Signal versus Noise: Antibiotics, Endocarditis, and the NHS

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No conflicts of Interest
The story so far

Mar 2008
NICE recommends against antibiotic prophylaxis for endocarditis

Mar 2013
Antibiotic prescriptions for endocarditis prophylaxis decline by 88%
420 additional hospitalizations and 18 additional deaths related to endocarditis a year compared with expectations from a historical trajectory

Interpreting observational analyses:
1. Is the association real?
2. Is the association causal?
3. What are the implications?
Q1. Is the observed association real?

For

- Nation-wide database with stable coding patterns
- Temporal association

Against

- Absence of a contemporaneous control
- Imperfect adjustment for secular trends:
  - Population estimates
  - Hospitalization rates
All NHS Hospitalizations (England, 2003-13)

The graph shows the trend of all NHS hospitalizations in England from 2003 to 2013. The x-axis represents the years from 2003 to 2013, and the y-axis represents the number of hospital discharge episodes in thousands. The trend line indicates a significant increase in hospitalizations over the period, peaking around 2008.
All NHS Hospitalizations (England, 2003-13)

After NICE there was a significant increase in the number of IE cases/month above the previous trend (0.62 cases/month, CI 0.35-0.89, p<0.001)

By March 2013 this amounted to an extra:
- 35 IE cases/month or
- 420 IE cases/year
Q2. Is the observed association causal?

For

- Biologic plausibility:
  - Fewer antibiotics → More endocarditis

Against

- No rise in endocarditis noted in other settings
  - US adults ¹
  - US children ²
- Case fatality = 4.3%
  (18 additional deaths/420 cases)

¹ Bor, et al. PLoS ONE 8(3):e60033
Q3. What are the implications?

- Additional analyses before these data can inform guidelines:
  - Endocarditis rates to all-cause hospitalizations
  - Temporal or geographic variation (is there a dose-response curve?)
  - Bacteriology

- As presented, these data are inadequate to alter the weight of evidence on which the prophylaxis guidelines are based, and should not prompt changes in prescribing practice at this time.
Thank You!

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