Estimating Vaccine Efficacy For Influenza Vaccine

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Reference

Basta NE, Halloran ME, Matrajt L, Longini, IM.

Estimating Influenza Vaccine Efficacy From Challenge and Community-based Study Data.

AJE. 2008;168(12):1343-52

Outline

- **Estimating influenza vaccine efficacy using existing data**
  - (1) Challenge Studies in Humans
  - (2) Community-based Trials
- **Relevant to both seasonal and pre-pandemic influenza vaccine**

Identifying Challenge Studies

- **PubMed Search**
  - "influenza, human" *and* "influenza vaccine" *and* [experiment* *or* challenge* *or* "wild type" *or* wildtype"]
  - Inclusion Criteria:
    - RCT with appropriate comparison groups and detailed outcome data
    - Participants seronegative to the challenge strain
    - Wild-type virus challenge

Published Challenge Studies

- Clements ML *et al.* Lancet 1984;1:705-8
- Clements ML *et al.* J Clin Micro 1986;23:73-6
- Sears SD *et al.* JID 1988;158:1209-19
- Clements ML *et al.* JID 1990;161:869-77
- Treanor JJ *et al.* Vaccine 1999;18:899-906

Vaccine Efficacy

VE = 1 - Relative Risk

Measures of Vaccine Efficacy

- VE_S - Vaccine efficacy against susceptibility
- VE_{SP} - Vaccine efficacy against infection-confirmed symptomatic illness
- VE_P - Vaccine efficacy against symptomatic illness among infecteds
- VE_I - Vaccine efficacy against infectiousness among infecteds

Halloran ME, Longini IM, Struchiner CJ. Design and interpretation of vaccine field studies. Epidemiol. Rev. 1999;21:73-88.

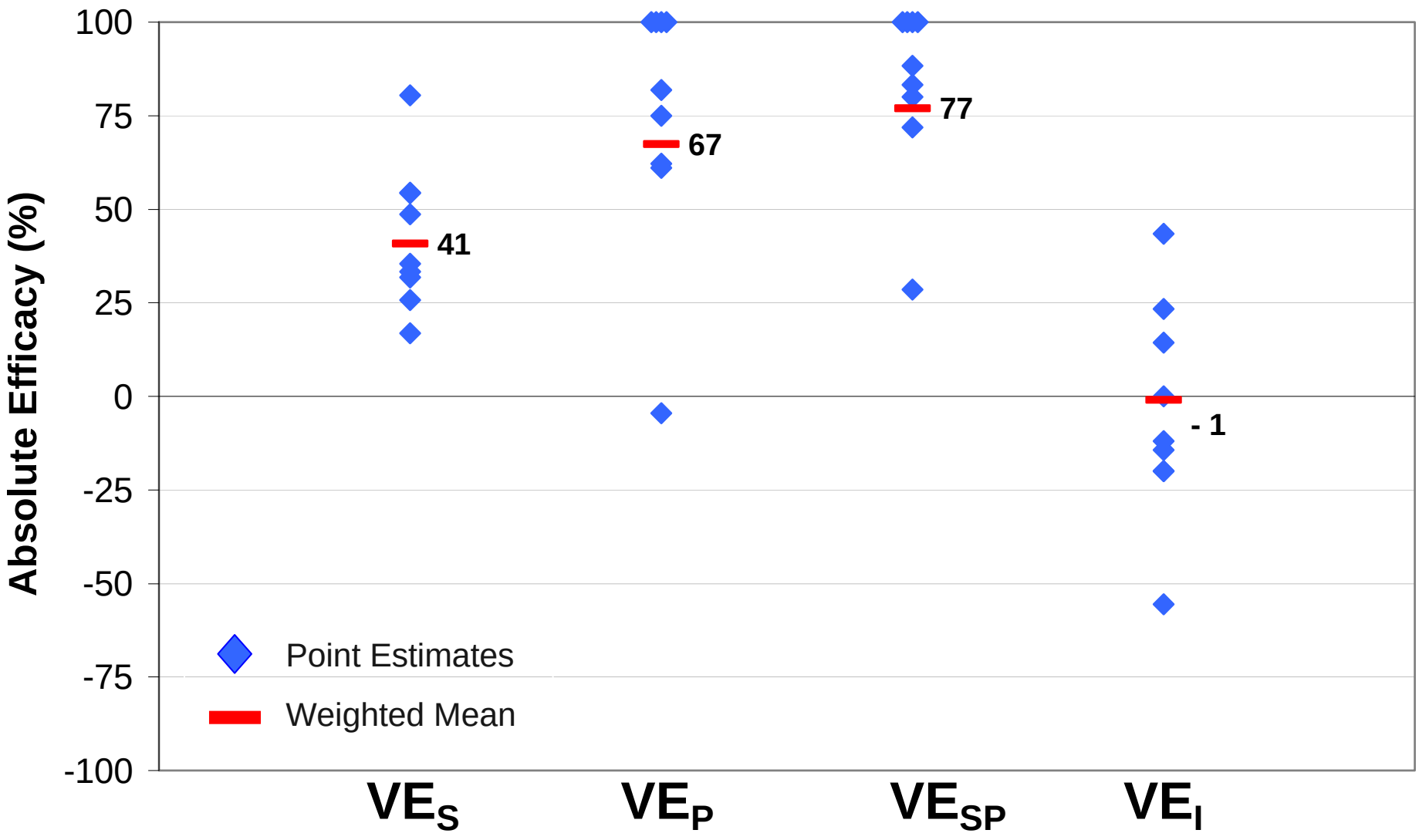
Challenge Study Endpoints

Efficacy Measure	Outcome
VE_S	Lab-confirmed infection
VE_{SP}	Lab-confirmed infection and influenza-like illness
VE_P	Influenza-like illness among lab-confirmed infecteds
VE_I	Viral shedding among lab-confirmed infecteds

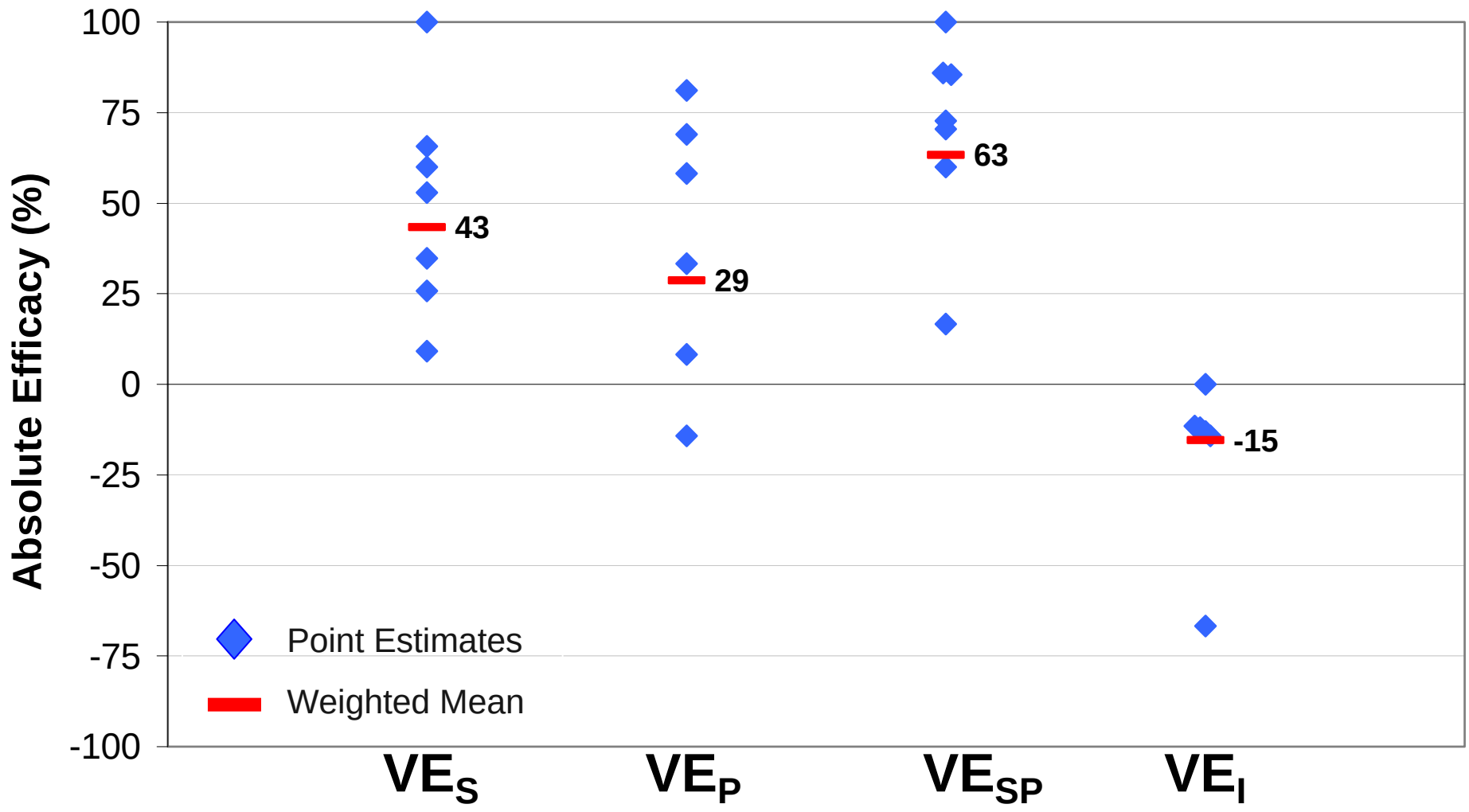
Estimating VE from Challenge Studies

- Based on the challenge study data, we calculated the weighted averages (95% CIs) for VE_S, VE_P, VE_{SP}, and VE_I for:
  - Absolute efficacy of live, attenuated vaccine
  - Absolute efficacy of inactivated vaccine
  - Relative efficacy of live vaccine compared to inactivated vaccine

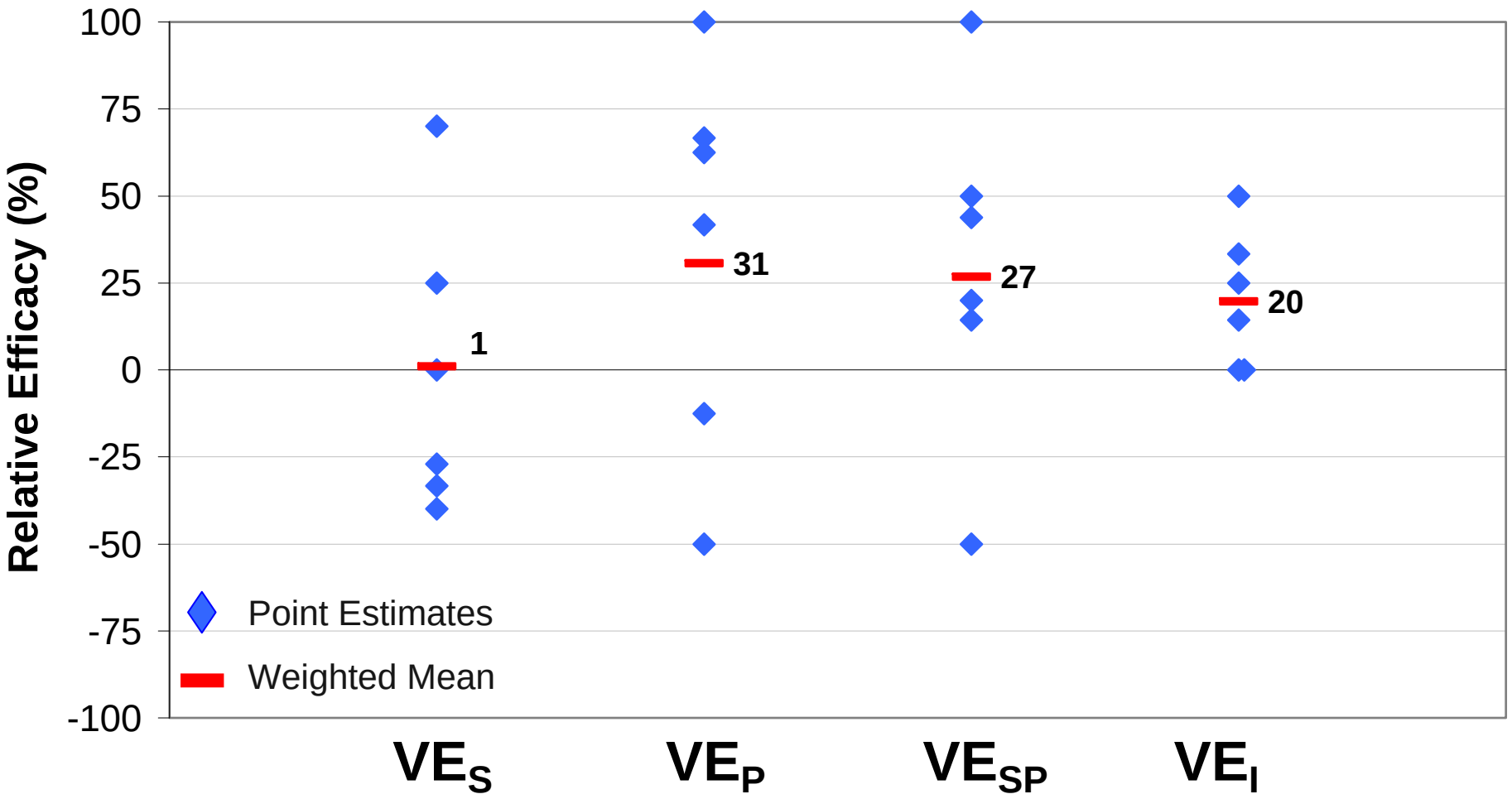
Absolute Efficacy of Live Influenza Vaccine



Absolute Efficacy of Inactivated Influenza Vaccine



Relative Efficacy of Live vs Inactivated Influenza Vaccine



Summary: Weighted VE Estimates

Table 2. Weighted Mean Vaccine Efficacy Estimates and 95% Confidence Intervals From a Secondary Analysis of 5 Experimental Influenza Challenge Studies in Adults[a]

	Live Vaccine: Absolute Efficacy		Inactivated Vaccine: Absolute Efficacy		Live vs. Inactivated Vaccine: Relative Efficacy	
	Weighted Mean %	95% CI	Weighted Mean %	95% CI	Weighted Mean %	95% CI
VE_S	41	15, 66	43	8, 79	1	−41, 43
VE_P	67	24, 100	29	−19, 76	31	−47, 100
VE_{SP}	77	27, 100	63	11, 100	27	−73, 100
VE_I	−1	−27, 25	−15	−51, 20	20	−15, 54

Basta NE, Halloran ME, Matrajt L, Longini IM. AJE (2008)

Estimates from Community-based Influenza Vaccine Trials

- VE_{SP} most commonly reported
  - Case ascertainment based on symptoms
- Vaccination of Children
  - Homologous Influenza Seasons
  - Heterologous Influenza Seasons
- Vaccination of Adults
  - Heterologous Influenza Seasons

What have we learned?

Table 3. Expected Vaccine Efficacies (%) for Live and Inactivated Seasonal Influenza Vaccine in Homologous and Heterologous Seasons

	Live Vaccine		Inactivated Vaccine	
	Homologous	Heterologous	Homologous	Heterologous
VE_S	40	30	40	30
VE_P	83	57	67	14
VE_{SP}	90	70	80	40
VE_I	50	30	40	20
VE_C	83	68	78	56

Basta NE, Halloran ME, Matrajt L, Longini IM. AJE (2008)

Future Studies

- Field studies should be designed to estimate all 4 components of VE
- More precise estimates of VE_I are needed
- Identification and validation of true correlates of immunity and surrogates of protection are needed

Conclusions

- **Feasibility of estimating 4 components of VE using existing data**
- **VE estimates can be used to plan vaccination strategies for:**
  - Seasonal influenza in children and
  - Pandemic influenza in the community