Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

Partial Evidence to Recommendations Framework for Dengue Vaccine TAK-003

Joshua Wong, MD

ACIP June 22, 2023

Dengue Branch, CDC

Goals for Partial EtR Presentation

- **Summarize** the extent of the Work Group deliberations to date

- **Present** three Evidence to Recommendations (EtR) domains*

- **Prepare** ACIP for the next meeting which will include a full EtR presentation, proposed recommendation, and vote.† During the full EtR presentation:
  - Domains presented today will be summarized.
  - Work Group opinions and relevant summaries of straw polls will be presented.

*Data from ND/CDC Modeling are preliminary and subject to change
†Subject to change

Evidence to Recommendations (EtR) Framework

EtR Domain	Question
Public Health Problem	• Is the problem *(dengue)* of public health importance?
Benefits and Harms	• What is the overall certainty of this evidence for the critical outcomes? • How substantial are the desirable anticipated effects of the intervention (*TAK-003 dengue vaccine*)? • How substantial are the undesirable anticipated effects? • Do the desirable effects outweigh the undesirable effects?
Values	• Does the target population feel the desirable effects are large relative to the undesirable effects? • Is there important variability in how patients value the outcomes?
Acceptability	• Is the intervention acceptable to key stakeholders?
Feasibility	• Is the intervention feasible to implement?
Resource Use	• Is the intervention a reasonable and efficient allocation of resources?
Equity	• What would be the impact of the intervention on health equity?

Public Health Problem

Is the problem (dengue) of public health importance?

Is dengue a problem of public health importance in dengue-endemic areas?

1. Should two doses of TAK-003 be administered routinely to **seropositive*** **persons aged 4–16 years** living in dengue-endemic areas?

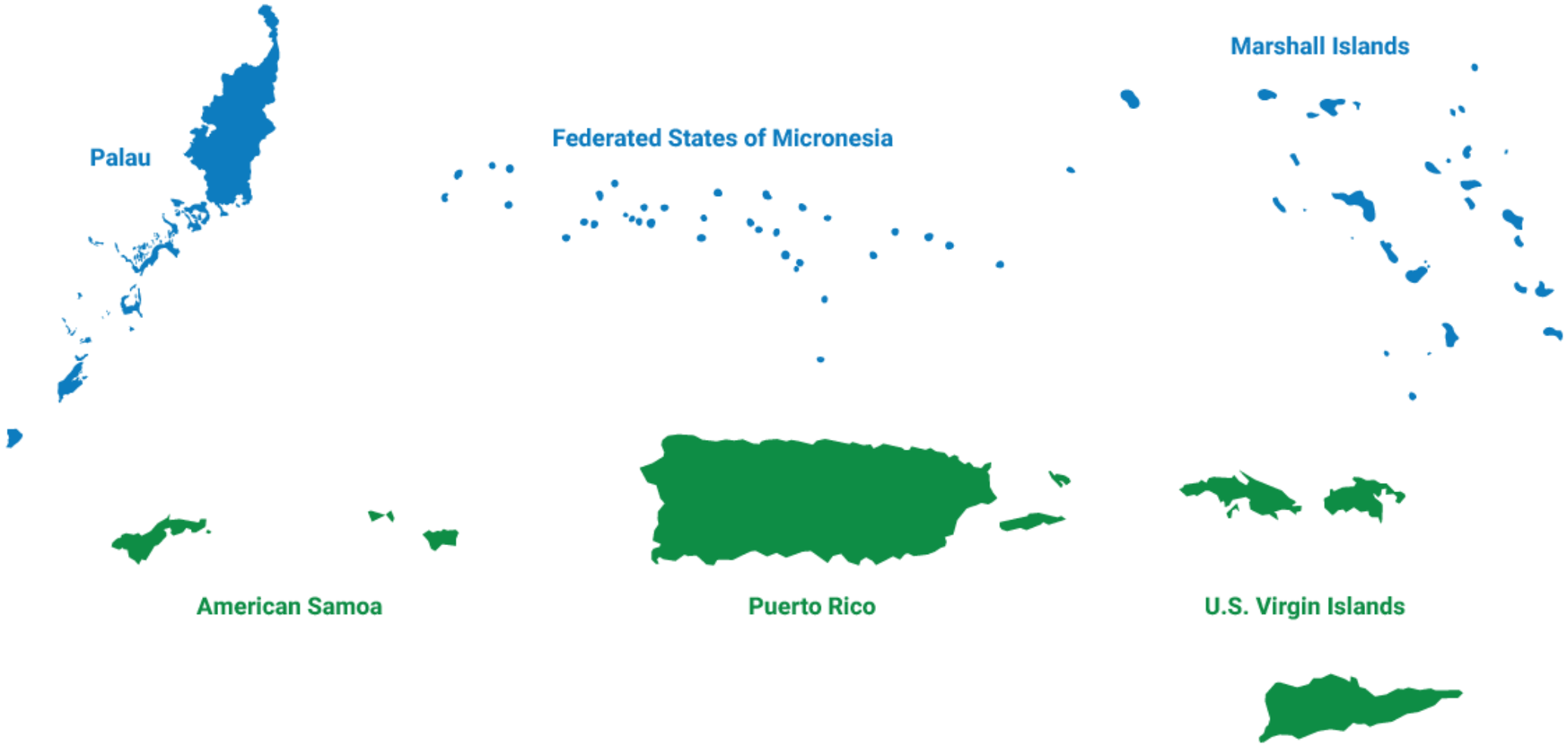
2. Should two doses of TAK-003 be administered routinely to **seronegative** **persons aged 4–16 years** living in dengue-endemic areas?

3. Should two doses of TAK-003 be administered routinely to **seropositive*** **persons aged 17–60 years** living in dengue-endemic areas?

4. Should two doses of TAK-003 be administered routinely to **seronegative** **persons aged 17–60 years** living in dengue-endemic areas?

*Recommendations for seropositive individuals only will require prevaccination screening for previous dengue virus infection.

Dengue is endemic in six U.S. territories and freely associated states.

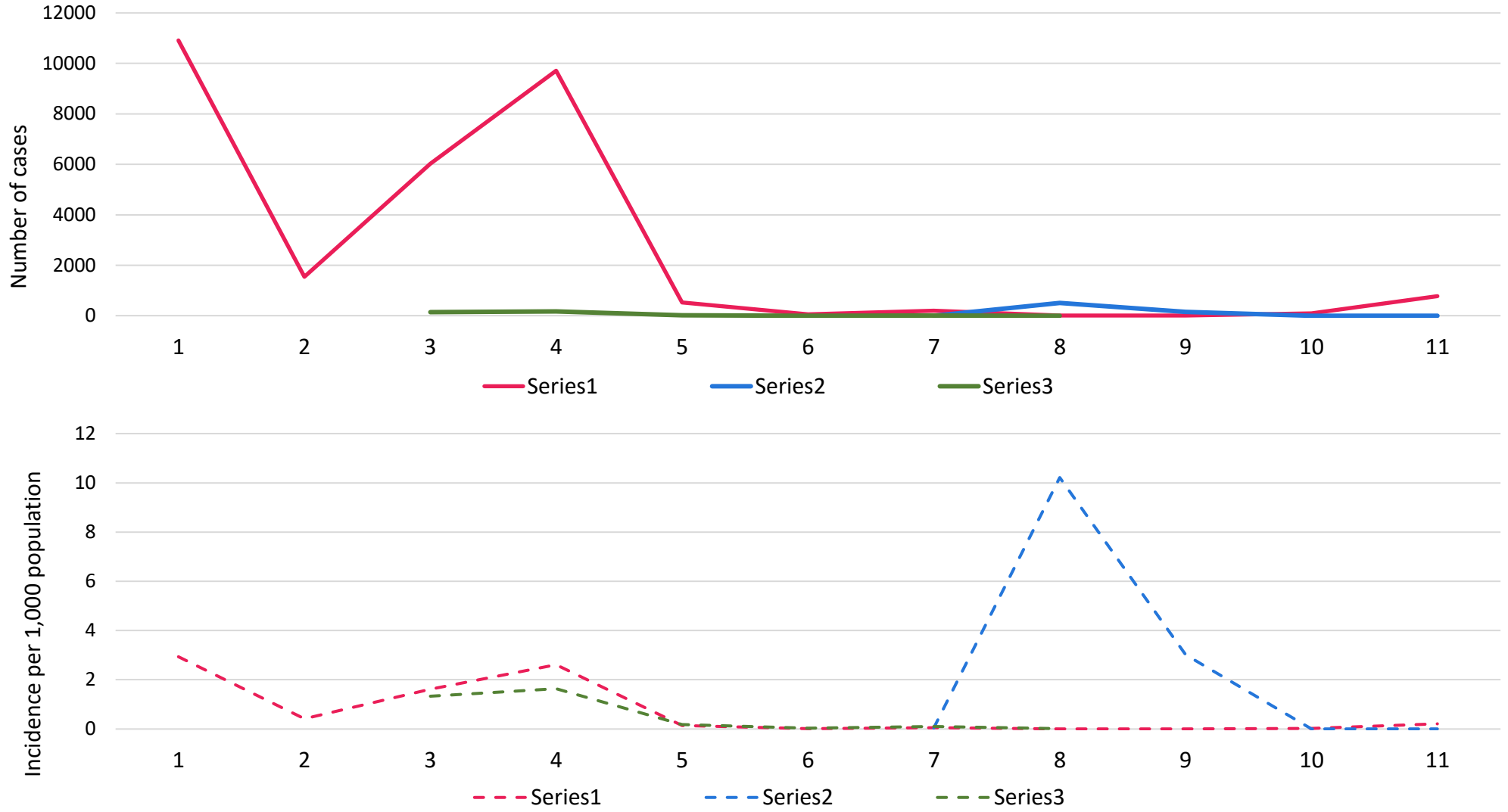


Puerto Rico has the largest population among territories with endemic dengue.

Territory	**Population**	**(%)**
Puerto Rico	3,285,874	(96.0%)
US Virgin Islands	87,146	(2.5%)
American Samoa	49,710	(1.5%)
Total population at risk	**3,422,730**	**(100%)**

2020 data - census.gov

Dengue cases and rates per 1,000 population in Puerto Rico, American Samoa, and USVI, 2010–2020



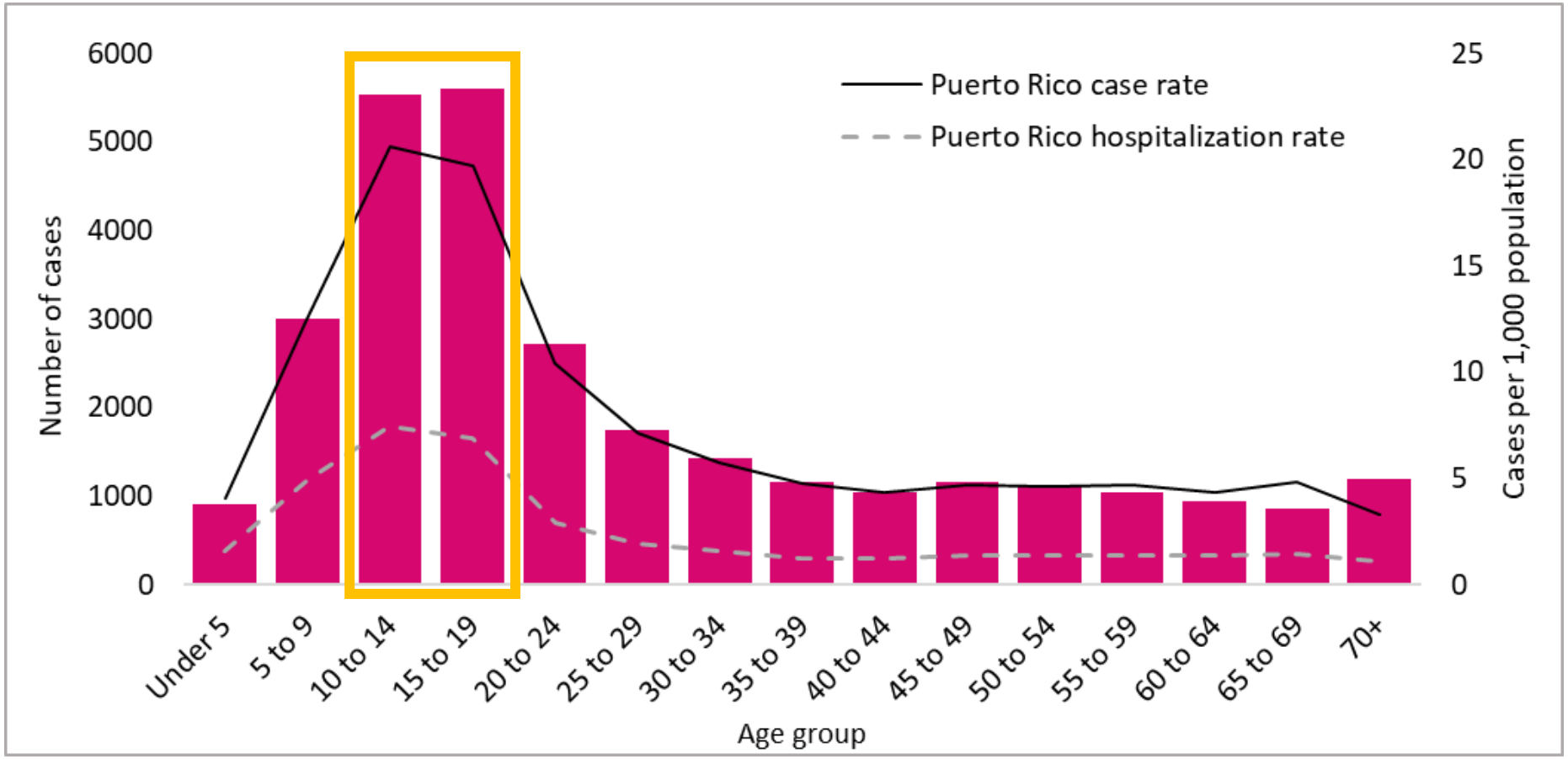
Ryff KR, Rivera A, Rodriguez DM, Santiago GA, Medina FA, Ellis EM, Torres J, Pobutsky A, Munoz-Jordan J, Paz-Bailey G, Adams LE. Epidemiologic Trends of Dengue in U.S. Territories, 2010-2020. MMWR Surveill Summ. 2023 May 19;72(4):1-12.

Is dengue a problem of public health importance for children/adolescents living in endemic areas?

	Seropositive	Seronegative
4–16 years Children/Adolescents		

Dengue cases and hospitalizations by age group in Puerto Rico, 2010–2020

Highest case rates occurred among children 10–19 years old



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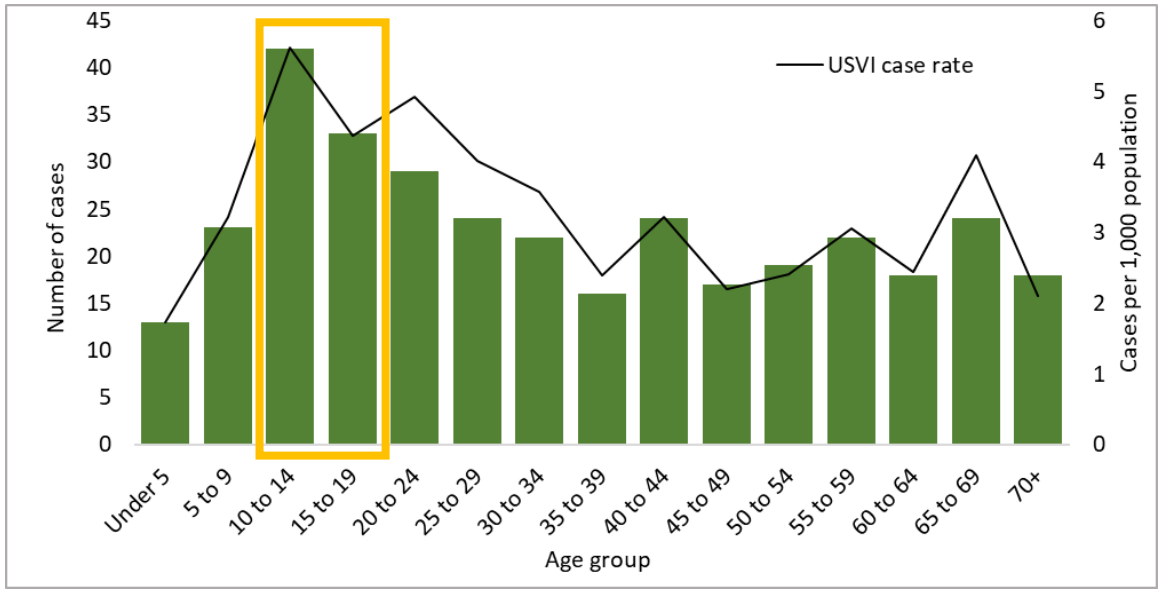
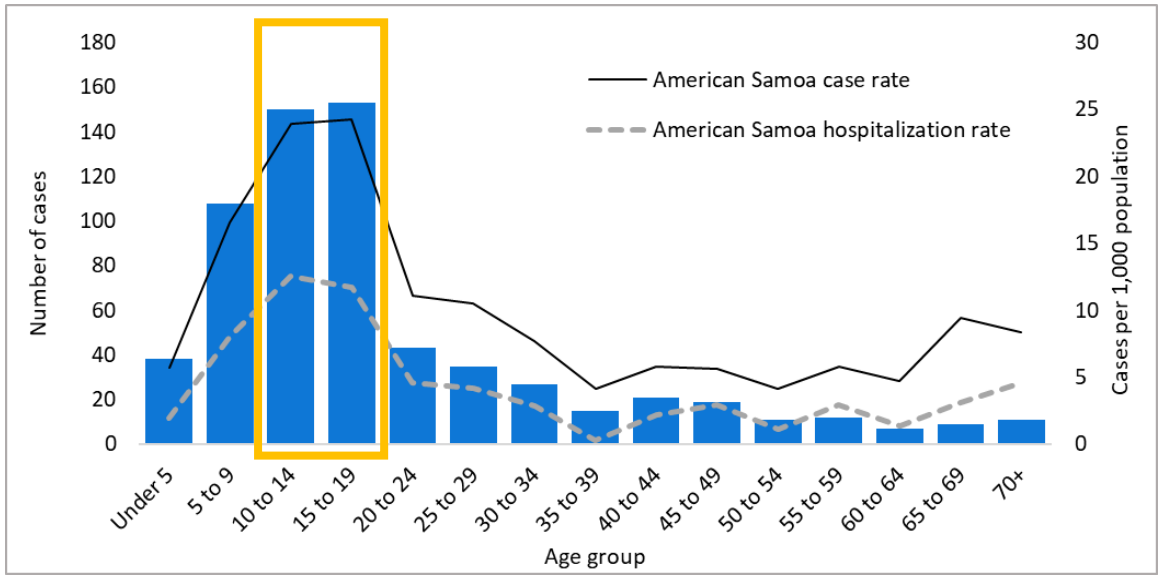
Dengue cases and hospitalizations by age group in US Virgin Islands and American Samoa, 2010–2020

Highest case rates occurred among children 10–19 years old





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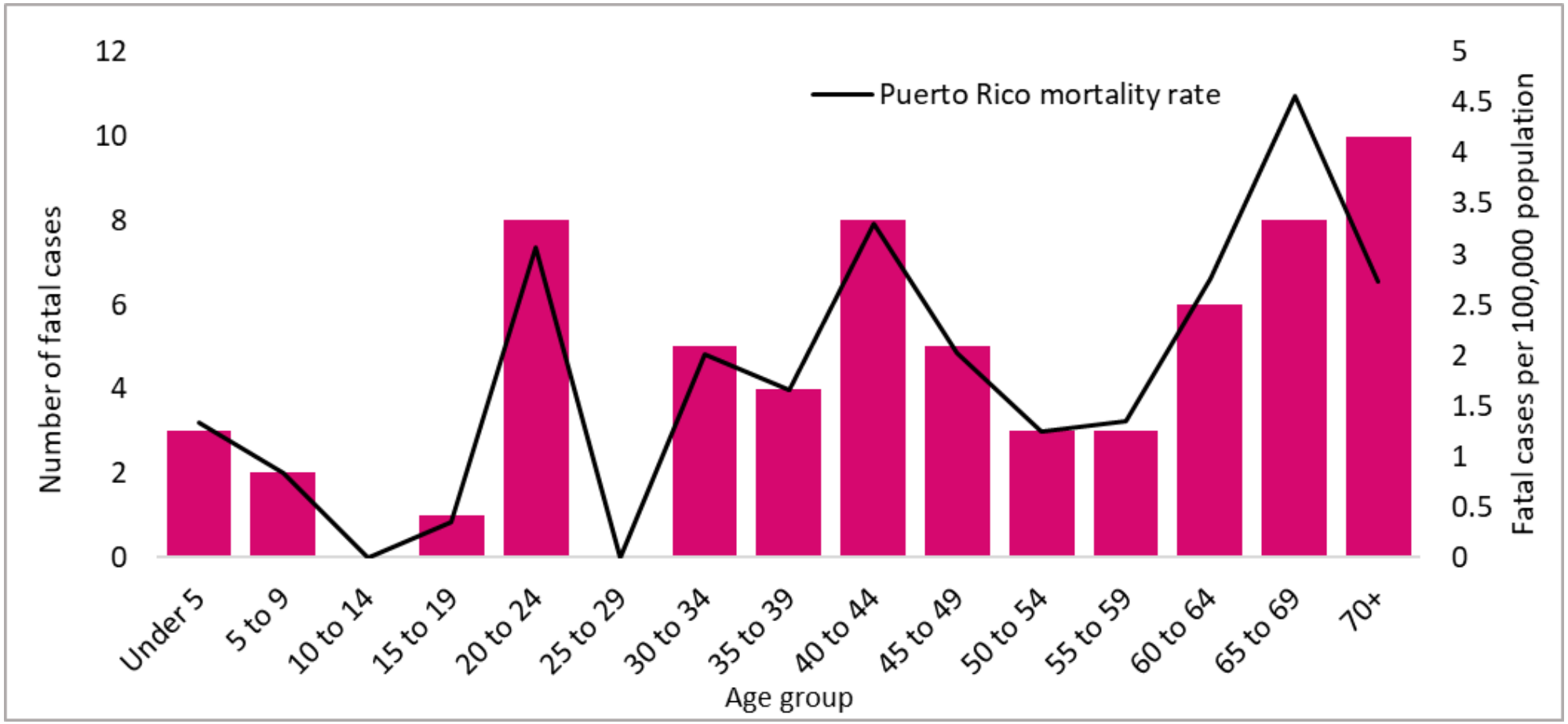
Is dengue a problem of public health importance for adults living in endemic areas?

	Seropositive	Seronegative
4–16 years Children/Adolescents		
17–60 years Adults		

Fatal dengue cases (N = 68) by age group in Puerto Rico, 2010–2020

Higher mortality rates occurred among adults



*All fatal dengue cases reported during 2010–2020 were from Puerto Rico. No deaths were reported from the other territories

Ryff KR, Rivera A, Rodriguez DM, Santiago GA, Medina FA, Ellis EM, Torres J, Pobutsky A, Munoz-Jordan J, Paz-Bailey G, Adams LE. Epidemiologic Trends of Dengue in U.S. Territories, 2010-2020. MMWR Surveill Summ. 2023 May 19;72(4):1-12.

Summary – Public Health Problem

- Dengue is endemic in six US territories and freely associated states.
  - Puerto Rico has the largest population among US territories where dengue is endemic.
- The highest case and hospitalization rates occur in individuals aged 10–19 years.
- The highest mortality rates occur in adults aged ≥20 years.

Public Health Problem

Is the problem (dengue) of public health importance?

Options: ○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know

Benefits and Harms

Benefits and Harms

What is the overall certainty of the desirable anticipated effects?

Outcomes: desirable anticipated effects

Outcome	Importance*
Virologically confirmed dengue due to any serotype	Critical
Hospitalization for dengue due to any serotype	Critical
Dengue hemorrhagic fever due to any serotype	Critical
Severe dengue (trial definition) due to any serotype	Critical

*Options are critical, important but not critical, not important for decision-making

Systematic review

- Systematic search identified 370 articles
  - 17 met inclusion/exclusion criteria including data on outcomes of interest from phase 1–3 trials.

- However, 0 articles contained the 57 month follow-up time of interest that has been presented to and discussed by Work Group and ACIP.

- All vaccine efficacy and safety data provided by Takeda.*

*One article regarding safety outcomes used in systematic review has been published (Patel, CID, 2022), but data stratified by PICO populations was provided by Takeda in personal communications with WG lead.

Multiple GRADE domains do not change for the populations assessed or outcomes.

Outcome	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Certainty
VCD	↑	↑	↑	↑			↑	
Hospitalization								
DHF								
Severe Dengue								

Indirectness and **imprecision** varied by population/outcome assessed and determined final certainty level.

Outcome	[redacted]	Indirectness	Imprecision	[redacted]	Certainty
VCD					
Hospitalization					
DHF					
Severe Dengue					
SAE					
Deaths					

How certain are the desirable effects in children/adolescents?

	Seropositive	Seronegative
4–16 years Children/Adolescents	• **Phase 3 Trial data**	• **Phase 3 Trial data**

Vaccine Efficacy* Outcome: **Virologically Confirmed Dengue**

Overall VE

61.2% (56.0, 65.8%)

VE in Seropositives

64.2% (58.4, 69.2%)

VE in Seronegatives

53.5% (41.6–62.9%)

VE in Seropositives by Serotype		
DENV-1	**56.1%**	**(44.6, 65.2%)**
DENV-2	**80.4%**	**(73.1, 85.7%)**
DENV-3	**52.3%**	**(36.7, 64.0%)**
DENV-4	**70.6%**	**(39.9, 85.6%)**

VE in Seronegatives by Serotype		
DENV-1	**45.4%**	**(26.1, 59.7%)**
DENV-2	**88.1%**	**(78.6, 93.3%)**
DENV-3	-15.5%	(-108.2, 35.9%)
DENV-4	-105.6%	(-628.7, 42.0%)

*57 months after first dose, significant results **bolded.** Number for seropositive placebo participants 4,855 and vaccine 9,666; Seronegative placebo 1,832 and vaccine 3,714.

Paz-Bailey. ACIP, February 17, 2023.

Vaccine Efficacy* Outcome: **Hospitalization**

Overall VE

84.1% (77.8, 88.6%)

VE in Seropositives

85.9% (78.7, 90.7%)

VE in Seropositives by Serotype

DENV-1	**66.8% (37.4, 82.3%)**
DENV-2	**95.8% (89.6, 98.3%)**
DENV-3	**74.0% (38.6, 89.0%)**
DENV-4	**100% (NE, NE)†**

†DENV-4 Placebo events: 3 TAK-003 events: 0

VE in Seronegatives

79.3% (63.5, 88.2%)

VE in Seronegatives by Serotype

DENV-1	**78.4%**	**(43.9, 91.7%)**
DENV-2	**100%**	**(NE, NE)§**
DENV-3	-87.9%	(-573.4, 47.6%)¶
DENV-4	100 %	(NE, NE)**

§DENV-2 Placebo events: 23 TAK-003 events: 0
¶DENV-3 Placebo events: 3 TAK-003 events: 11
**DENV-4 Placebo events: 1 TAK-003 events: 0

*57 months after first dose, significant results **bolded.** Number for seropositive placebo participants 4,855 and vaccine 9,666; Seronegative placebo 1,832 and vaccine 3,714.

Vaccine Efficacy* Outcome: **Hospitalization**

Overall VE

84.1% (77.8, 88.6%)

VE in Seronegatives

79.3% (63.5, 88.2%)

VE in Seronegatives by Serotype

DENV-1	**78.4%**	**(43.9, 91.7%)**
DENV-2	**100%**	**(NE, NE)[§]**
DENV-3	-87.9%	(-573.4, 47.6%)[¶]
DENV-4	100 %	(NE, NE)**

Data insufficient to rule out an increased risk

[§]DENV-2 Placebo events: 23 TAK-003 events: 0
[¶]DENV-3 Placebo events: 3 TAK-003 events: 11
**DENV-4 Placebo events: 1 TAK-003 events: 0

*57 months after first dose, significant results **bolded.** Number for seropositive placebo participants 4,855 and vaccine 9,666; Seronegative placebo 1,832 and vaccine 3,714.

Dengue Hemorrhagic Fever (1997 Definition)

Overall VE

70.0% (31.5, 86.9%)

VE in Seropositives

80.9% (46.3, 93.2%)

Events by Serotype

	Placebo	TAK-003
DENV-1	*<10*	*<10*
DENV-2	*<10*	*<10*
DENV-3	*<10*	*<10*
DENV-4	*<10*	*<10*
Total	*13*	*5*

VE in Seronegatives

-3.4% (-464.7, 81.1%)

Events by Serotype

	Placebo	TAK-003
DENV-1	*<5*	*<5*
DENV-2	*<5*	*<5*
DENV-3	*<5*	*<5*
DENV-4	*<5*	*<5*
Total	*2*	*4*

*57 months after first dose, significant results for vaccine efficacy **bolded.** Number for seropositive placebo participants 4,855 and vaccine 9,666; Seronegative placebo 1,832 and vaccine 3,714.

Severe Dengue Trial-specific Definition

Overall VE

70.2% (-24.7, 92.9%)

VE in Seropositives

90.2% (16.4, 98.9%)

Events by Serotype

	Placebo	TAK-003
DENV-1	*<5*	*<5*
DENV-2	*<5*	*<5*
DENV-3	*<5*	*<5*
DENV-4	*<5*	*<5*
Total	*5*	*1*

VE in Seronegatives

-999.0% (NE, NE)

Events by Serotype

	Placebo	TAK-003
DENV-1	*<5*	*<5*
DENV-2	*<5*	*<5*
DENV-3	*<5*	*<5*
DENV-4	*<5*	*<5*
Total	*0*	*2*

Paz-Bailey. ACIP, February 17, 2023.

Outcomes: desirable anticipated effects

Outcome	Importance*
Virologically confirmed dengue **due to any serotype**	Critical
Hospitalization for dengue **due to any serotype**	Critical
Dengue hemorrhagic fever **due to any serotype**	Critical
Severe dengue (trial definition) **due to any serotype**	Critical

*Options are critical, important but not critical, not important for decision-making

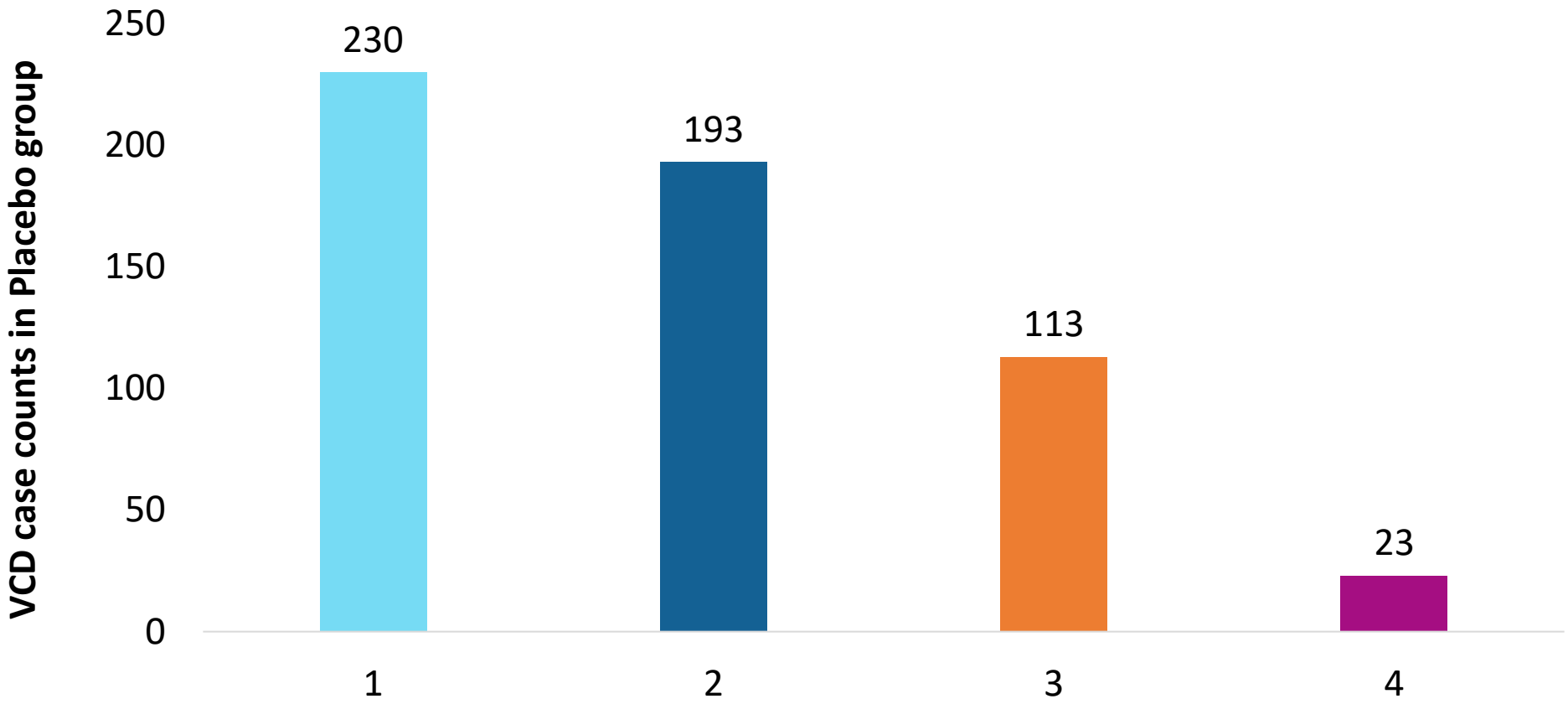
What is the overall certainty of the desirable anticipated effects in children/adolescents aged 4–16 years?

Seropositive children/adolescents aged 4–16 years				
Outcome (Desirable)	**Vaccine Efficacy**	**Imprecision**	**Indirectness**	**Certainty**
Virologically confirmed dengue	64.2 (58.4, 69.2)	Not serious		
Hospitalization	85.9 (78.7, 90.7)	Not serious		
Dengue hemorrhagic fever	80.9 (46.3, 93.2)	Not serious		
Severe dengue (trial definition)	90.2 (16.4, 98.9)	Not serious		

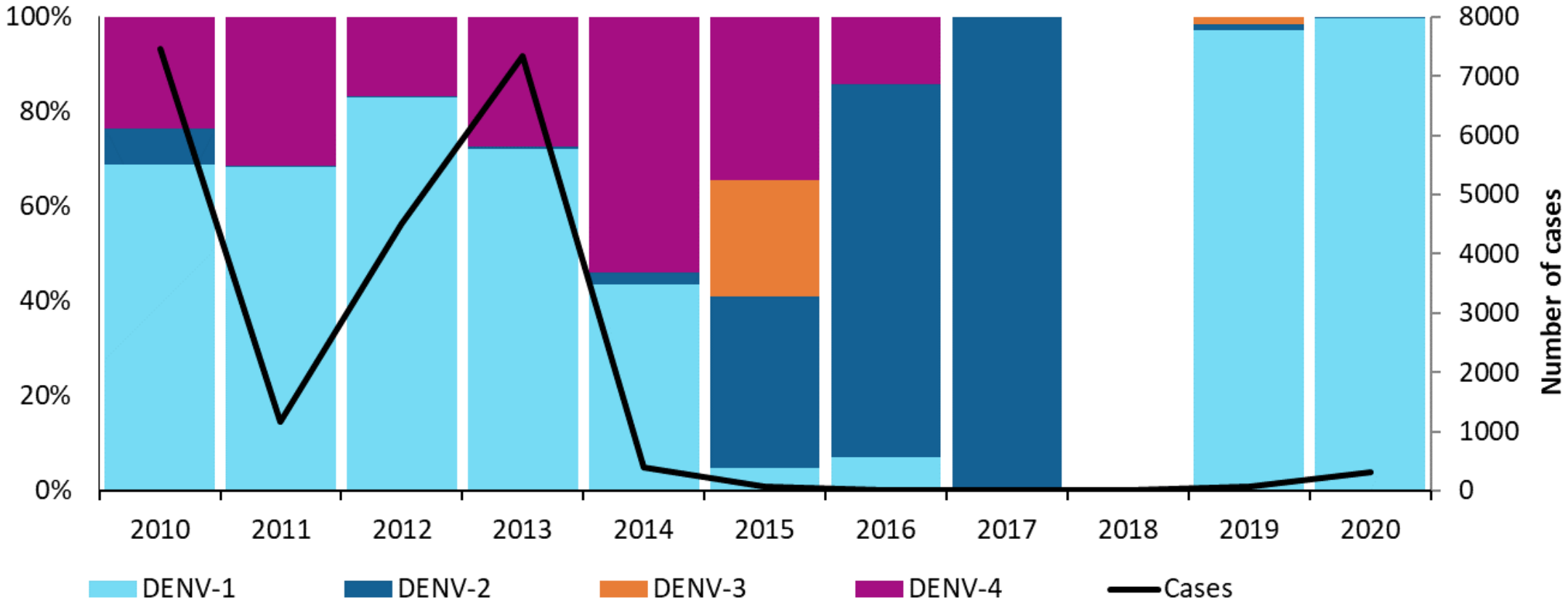
Seronegative children/adolescents aged 4–16 years				
Outcome (Desirable)	**Vaccine Efficacy**	**Imprecision**	**Indirectness**	**Certainty**
Virologically confirmed dengue	53.5 (41.6, 62.9)	Not serious		
Hospitalization	79.3 (63.5, 88.2)	Not serious		
Dengue hemorrhagic fever	-3.4 (-464.7, 818.1)	Serious		
Severe dengue (trial definition)	NE (NE, NE)	Serious		

Does the study population differ from the population of interest?

DENV-1 and DENV-2 were the most common serotypes in the TAK-003 Phase 3 trial.



All four serotypes have circulated in PR from 2010–2020.



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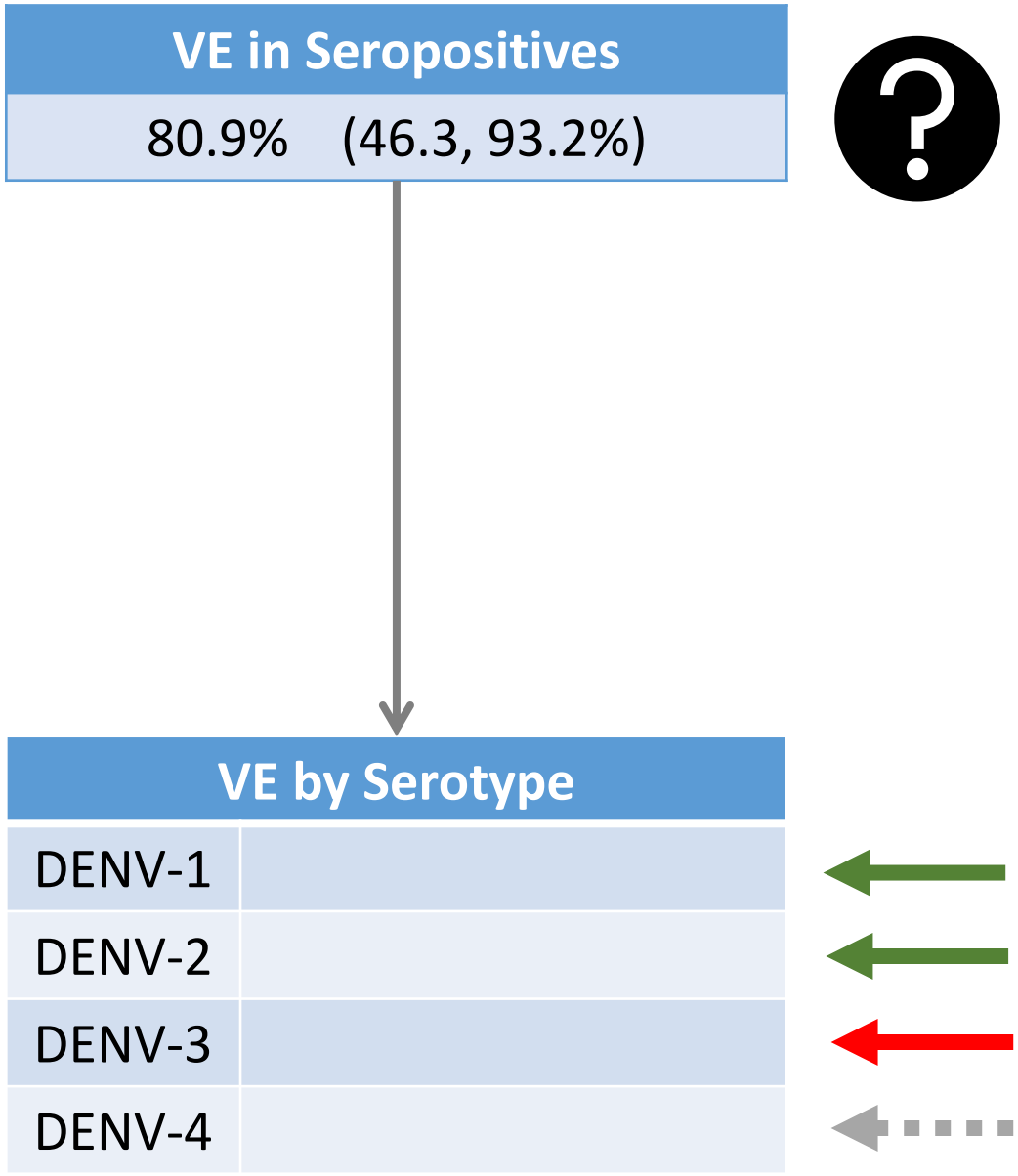
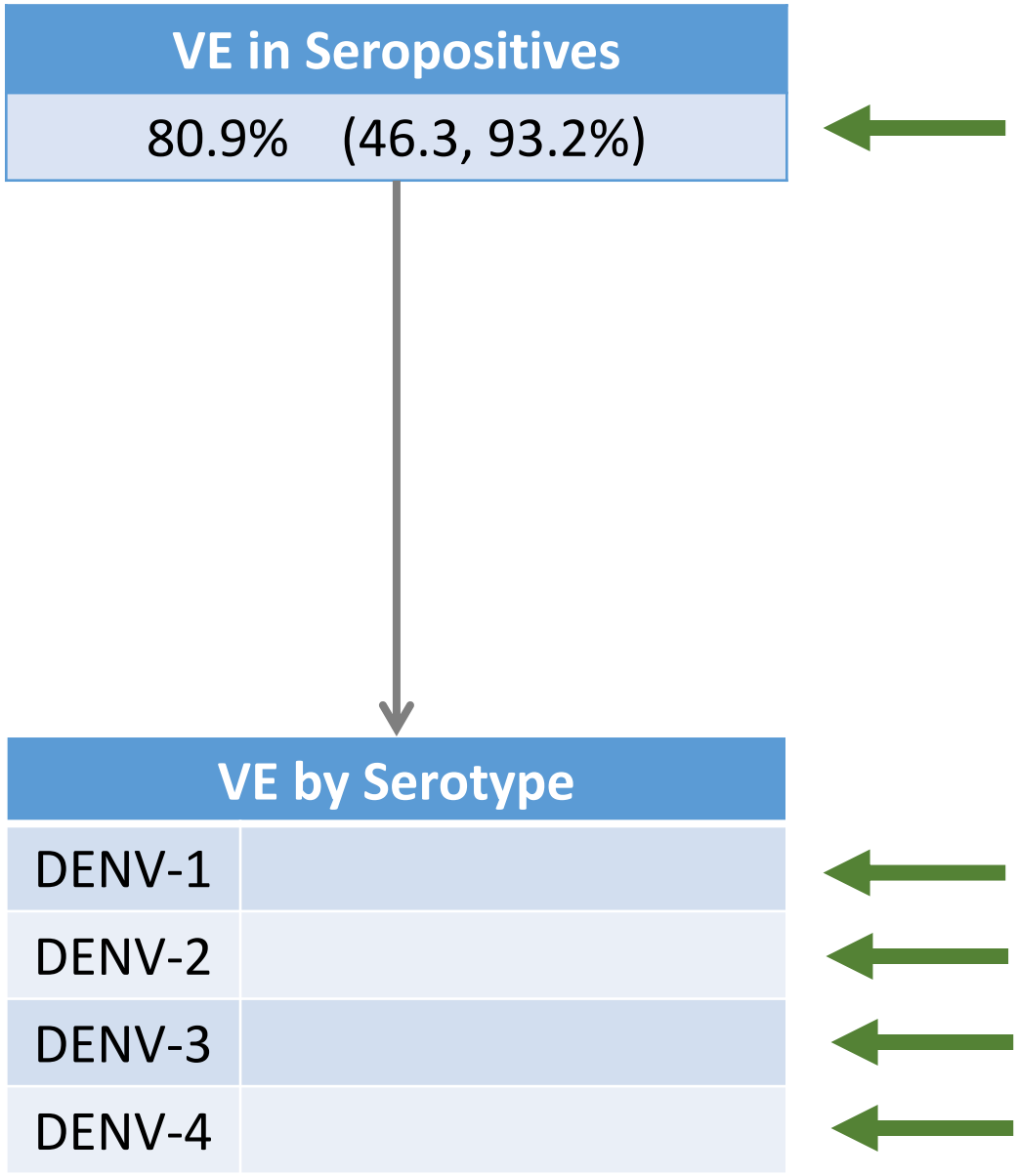


The VE for all serotypes combined from the phase 3 trials

does **not directly** apply to our population of interest and their future risk of dengue if

it does not protect against one or more of the 4 serotypes.



The VE for all serotypes combined from the phase 3 trials

is only **directly** applicable to our population of interest and their future risk of dengue if there is

significant protection against all 4 serotypes.

What is the overall certainty of the desirable anticipated effects in children/adolescents aged 4–16 years?

Seropositive children/adolescents aged 4–16 years				
Outcome (Desirable)	**Vaccine Efficacy**	**Imprecision**	**Indirectness**	**Certainty**
Virologically confirmed dengue	64.2 (58.4, 69.2)	Not serious	Not serious	High
Hospitalization	85.9 (78.7, 90.7)	Not serious	Not serious	High
Dengue hemorrhagic fever	80.9 (46.3, 93.2)	Not serious	Serious	Moderate
Severe dengue (trial definition)	90.2 (16.4, 98.9)	Not serious	Serious	Moderate

Seronegative children/adolescents aged 4–16 years				
Outcome (Desirable)	**Vaccine Efficacy**	**Imprecision**	**Indirectness**	**Certainty**
Virologically confirmed dengue	53.5 (41.6, 62.9)	Not serious	Serious	Moderate
Hospitalization	79.3 (63.5, 88.2)	Not serious	Serious	Moderate
Dengue hemorrhagic fever	-3.4 (-464.7, 818.1)	Serious	Serious	Low
Severe dengue (trial definition)	NE (NE, NE)	Serious	Serious	Low

How certain are the desirable effects in adults?

	Seropositive	Seronegative
4–16 years Children/Adolescents		
17–60 years Adults		• **Outcomes assessed through immunobridging**

Antibody titers in seronegative adults (18–60) were **noninferior* at 1 and 6 months** for almost all serotypes compared to participants aged 4–16.

Outcome (desirable)	Time after 2nd dose	N (4–16 years)	N (18–60 years)	Geometric Mean Ratio	Met noninferiority objective*
GMR DENV-1	1 month	641	367	0.69 (0.58, 0.82)	Yes
GMR DENV-2	1 month	641	367	0.59 (0.52, 0.66)	Yes
GMR DENV-3	1 month	641	367	1.77 (1.53, 2.04)	No
GMR DENV-4	1 month	641	367	1.05 (0.92, 1.20)	Yes
GMR DENV-1	6 months	607	353	0.62 (0.51, 0.76)	Yes
GMR DENV-2	6 months	607	355	0.66 (0.57, 0.76)	Yes
GMR DENV-3	6 months	607	355	0.98 (0.84, 1.14)	Yes
GMR DENV-4	6 months	607	354	1.01 (0.86, 1.18)	Yes

*Non-inferiority was defined as a geometric mean ratio (GMR) with the upper bound of the 95% CI below 2.0.

Rivera L, Biswal S, Sáez-Llorens X, Reynales H, López-Medina E, Borja-Tabora C, et al. Three years efficacy and safety of Takeda's dengue vaccine candidate (TAK-003). Clin Infect Dis. 2021 Oct 4.

What is the overall certainty of the desirable anticipated effects in adults aged 17–60 years?

Seronegative adults aged 17–60 years					
Outcome (Desirable)	**N (4–16 years)**	**N (18–60 years)**	**Met noninferiority objective**	**Indirectness**	**Certainty**
VCD, hospitalization, DHF, severe dengue (**assessed with immunobridging**)	607-641	353-367	Yes for all serotypes, except for DENV-3 assessed at 1 month	Serious*	Moderate

*Downgraded once for indirectness due to immunobridging.

How certain are the desirable effects in adults?

	Seropositive	Seronegative
4–16 years Children/Adolescents		
17–60 years Adults	• **Outcomes assessed through immunobridging in seronegatives***	• Outcomes assessed through immunobridging

*Immunogenicity in seropositive adults expected to be at least as robust as in seronegative adults; downgraded twice for indirectness.

What is the overall certainty of the desirable anticipated effects in adults aged 17–60 years?

Seronegative adults aged 17–60 years					
Outcome (Desirable)	**N (4–16 years)**	**N (18–60 years)**	**Met noninferiority objective**	**Indirectness**	**Certainty**
VCD, hospitalization, DHF, severe dengue (**assessed with immunobridging**)	607-641	353-367	Yes for all serotypes, except for DENV-3 assessed at 1 month	Serious	Moderate

Seropositive adults aged 17–60 years		
Outcome (Desirable)	**Indirectness**	**Certainty**
VCD, hospitalization, DHF, severe dengue **(assessed with immunobridging in seronegative adults)**	Very Serious*	Low

*Downgraded twice for indirectness, because outcomes are assessed with immunobridging data from seronegative adults and assumption of equal or greater immunogenicity in seropositive adults

Summary of Desirable Outcomes

4–16 years
Children/Adolescents

Seropositives

Outcome	VE	Certainty
VCD	64.2 (58.4, 69.2)	High
Hospitalization	85.9 (78.7, 90.7)	High
DHF	80.9 (46.3, 93.2)	Moderate
Severe dengue	90.2 (16.4, 98.9)	Moderate

Seronegatives

Outcome	VE	Certainty
VCD	53.5 (41.6, 62.9)	Moderate
Hospitalization	79.3 (63.5, 88.2)	Moderate
DHF	-3.4 (-464.7, 818.1)	Low
Severe dengue	NE (NE, NE)	Low

17–60 years
Adults

Seropositives

Outcome (Desirable)	Certainty
All outcomes (assessed with **immunobridging in seronegatives***)	Low

Seronegatives

Outcome (Desirable)	Certainty
All outcomes (assessed with **immunobridging**)	Moderate

*Immunogenicity in seropositive adults is expected to be at least as high as in seronegative adults.

Summary of Certainty for All Desirable Outcomes

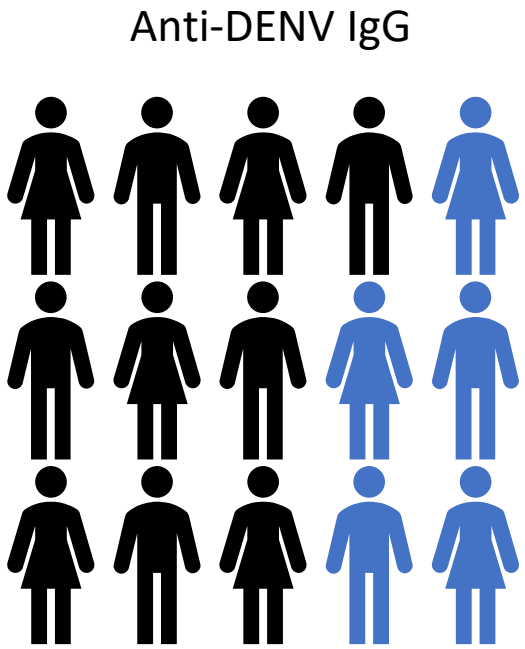
	Seropositives	Seronegatives
4–16 years Children/Adolescents	**High – Moderate**	**Moderate – Low**
17–60 years Adults	**Low**	**Moderate**

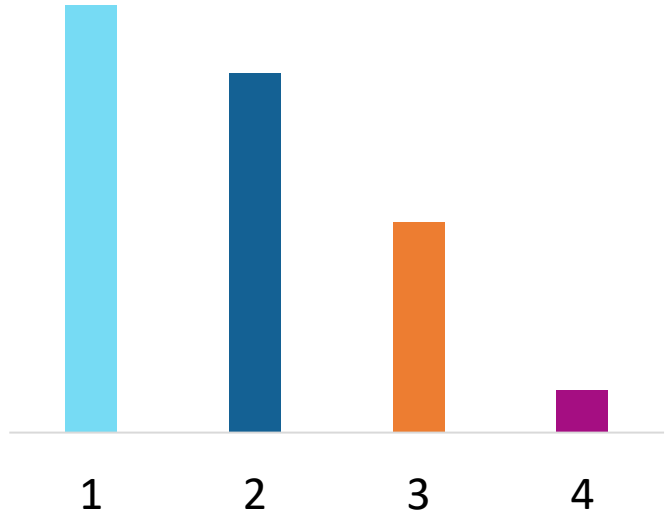
*Immunogenicity in seropositive adults is expected to be at least as high as in seronegative adults.

Benefits and Harms

How substantial are the desirable anticipated effects?

The population level effects of TAK-003 implementation will vary by…





seroprevalence of past infection AND serotype circulation.

Preliminary Modeled Estimates of Population-level Impacts in San Juan, PR* over 10 years

Recommendation	Reduction in VCD†	Reduction in hospitalizations†
4–16, seropositive (**screening**‡)	1%	3%
4–16, all serostatuses (no screening)	3%	3%
17–60, seropositive (**screening**‡)	6%	10%
17–60, all serostatuses (no screening)	8%	13%
4–60, seropositive (**screening**‡)	7%	12%
4–60, all serostatuses (no screening)	9%	15%

*The model assumes a seroprevalence of 40% at age 9, a vaccine coverage increasing from 0 to 40% over 10 years in all ages eligible, and serotype distribution simulated from 20 years of historical data (1996–2016) from San Juan, Puerto Rico (PR).
†Averted symptomatic and hospitalizations are for all ages in San Juan and include direct and indirect effects.
‡Screening test with 80% sensitivity and 98% specificity

Summary of Desirable Anticipated Effects

- Modeling* shows a **reduction in VCD and hospitalizations** following implementation of TAK-003 in **all populations** explored in the policy questions.

- Reductions in VCD and hospitalizations are **higher** when vaccination is implemented in **broader age ranges** and for **both seropositive and seronegative** individuals.

*Model based on preliminary data from Dr. España presented to ACIP on June 22, 2023.

Benefits and Harms

How substantial are the desirable anticipated effects?

Options: ○ Minimal ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know

Benefits and Harms

How substantial are the undesirable anticipated effects?

What is the overall certainty?

Outcomes: undesirable anticipated effects

Outcome	Importance*
Serious adverse events (SAEs)	Critical
Deaths	Critical
Systemic reactions†	Important
Local reactions†	Important
Interference with co-administered vaccines†	Important

*Options are **critical**, **important** but not critical, **not important** for decision-making

†Not assessed in GRADE analysis

How certain are the undesirable effects in children/adolescents?

	Seropositive	Seronegative
4–16 years Children/Adolescents	• **Phase 2 and 3 trials**	• **Phase 2 and 3 trials**

What is the overall certainty of the undesirable anticipated effects in children/adolescents aged 4–16 years?

Seropositive children/adolescents aged 4–16 years						
Outcome (Undesirable)	**n/N TAK-003**	**n/N placebo**	**Hazard Ratio**	**Imprecision**	**Indirectness**	**Certainty**
SAEs	826/9725 (8.5%)	503/4944 (10.2%)*	0.82 (0.74, 0.92)	Not serious	Not serious	High
Deaths†	14/9725 (0.14%)	6/4944 (0.12%)	1.18 (0.45, 3.07)	Not serious	Not serious	High

Seronegative children/adolescents aged 4–16 years						
Outcome (Undesirable)	**n/N TAK-003**	**n/N placebo**	**Hazard Ratio**	**Imprecision**	**Indirectness**	**Certainty**
SAEs	323/3984 (8.1%)	183/1979 (9.3%)*	0.88 (0.73, 1.05)	Not serious	Not serious	High
Deaths†	2/3984 (0.05%)	1/1979 (0.05%)	1.00 (0.09, 11.04)	Not serious	Not serious	High

*Higher dengue SAEs in placebo (n=100) compared to TAK-003 (n=51) resulted in HR <1 for all SAEs in TAK-003 compared to placebo.

†None of the deaths in the trial were due to dengue

Communication with Takeda. April 25, 2023.

How certain are the undesirable effects in adults?

	Seropositive	Seronegative
4–16 years Children/Adolescents	• Phase 2 and 3 trials	• Phase 2 and 3 trials
17–60 years Adults	• **Phase 2 and 3 trials**	• **Phase 2 and 3 trials**

What is the overall certainty of the undesirable anticipated effects in adults aged 17–60 years?

Seronegative adults aged 17–60 years						
Outcome (Undesirable)	**n/N TAK-003**	**n/N placebo**	**Hazard Ratio**	**Imprecision**	**Indirectness**	**Certainty**
SAEs	9/488 (1.8%)	3/84 (3.6%)	0.499 (0.14, 1.84)	Not serious	Not serious	High
Deaths	0/488	0/84	N/A	Not serious	Not serious	High

Seropositive adults aged 17–60 years						
Outcome (Undesirable)	**n/N TAK-003**	**n/N placebo**	**Hazard Ratio**	**Imprecision**	**Indirectness**	**Certainty**
SAEs	3/83 (3.6%)	0/31	N/A	Serious	Not serious	Moderate
Deaths	0/83	0/31	N/A	Serious	Not serious	Moderate

Communication with Takeda. April 25, 2023.

Summary of Undesirable Outcomes Certainty

4–16 years
Children/Adolescents

Seropositives

Outcome (Undesirable)	n/N TAK-003	n/N placebo	Certainty
SAEs	826/9725 (8.5%)	503/4944 (10.2%)	High
Deaths	14/9725 (0.14%)	6/4944 (0.12%)	High

Seronegatives

Outcome (Undesirable)	n/N TAK-003	n/N placebo	Certainty
SAEs	323/3984 (8.1%)	183/1979 (9.3%)*	High
Deaths	2/3984 (0.05%)	1/1979 (0.05%)	High

17–60 years
Adults

Seropositives

Outcome (Undesirable)	n/N TAK-003	n/N placebo	Certainty
SAEs	3/83 (3.6%)	0/31	Moderate
Deaths	0/83	0/31	Moderate

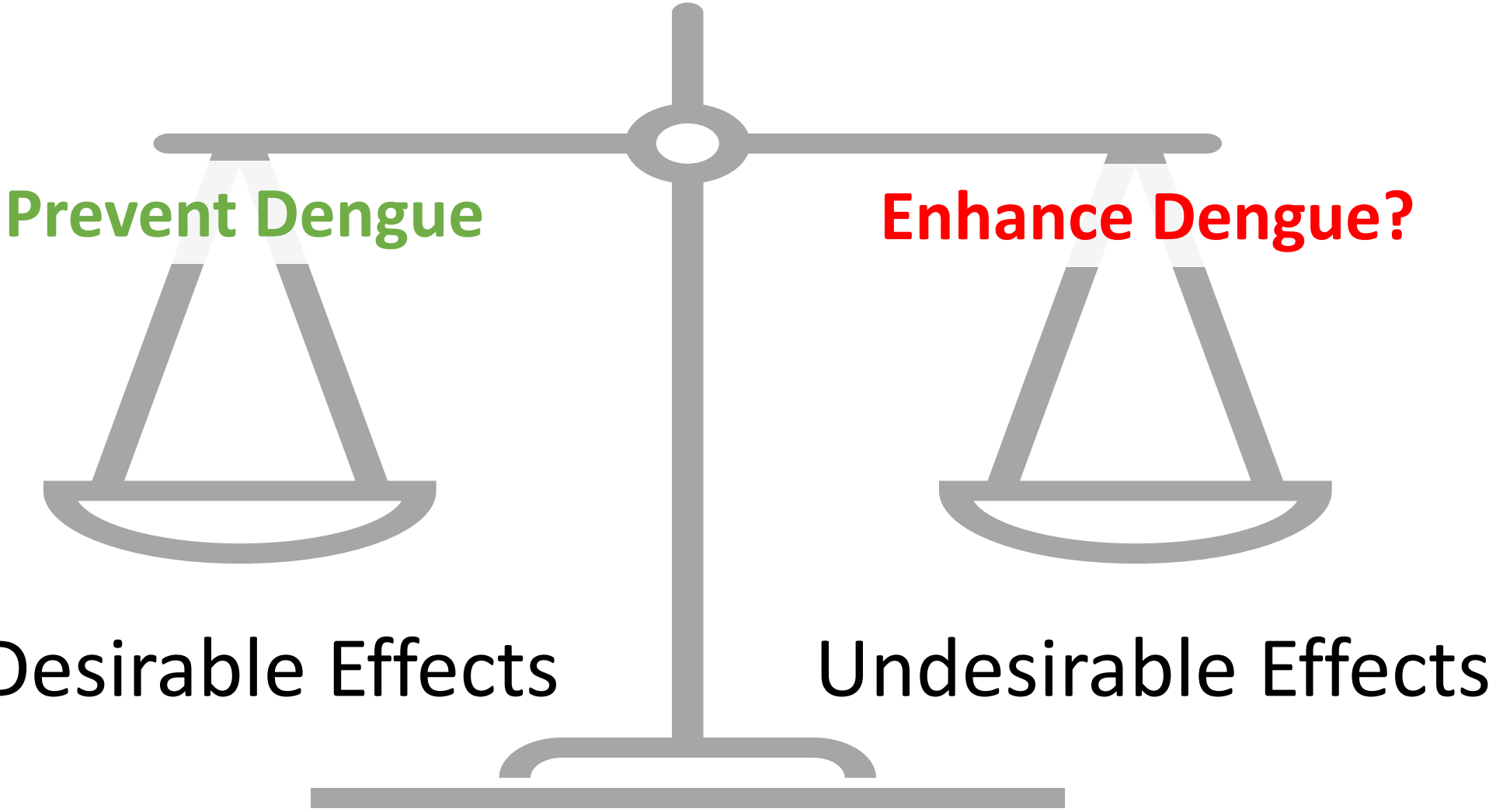
Seronegatives

Outcome (Undesirable)	n/N TAK-003*	n/N placebo	Certainty
SAEs	9/488 (1.8%)	3/85 (3.6%)	High
Deaths	0/488	0/85	High

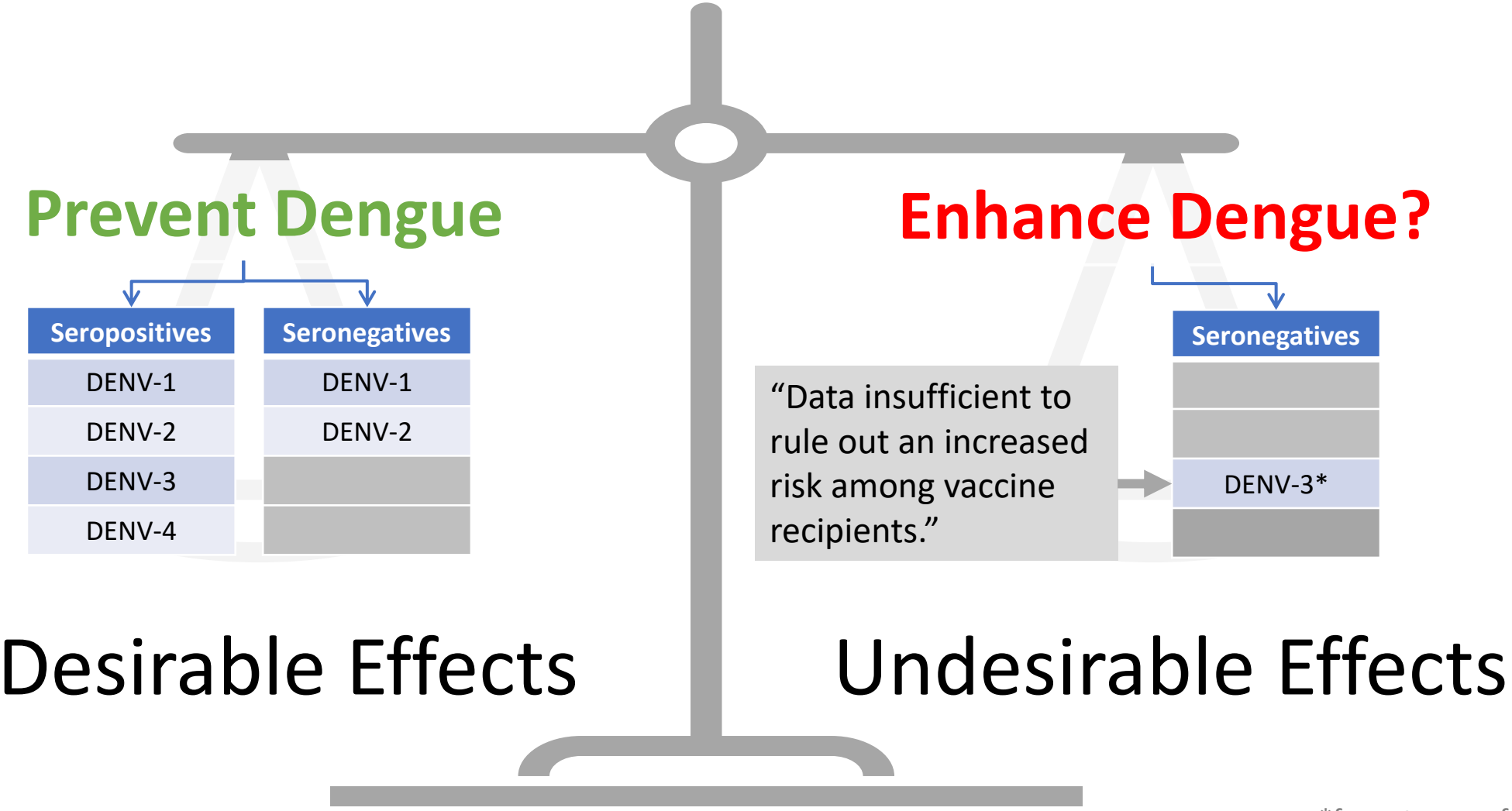
Summary of Certainty for All Undesirable Outcomes

	Seropositives	Seronegatives
4–16 years Children/Adolescents	**High**	**High**
17–60 years Adults	**Moderate**	**High**

Dengue vaccine outcomes of interest can be a desirable **and** an undesirable outcome.



The effects differ by **vaccinee serostatus** and **serotype.**

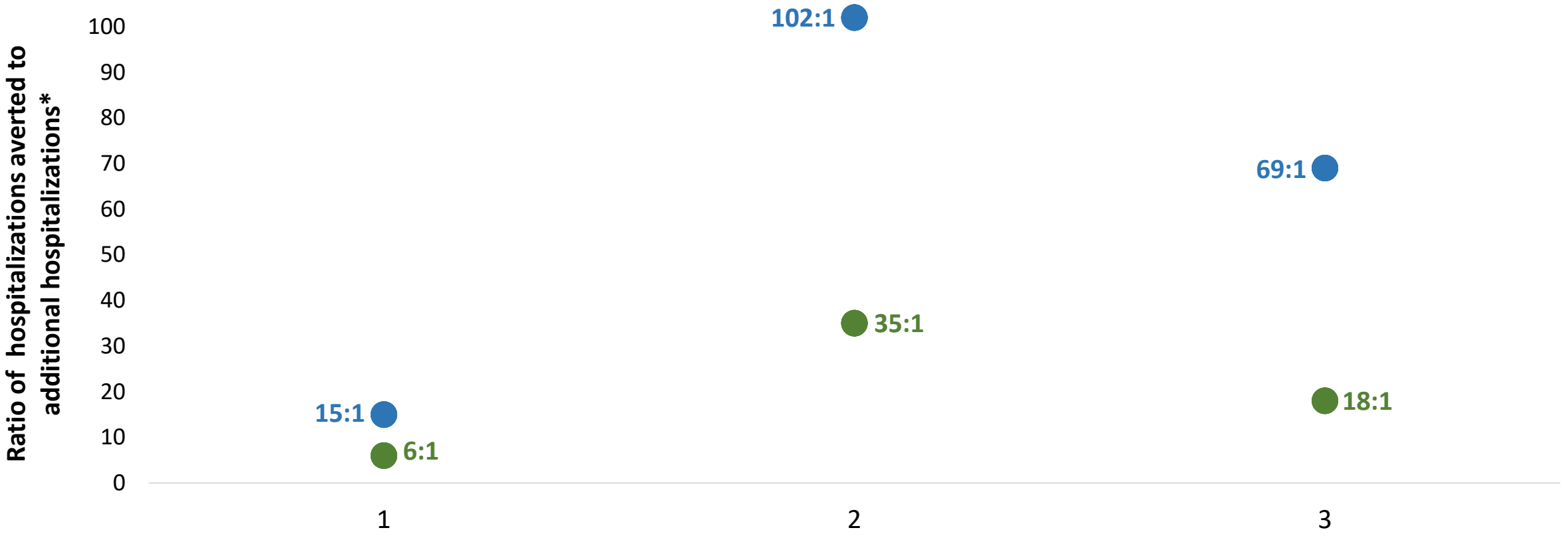


*for outcome of hospitalization.

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

Screening decreased the ratio of averted to additional hospitalizations compared to no pre-vaccination screening but may lead to lower absolute hospitalizations averted.



*Hospitalizations among vaccinees in a no screening scenario represent hospitalizations among seronegative persons who are infected by DENV-3 post-vaccination. In the screening scenario, they represent hospitalizations among seronegative persons with false positive test results who are infected with DENV-3 and are subsequently hospitalized. Model based on 40% seroprevalence at 9 years old. Other model assumptions described by Dr. España (ACIP, June 22, 2023).

Summary of Balance of Desirable and Undesirable Anticipated Effects

- Modeling* shows that the ratio of **hospitalizations averted** to **additional hospitalizations caused by vaccination** increases with screening and vaccination of seropositive individuals only.

- This **ratio is higher** in the population aged 17–60 years compared to the population aged 4–16 years under both screening and no screening scenarios.

- The **benefits** of screening and vaccinating seropositive individuals will be weighed against the **lower overall reduction** in VCD and hospitalizations in this scenario.

*Models based on preliminary data from Dr. España presented to ACIP on June 22, 2023.

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

Options: ○ Favors intervention ○ Favors comparison ○ Favors both ○ Favors neither ○ Varies ○ Don't know

Resource Use

Is the intervention a reasonable and efficient allocation of resources?

Preliminary Modeled Estimates of Cost-effectiveness in San Juan, PR over 10 years

Population and Strategy†	ICER per hospitalization averted (USD) §	ICER per QALY gained (USD)§¶
4–16 (screening)	16,800	181,918
4–16 (no screening)	46,813	254,751
17–60 (screening)	48,989	396,574
17–60 (no screening)	39,886	314,597
4–60 (screening)	48,305	384,830
4–60 (no screening)	45,495	326,412

Estimates modeled on San Juan, PR, population 326,953. Puerto Rico has a total population of 3.264 million) (US Census Bureau). For estimates with screening, the model assumes a test with 80% sensitivity and 98% specificity.
†The model assumes a seroprevalence of 40% at age 9 and a vaccine coverage increasing from 0 to 40% over 10 years.
§Cost of full vaccination was $330 US; cost of a test was $30 with annual retesting for negative individuals.
¶ICER per QALY gained was modeled from a societal perspective with a 3% discounting rate.

Resource Use

Is the intervention a reasonable and efficient allocation of resources?

Options: ○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know

Summary

- Presented 3 of 7 EtR domains:
  - Public Health Problem
  - Benefits and Harms
  - Resource Use
- Certainty assessment of the evidence for outcomes by policy question **ranged from high to low**.
- Weighing the **risks and benefits** of dengue vaccination is complex.
- Work Group discussions will continue this summer.
- Draft recommendation and vote will occur at the **next meeting**.

Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

ACIP Dengue Vaccines Workgroup and Support Team

ACIP Members
Wilbur Chen (Chair)
Kathy Poehling
Beth Bell
Veronica McNally

CDC Co-Leads
Gabriela Paz-Bailey
Laura Adams

Ex Officio Members
Kaitlyn Morabito (NIH)
Ralph LeBlanc (FDA)
Ihid Carneiro Leao (FDA)
Kirk Prutzman (FDA)
Srihari Seshadri (DOD)

Liaison Representatives
Elizabeth Barnett (AAP)
Rob Schechter (AIM)

Consultants
Edwin Asturias
Robert Atmar
Alan Barrett
Iris Cardona
Anna Durbin
Tony Marfin
Kristen Pierce
Anita Shet

CDC Contributors
Joshua Wong
Nicole Medina
Mimi Eckert
Rachel Eidex
Alfonso Hernandez
Susan Hills
Terri Hyde
Mike McNeil
Jorge Munoz
Erin Staples
Cindy Weinbaum
Rita Helfand

GRADE Consultants
Doug Campos-Outcalt
Rebecca Morgan

GRADE Analysis Team
Joshua Wong (Co-lead)
Alfonso Hernandez (Co-Lead)
Cameron Adams
Arlene Rivera
Daniel Milan

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.