Evidence for selection bias in influenza vaccine effectiveness studies: systematic review

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Background & Question

- Evidence on influenza vaccine effectiveness (VE)
  - is frequently derived from observational studies
  - is often used to support recommendations on influenza vaccination made by vaccination committees (ACIP, WHO-SAGE, STIKO)
- However:
  - these studies are prone to bias, particularly selection bias, and have been suspected to overestimate VE if unspecific outcomes are used (e.g. mortality)

Research questions

1) How often do observational studies on influenza VE show indication of selection bias?
2) What is the impact on VE estimates?
3) How many of these studies show indication of residual confounding in the adjusted analyses?

Methods

- Systematic searches (Medline, Embase, Cochrane; last search: 25 May 2014)
- Inclusion criteria: i) observational study; ii) calculated influenza VE; iii) reported baseline characteristics; iv) reported crude and adjusted VE; v) investigated off-season VE
- Assessment of risk of selection bias: according to baseline characteristics (vacc. vs. unvacc.)
- Comparison of unadjusted vs. confounder-adjusted VE estimates
- Comparison of season vs. off-season estimates

Results

- Total studies = 23
  - Season and off-season VE estimates (part 1)
  - Forms of selection bias in vaccination studies:
    - Confounding by indication: patients with underlying chronic diseases are more likely to be vaccinated → underestimation of VE
    - Healthy vaccinee bias: patients who are in better health are more likely to be vaccinated → overestimation of VE

Conclusions

- Both forms of selection bias are likely to operate simultaneously in observational studies on influenza vaccine effectiveness.
- Although adjustment can correct for confounding by indication to some extent, the resulting estimates are still prone to healthy vaccinee bias.
- Cohort study designs using unspecific outcomes should no longer be used to assess influenza vaccine effectiveness.
- Instead, other study types, such as test-negative design or quasi-randomised studies with influenza-specific outcomes should be preferred.