmission settings (SP9 > 70%) by 13%–25% (all simulations: 10%–34%).

In settings with low transmission intensity (SP9 <= 30%), the models predicted that vaccination could lead to a substantial increase in hospitalization because of dengue.

Modelling reduced vaccine coverage or the addition of catch-up campaigns showed that the impact of vaccination scaled approximately linearly with the number of people vaccinated.
THE PUBLIC HEALTH VALUE OF DENGUE VACCINE

- Vaccine (2016)
- Estimating the public health importance of the CYD-tetravalent dengue vaccine: Vaccine preventable disease incidence and numbers needed to vaccinate
- Bradford D. Gessner, Annelies Wilder-Smith
- http://dx.doi.org/10.1016/j.vaccine.2016.03.017
LAC Region
vaccine efficacy: dengue

Vaccine Preventable Disease Incidence

Vaccine Efficacy

Hosp VCD 80%
VCD 65%
Severe VCD 96%

http://dx.doi.org/10.1016/j.vaccine.2016.03.017
LAC Region: Public health impact can be greater in settings where vaccine efficacy is lower: dengue
LAC Region: Public health impact can be greater in settings where vaccine efficacy is lower: dengue

Gessner and Wilder-Smith. Vaccine (2016). http://dx.doi.org/10.1016/j.vaccine.2016.03.017
LAC Region Summary - Dengue

- CYD-TDV shows high efficacy against severe clinical disease (96%) and health care utilization (80%)
- CYD-TDV also shows an ability to reduce dengue disease burden
  - Dengue VPDI is very high (1707)
  - Dengue NNV is very low (28)
- In addition, analyses found that the CYD-TDV dengue vaccine had favorable VPDI and NNV when compared to vaccines already used in the LAC region (Hib, rotavirus, PCV)
- CYD-TDV is important from different perspectives
  - Prevention of severe clinical disease
  - Reduction in health services utilization
  - Reduction in overall disease burden

http://dx.doi.org/10.1016/j.vaccine.2016.03.017
Conclusions

• Vaccine is recommended for endemic areas and a negative impact on the entire population can be avoided by choosing a target age for vaccination in which average seroprevalence exceeds ~50%.

• Understanding any differences between naturally and vaccine-acquired immunity will be critical in assessing the overall impact of vaccination on this group.

• To maximize the population impact of vaccination and to prevent negative impacts, it will be necessary to carefully tailor vaccination strategies to local epidemiological conditions.

• Population serosurveys can mitigate risks in planning routine vaccination.
Obrigado

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