

Draft Recommendations of the SAGE Working Group on Hepatitis E

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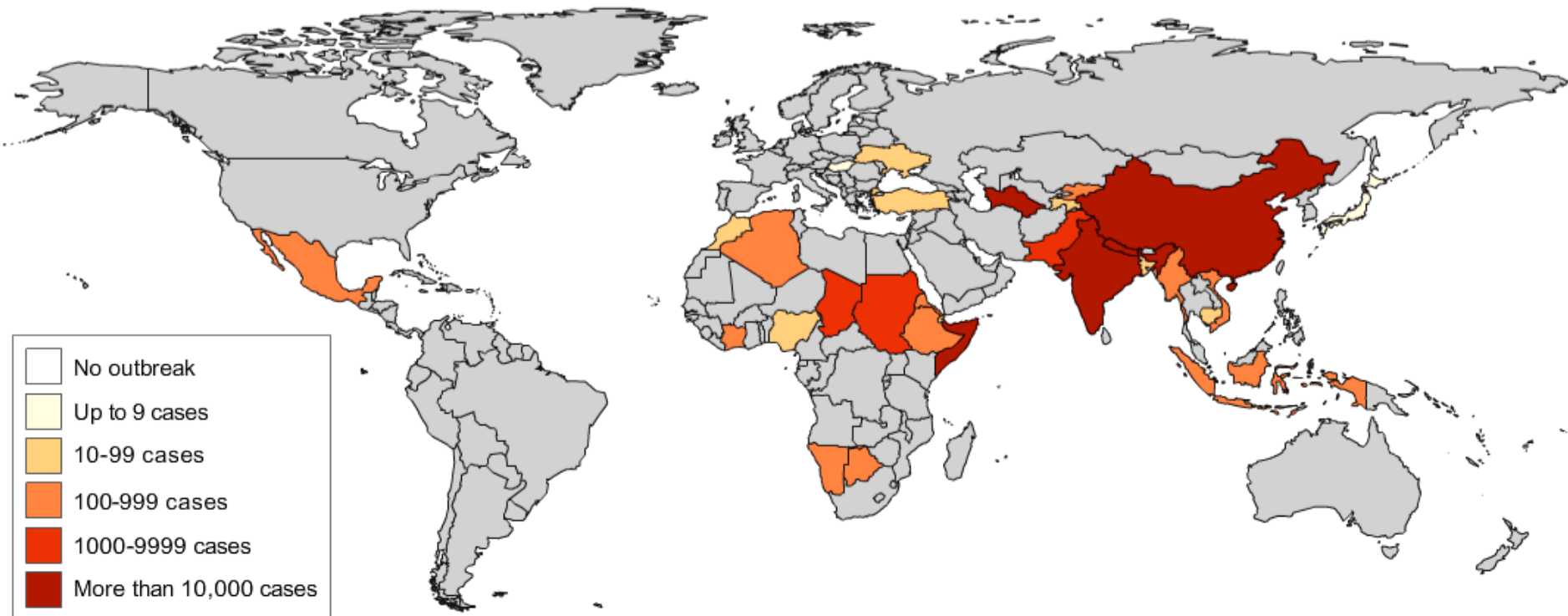
Questions for SAGE

- Should HEV vaccine be recommended for
 - General population in HEV endemic areas and areas at risk for outbreaks
 - Special high risk groups (pregnant women, individuals with chronic liver diseases, immuno-suppressed)
 - Special situations where the risk of disease or that of serious disease or mortality could be particularly high

HEV Burden of disease: Provisional estimates

- Annual global burden of hepatitis E
 - 3.3 million symptomatic cases (95% CI = 0.5-6.5 million)
 - ~ 70,000 (95% CI 12,400-133,000) deaths
 - 3,000 (95% CI 1,900-4,400) stillbirths
- Based essentially on genotype 1 disease
- True burden may be larger if other genotypes contribute significantly to disease

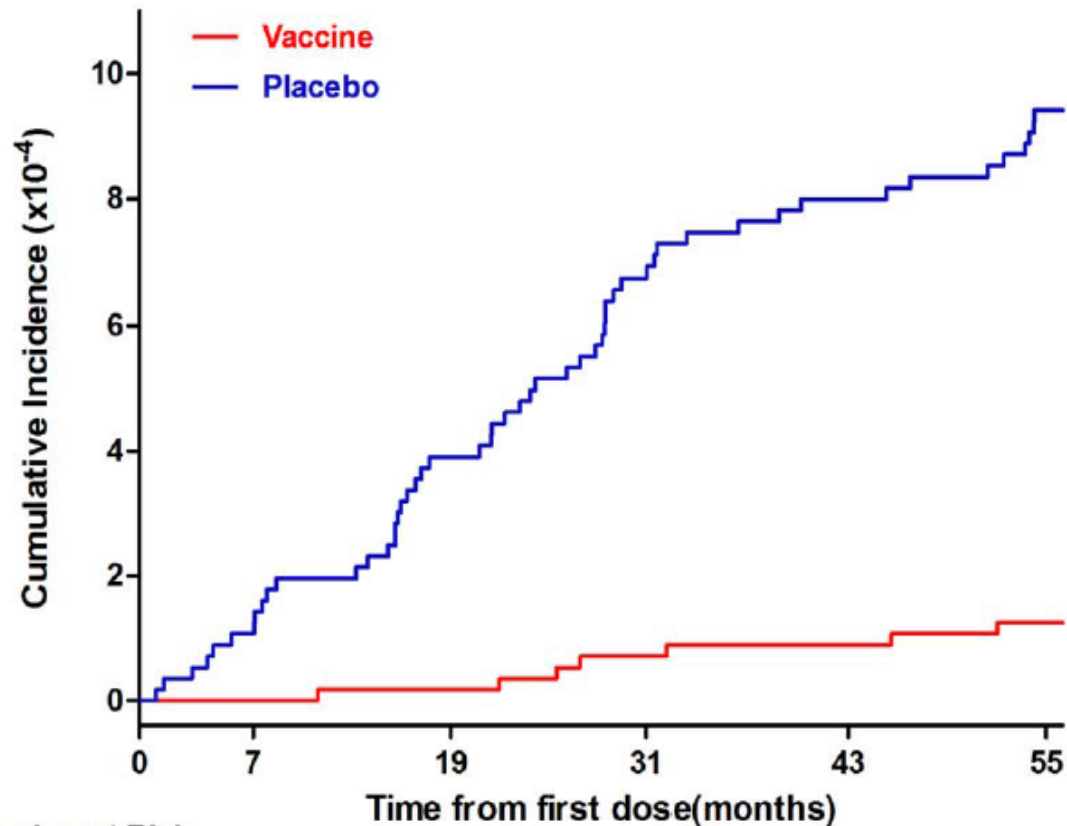
Hepatitis E: Outbreaks (1980-2007)



Hecolin – licensed HEV Vaccine

- Available in Chinese market since 2012
- Purified recombinant HEV antigen: 30 µg
- Three doses at 0-1-6 mo
- Shelf life: 36 (stable for 45 months)

Extended follow-up data: Efficacy



Number at Risk

Vaccine	56302	56215	56022	55774	55484	55240
Placebo	56302	56209	55977	55718	55436	55185

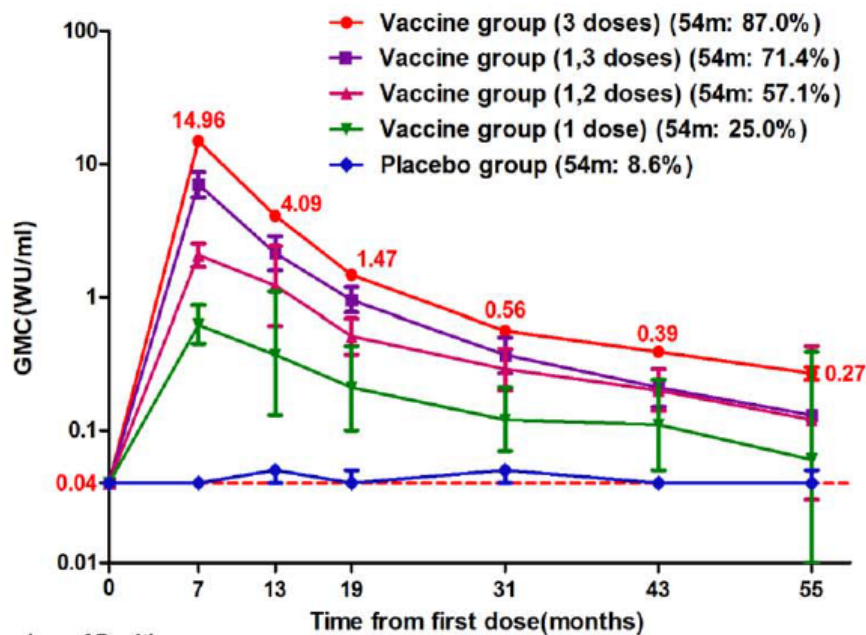
Cumulative Number of participants with Hepatitis E

Vaccine	0	0	1	4	5	7
Placebo	0	6	22	38	45	53

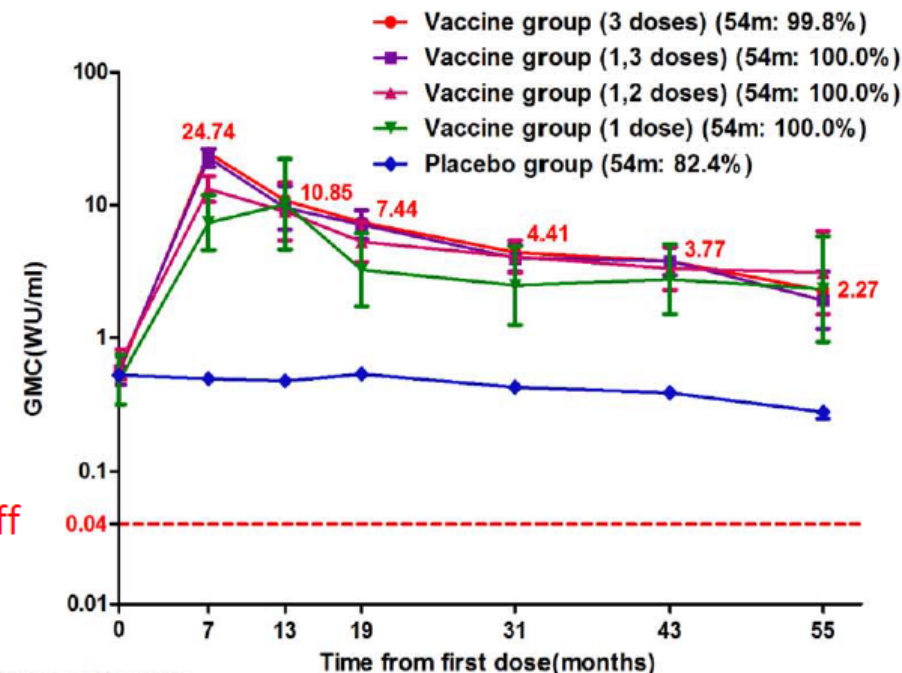
Unpublished data:
Innovax (confidential)

Extended follow-up data: Antibody persistence

Seronegative subjects



Seropositive subjects



Draft recommendation on use of Hepatitis E vaccine in general population in areas with high endemicity

- The only available trial was conducted in an area with very low disease incidence. Efficacy of vaccine in areas with or during periods of high rate of transmission of HEV is not known
- The phase III trial with the vaccine primarily assessed its efficacy against genotype 4 (>90% infections in the placebo group were due to gn 4), and to only limited extent against genotype 1.
- There is lack of data on protection against severe disease and death.
- The protective level of antibodies, duration of protection following hepatitis E vaccine and the possible need for boosters are not known.

Draft recommendation on use of Hepatitis E vaccine in general population in areas with high endemicity

- Data on efficacy are limited to persons in the age group of 16-65 years. Data are not available in children below 16 years of age and in those older than 16 years of age.
- Data on the incidence of hepatitis E infection & disease, and its contribution to mortality in general population even in areas where hepatitis E disease is common, are quite limited

It is a promising vaccine which showed high efficacy in 16-65 year old health Chinese subjects. In view of the above reasons, introduction of this vaccine in routine national programs in populations where epidemic & sporadic hepatitis E disease is common, is not recommended at this time. However, the national authorities may

Draft Recommendations on the Use of Hepatitis E vaccine

- Limited/lack of information at this time **does not** allow us to **recommend** the use of the vaccine for the following population sub-groups:
 - pregnant women or in women of child-bearing age living in areas where hepatitis E disease is common
 - chronic liver disease patients
 - persons on organ transplant wait-list
 - travellers from low-endemicity areas to high-endemicity areas

Draft Recommendations on the Use of hepatitis E vaccine

- The Group recognizes that there could be special situations where the risk of disease or that of serious disease or mortality could be particularly high, and that these may override other considerations. The Group's recommendations should not preclude the use of this vaccine in these special situations.
- Use of the vaccine during **outbreaks** of hepatitis E **could be** considered
- In all such situations, experience with the use of vaccine, including the occurrence of any adverse events, should be documented.

HEV vaccine: Information gaps

- Data on protection
 - Duration of protection and protective antibody titer
 - Protection against high viral dose
 - Protection against severe disease
 - Protection in children (<16 years) and older age (>65 years)
- Data on specific population subgroups
 - Persons with liver disease or immunosuppression
 - Pregnant women
 - Outbreak settings
- Vaccine target: High-risk groups versus general population
 - Better disease burden data
 - Cost-benefit ratio

As and when data on some of the current information gaps become available, the recommendations for one or more of the situations discussed above will need reconsideration.