Do influenza vaccines actually work in the elderly?

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Do influenza vaccines really work in the elderly?

If they don't, why do we persist in vaccinating the elderly across Europe every winter?

Presenter's declaration

Between October 2007 and September 2010, *ad hoc* paid consultancy to several influenza vaccine manufacturers (Sanofi-Pasteur MSD, Sanofi-Pasteur, GlaxoSmithKline plc, Baxter AG, Solvay, Novartis). Former employee of SmithKline Beecham (now part of GSK) 2000 - 2001.

No outstanding interests related to shares, share options or accrued pension rights since 2004. Current or past research funding, related to influenza vaccination from GSK and Astra-Zeneca.

Is it any surprise that policy makers are confused?

- Osterholm MT, Kelley NS, Sommer A, Belongia EA. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. Lancet Infect Dis. 2012 Jan;12(1):36-44.

- "Influenza vaccines can provide moderate protection against virologically confirmed influenza, but such protection is greatly reduced or absent in some seasons. Evidence for protection in adults aged 65 years or older is lacking. LAIVs consistently show highest efficacy in young children (aged 6 months to 7 years)."

Is it any surprise that policy makers are confused?

- Jefferson T, Di Pietrantonj C, Al-Ansary LA, Ferroni E, Thorning S, Thomas RE. Vaccines for preventing influenza in the elderly. Cochrane Database Syst Rev. 2010 Feb 17; (2):CD004876.

- "Due to the general low quality of non-RCTs and the likely presence of biases, which make interpretation of these data difficult and any firm conclusions potentially misleading, we were unable to reach clear conclusions about the effects of the vaccines in the elderly. The available evidence is of poor quality and provides no guidance regarding the safety, efficacy or effectiveness of influenza vaccines for people aged 65 years or older."

Cochrane approach

- 75 eligible studies, 100 datasets, 14 different outcomes, 4 sub-groups. Highly stratified approach.
- Some errors in assignment of studies to virus circulation/non-circulation periods.
- Mosaic of results, leading to lack of overall interpretability ("we were unable to reach clear conclusions about the effects of the vaccines in the elderly").

Is there an alternative view?

- If the lack of evidence for effectiveness in the elderly is so convincing, why don't Member States stop and spend the money on something else?

- If the lack of evidence for effectiveness in the elderly is so convincing, why do major EU based independent advisory committees (ACIP, JCVI, STIKO) continue to recommend vaccination for the elderly?

- A demonstration project, illustrating an alternative view, based on a consideration of exactly the same data (no more, no less) as considered in the Cochrane Review

Why are the data we have so confusing?

- When virus is not circulating, the vaccine cannot protect against a non-existent entity (VE tends towards zero and studies will be underpowered)

- VE estimates will vary according to outcome. If lab confirmed influenza infection is the outcome then the answer will be as accurate as it can be.

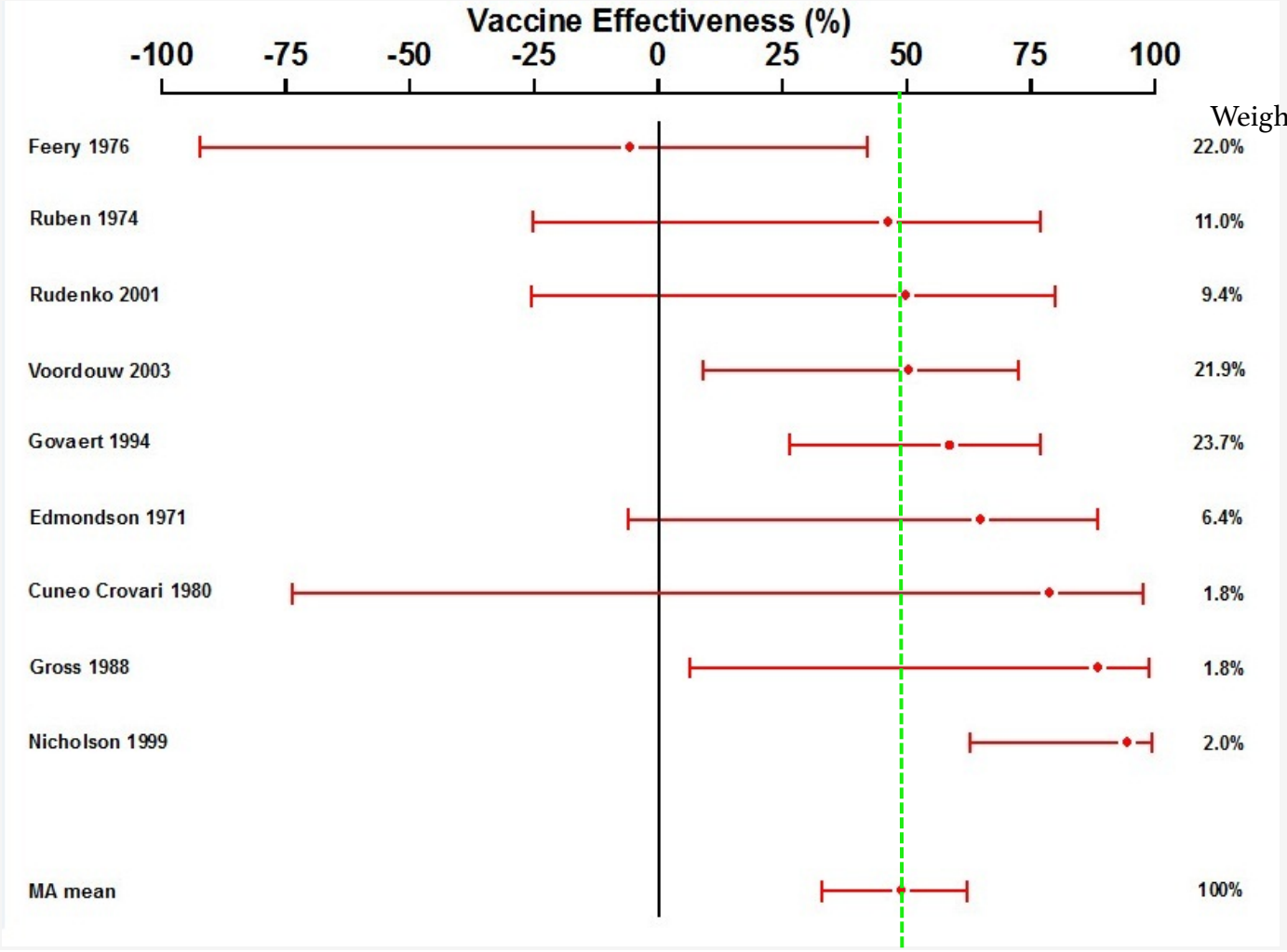
- If you choose syndromic illness (ILI) or complications or mortality, tendency to include illness that is not due to influenza, i.e. not-vaccine preventable = 'white noise'; so 'effectiveness' estimates are reduced.

- Vaccines are not perfectly matched every season

An alternative approach

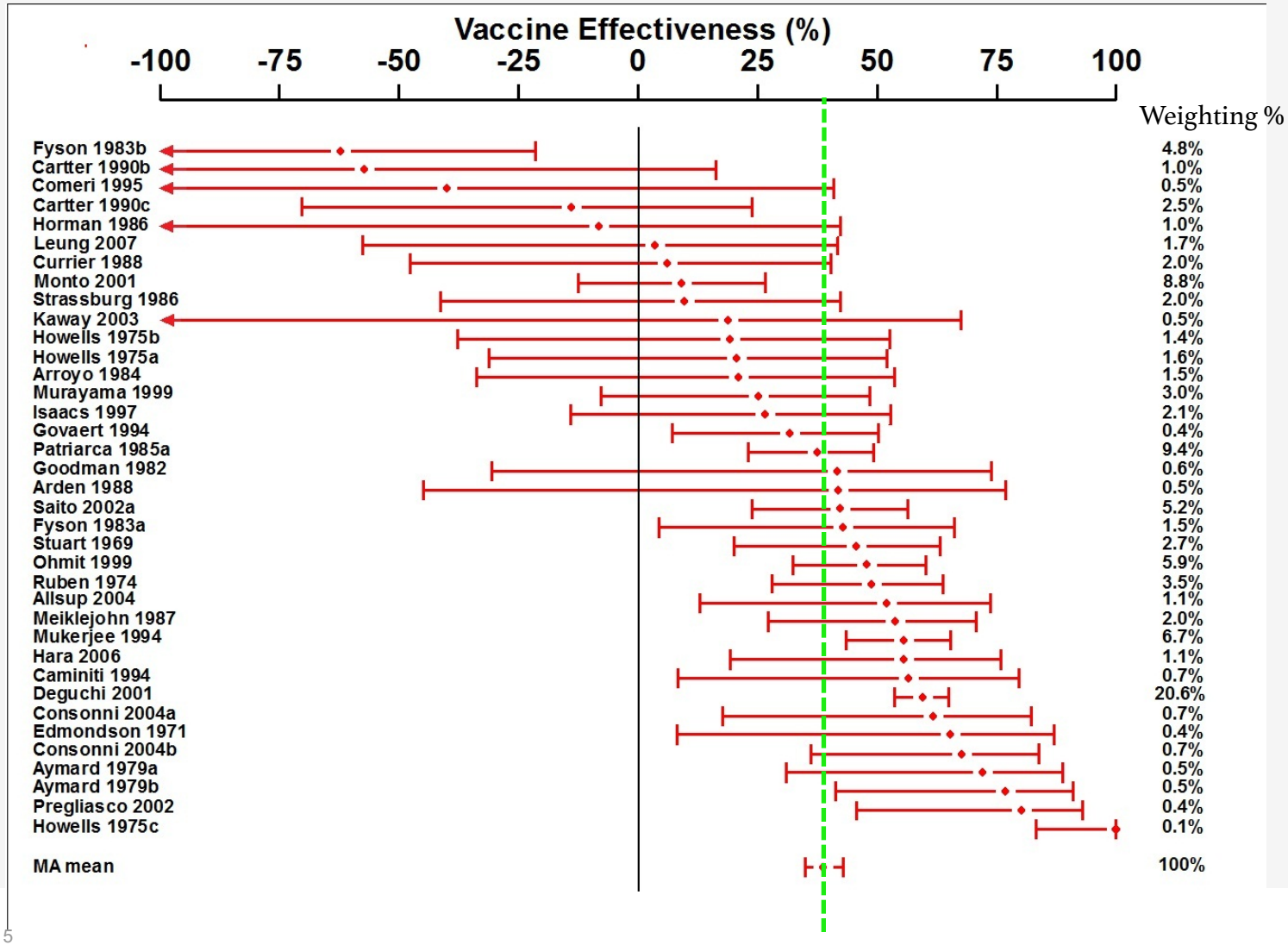
- Take the same 75 eligible studies
- Correct small number of errors in assignment of studies to virus circulation periods.
- Take the data as extracted by previous authors (no re-interpretation of data from individual studies)
- Re-plot outcomes based on simple, policy-relevant scenarios: 1) laboratory confirmed influenza; 2) syndromic influenza-like illness (ILI); 3) complications; 4) no virus circulation.
- Simple meta-analysis – inverse variance-weighted method

Laboratory confirmed influenza (virus active)



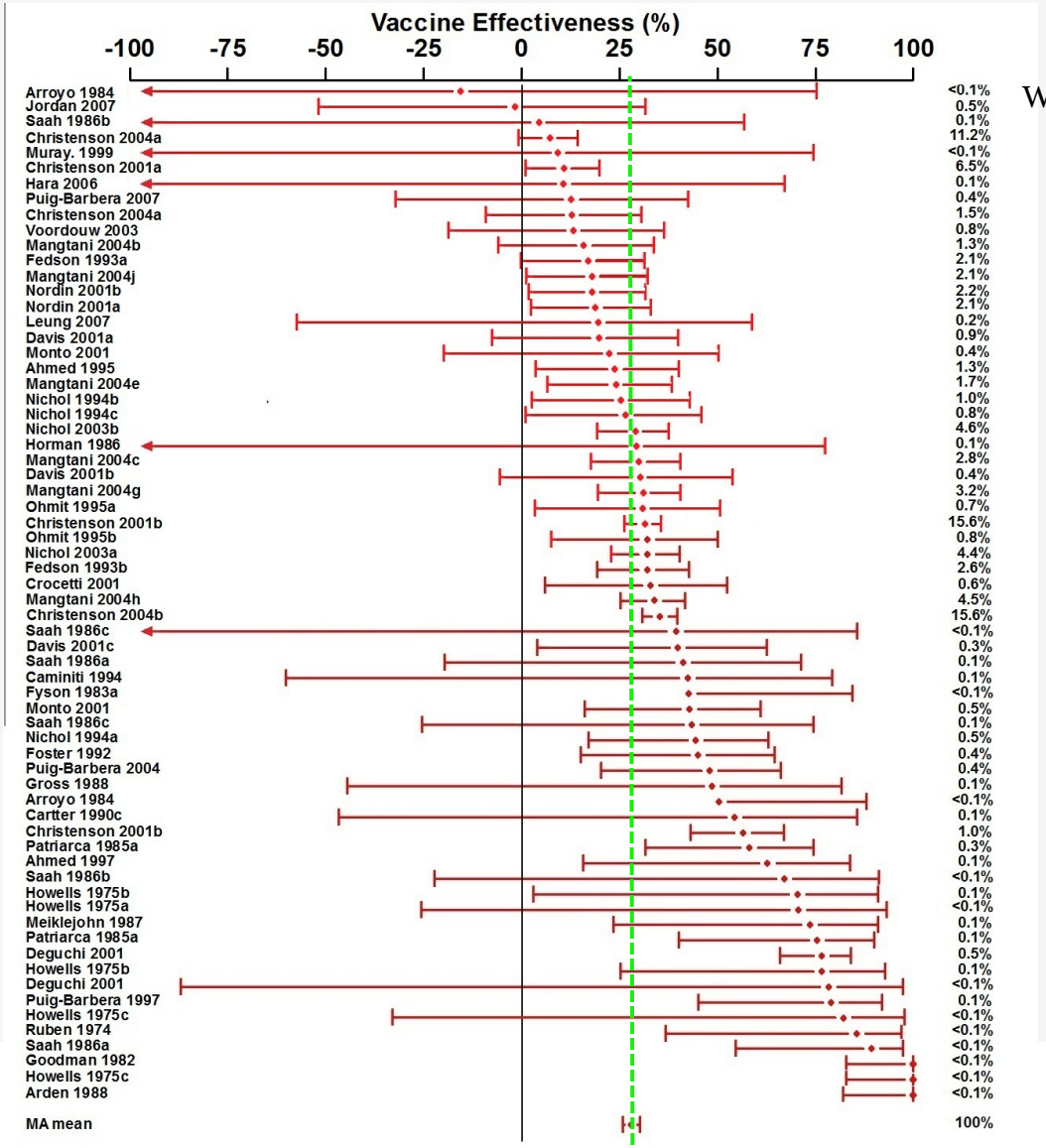
Inverse variance-weighted meta-analysis

Influenza-like illness (virus active)



Inverse variance-weighted meta-analysis

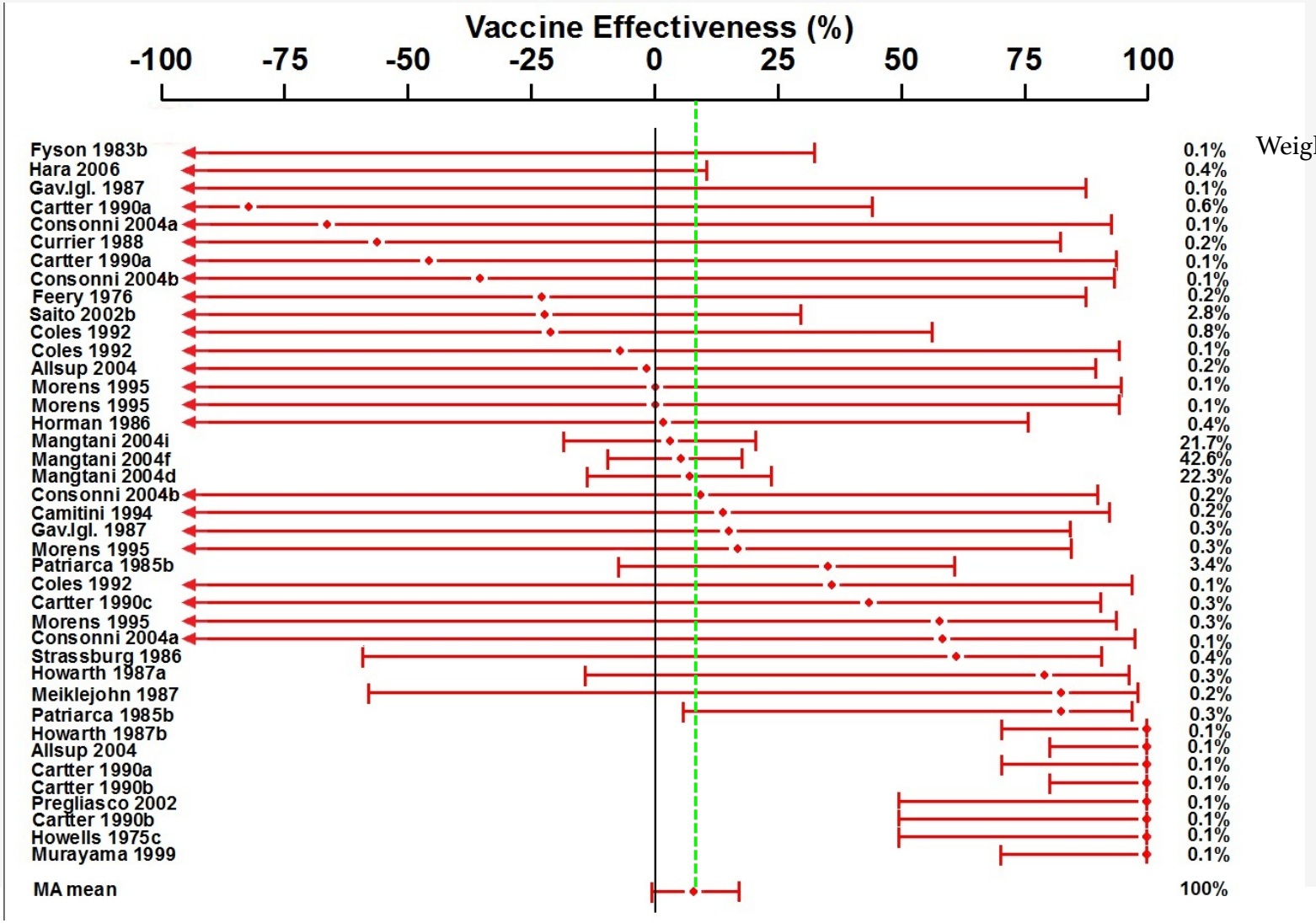
Complications inc. death (virus active)



Weighting %

Inverse variance-weighted meta-analysis

No virus circulation (all outcomes)



Inverse variance-weighted meta-analysis

Summary

- Take the same 75 eligible studies, apply a simpler framework of analysis

  - VE against lab-confirmed disease* : around 50%
  - VE against ILI without virus confirmation: around 40%
  - VE against influenza-related fatal and non-fatal complications: around 30% with large dispersion

  And the data now seem more logical

Based on:

Vaccine 31 (2013) 6030–6033

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Cochrane re-arranged: Support for policies to vaccinate elderly people against influenza

Walter E.P. Beyer[a], Janet McElhaney[b], Derek J. Smith[c,d,a], Arnold S. Monto[e], Jonathan S. Nguyen-Van-Tam[f], Albert D.M.E. Osterhaus[a,*]

Key actors

- Member States
- ECDC
- Healthcare workers (recommending to their patients; practicing what they preach)

Key messages

- Influenza vaccines are not a perfect tool in the elderly
- There is room for substantial improvement
- Nevertheless, taken year on year, evidence for the ability of influenza vaccines to reduce the risk of influenza infection, ILI and influenza-related complications in the elderly.
- Year on year likely meaningful individual patient benefit
- Meaningful public health benefits when applied at the elderly population level