



DISCUSSION ISSUES FOR DENGUE VACCINE USE

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INTRODUCTION CRITERIA



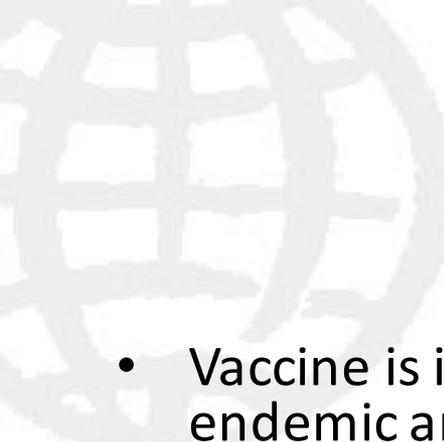
FUNDAMENTAL QUESTION 1: DOWNSIDE OF VACCINE USE?

- Vaccine safety concerns? Little evidence.
- New schedule/age group? Similar to HPV
- Waning immunity/booster requirement? Unknown but almost all LA countries have seasonal influenza policies
- Other interventions exist? Incidence increasing
- Other interventions soon to come? Which and on what timeline and with what evidence they will be marginally better than vaccine?
- Wait for better vaccine?
- Cost?
- Other public health priorities higher than dengue?



FUNDAMENTAL QUESTION 2: UPSIDE OF VACCINE USE?

- Disease reduction?
- Transmission reduction?
- Outbreak and health system disruption reduction?
- Strengthen HPV and more generally adolescent immunization?
- Learn about dengue vaccine use in anticipation of different vaccine?
- Reduce health inequities?



OTHER QUESTIONS

- Vaccine is indicated in endemic areas. What is the definition of endemic areas?
- Introduction through the National Immunization Program or also outbreak motivated?
- What programmatic criteria must be met for introduction?
 - Storage capacity
 - Cold chain
 - Communication/public health messaging
 - Education
 - Training
 - Development of school clinics
 - Etc.
- What surveillance (safety/impact) should exist pre-introduction?
- What advisory body recommendations? E.g., NITAGs, PAHO, WHO.
- What licensing body authorization?



VACCINE IMPLEMENTATION



PRINCIPLES

- Dengue vaccine introduction should complement and promote rather than disrupt existing public health interventions such as vector control, education, and case identification and referral.
- Dengue vaccine introduction should complement and promote rather than disrupt current national immunization program vaccine delivery.
- Dengue vaccine should be introduced only when the supply chain capacity is adequate at all health system levels
- Emphasis should be placed on sustainable strategies and those that are most efficient in achieving program goals (i.e., largest impact for least relative cost)
- Dengvaxia[®] should be used in routine immunization programs for the control of endemic disease and outbreaks. If within the context of an outbreak the decision to vaccinate is accelerated, program launch (routine + catch-up cohorts) should start as soon as is feasible with attention to planning for the delivery of all three doses of vaccine and according to the approved vaccine guidance.



ISSUES

- How should populations be prioritized?
 - Incidence (mortality, severe disease, disease)
 - Case density
 - Health care access
 - Economic impact
- Target age groups
 - 9 year old
 - All adolescents
 - All ages within label indication



IMPLEMENTATION STRATEGIES



STRATEGIES 1

- Health facility based
 - Least cost, as integrated into existing system
 - May achieve less impact where there is no history of adolescents presenting for immunization
 - Most effective where a large percentage of population lives relatively close to a health care facility/immunization clinic
- School-based
 - Requires new system if not implemented previously (e.g., for HPV), so may be costly
 - Where school attendance is high can lead to high coverage
 - Provides opportunity for integration of school based education regarding dengue and other mosquito-borne diseases
 - Can mobilize advocacy from teachers, who interact daily with target population



STRATEGIES 2

- Outreach
 - May be critical to reach underserved populations
 - Can facilitate catch-up campaigns
 - Requires additional considerations, such as training level of staff permitted to administer vaccines
- Integrated services
 - Refers to packaging vaccine delivery with other health interventions
 - Few health interventions routinely delivered for adolescents
 - Difficult with Dengvaxia[®], since 3 doses at specific intervals are required and this would be hard to coordinate with other interventions.



STRATEGIES 3

- Roll-out over time, including step-wedge design
 - Not exclusive of other designs.
 - Provides little advantage over a systematic prioritization process if the goal is to maximize public health impact.
 - Provides little advantage over a cluster-randomized trial if the goal is to study vaccine impact: a stepped-wedge design can be thought of as a non-randomized cluster-based introduction with too few intervention units for robust analysis.
- Integration with HPV vaccine
 - HPV is provided in a 0, 1, 6 month or 0 and 6 month schedule targeting adolescent females and in some cases adolescent males.
 - In countries using HPV vaccine, dengue vaccine can be combined with the 0 and 6 month HPV doses in targeted populations
 - Can be implemented in any setting (school, health facility, outreach)
 - If HPV targets only females, it may lead to confusing public health messaging as well as confusion at immunization clinics; moreover, a separate strategy will be required to reach males.



POST-INTRODUCTION SURVEILLANCE AND IMPACT EVALUATION



PURPOSE

- Measure local vaccine impact
- Assess program implementation
- Strengthen program support
- Counter rumors
- Identify unexpected effects



IMPACT DESIGNS

- Randomized clinical trial
- Non-randomized prospective cohort study
- Pre/post vaccine evaluation
- Case-control design



OUTCOMES AND ISSUES

POTENTIAL OUTCOMES

- Randomized clinical trial
- Non-randomized prospective cohort study
- Pre/post vaccine evaluation
- Case-control design

ISSUES

- Ethics
- Ability to provide incidence rates
- Cost
- Timeliness
- Rarity of outcome
- Ability to identify sufficient unimmunized people
- Comparability of unimmunized to immunized people
- Ability to incorporate into routine surveillance systems
- Degree and type of confounding
- Requirement for pre-vaccine data

OUTCOMES AND ISSUES

POTENTIAL OUTCOMES

- Hospital
 - Confirmed dengue case counts or incidence
 - Confirmed severe dengue case counts or incidence
 - Suspected dengue
 - Acute febrile illness
- Community cases/incidence
- Work/school absenteeism
- Number of outbreaks

ISSUES

- Cost
- Simplicity/speed
- Sensitivity/specificity
- Utility for economic models
- Need for laboratory diagnosis
- Variability due to issues other than vaccine
- Need for population data/residence information
- Severity vs. frequency of outcome



SUMMARY PUBLIC HEALTH MEASURES

- Vaccine preventable disease incidence
- Number needed to vaccinate
- Case count reduction