Deviations from HEAPs: Can they ever be justified?

Professor Dyfrig Hughes

PRIFYSGOL BANGOR UNIVERSITY

MRC Hubs for Trials Methodology Research
North West Hub

CHEME
Canolfan Economeg Iechyd a Gwerthuso Meddygiaethau
Centre for Health Economics and Medicines Evaluation

Experience from FolATED

- Folate Augmentation of Treatment – Evaluation for Depression (FolATED): randomised trial
- Aim to assess the clinical effectiveness and cost-effectiveness of adding folic acid (5mg daily) to the antidepressant treatment of moderate to severe depression

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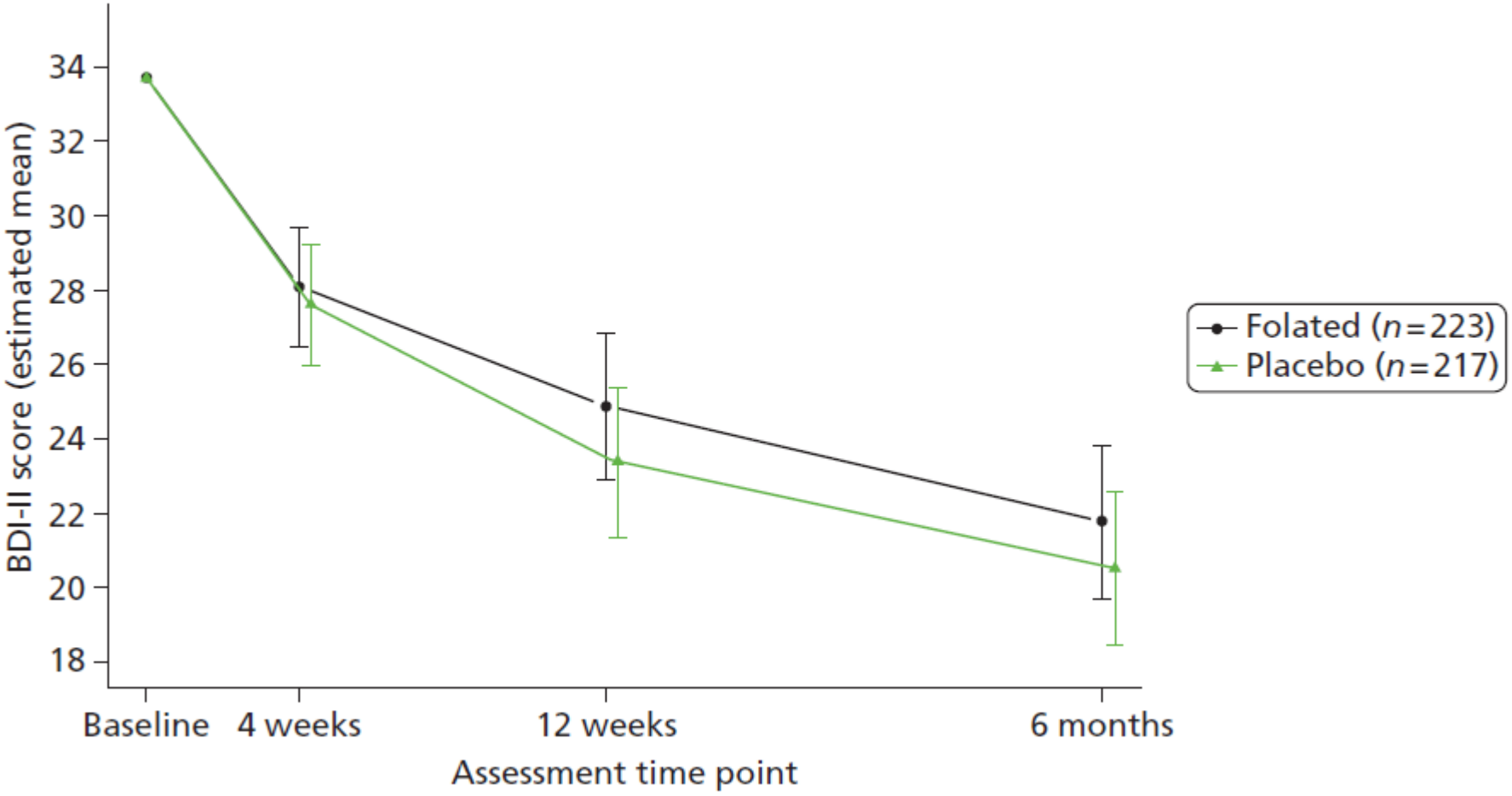
Outcomes

- Primary outcome: patient-rated BDI-II
- Economic outcome: cost per QALY gained

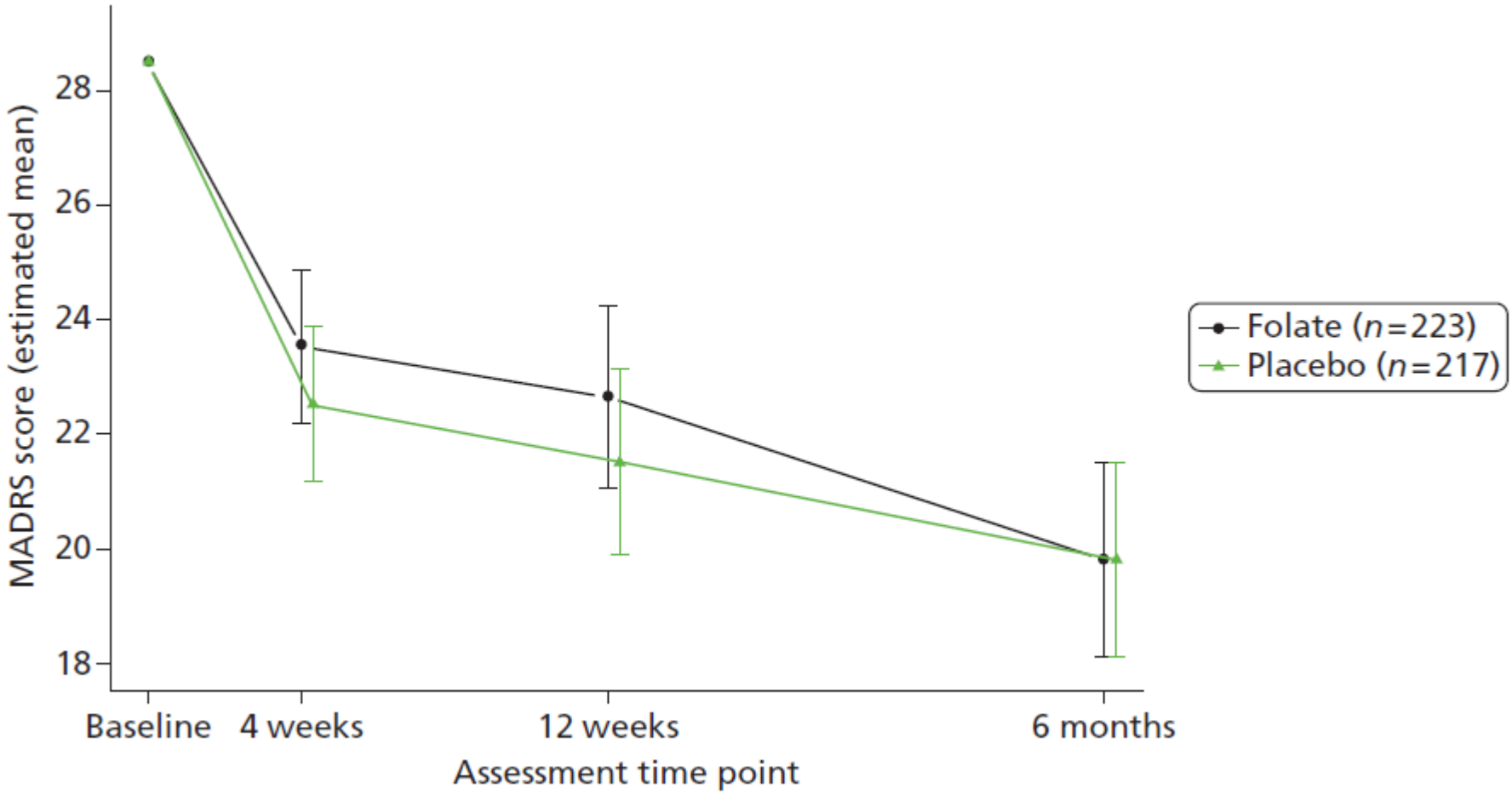
FOLATED HEAP

- Aim
- Data
  - Healthcare resource utilisation
  - Unit costs
  - Health Outcomes
- Analysis
  - Cost analysis
  - Analysis of health outcomes
  - Incremental analysis
  - Uncertainty analysis
  - Secondary analysis

BDI-II


BDI-II score (estimated mean)
34
32
30
28
26
24
22
20
18
Baseline
4 weeks
12 weeks
6 months
Assessment time point
Folated (n=223)
Placebo (n=217)

MADRS


MADRS score (estimated mean)
28
26
24
22
20
18
Baseline
4 weeks
12 weeks
6 months
Assessment time point
Folate (n=223)
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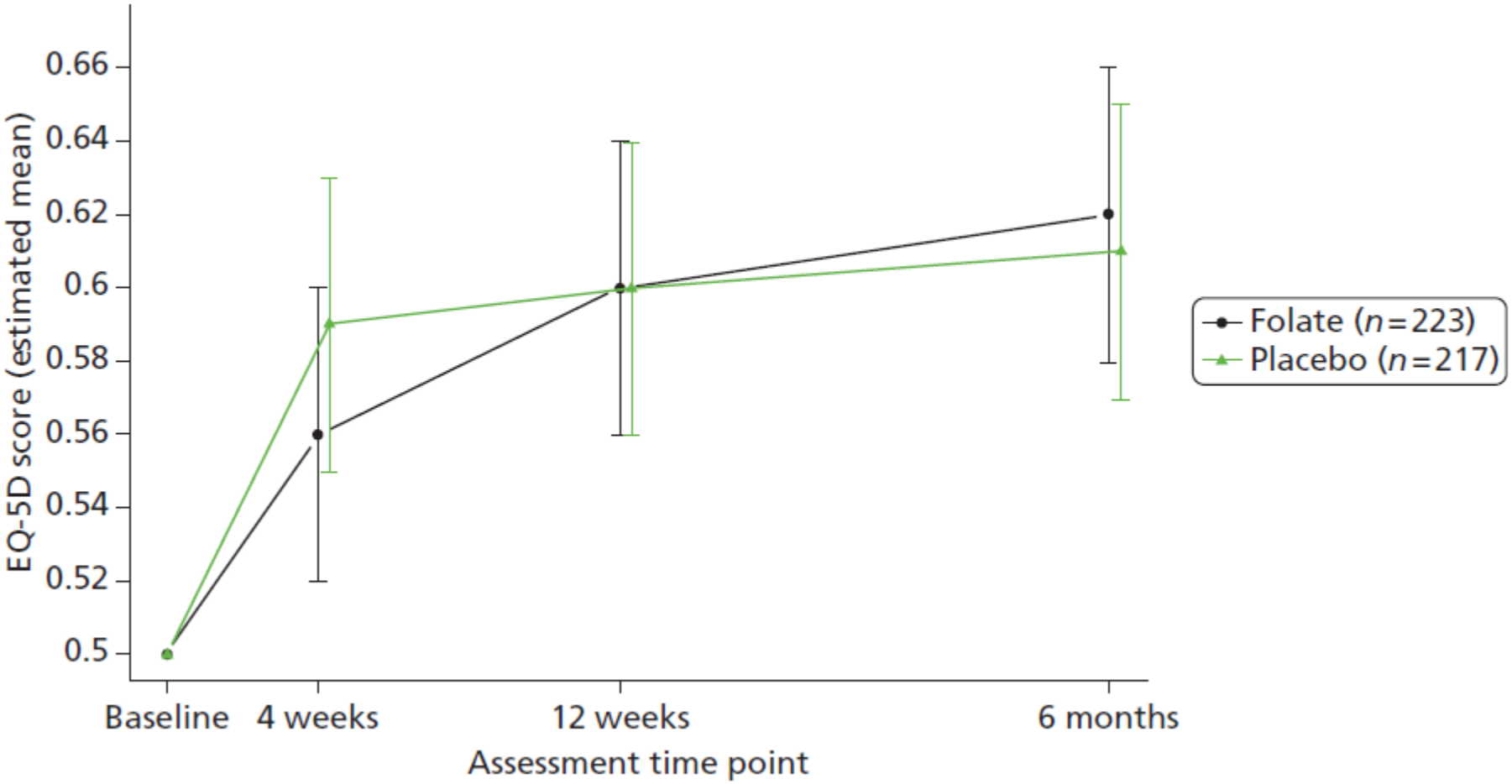
EQ-5D


EQ-5D score (estimated mean)
0.66
0.64
0.62
0.6
0.58
0.56
0.54
0.52
0.5
Baseline
4 weeks
12 weeks
6 months
Assessment time point
Folate (n=223)
Placebo (n=217)

Clinical conclusion

- FolATED generated no evidence that folic acid is effective or harmful in augmenting antidepressants

Economic questions

- Is there a need to conduct an economic evaluation of an intervention that doesn't work?
- Might folic acid be cost-effective even if not clinically effective?
  - Perhaps wrong / insensitive measures of effect
  - There may be cost advantages
- Would GPs ever start prescribing folic acid, knowing it isn't effective (at improving depression), on the basis of potential cost benefits?

NO!

Deviation from the HEAP

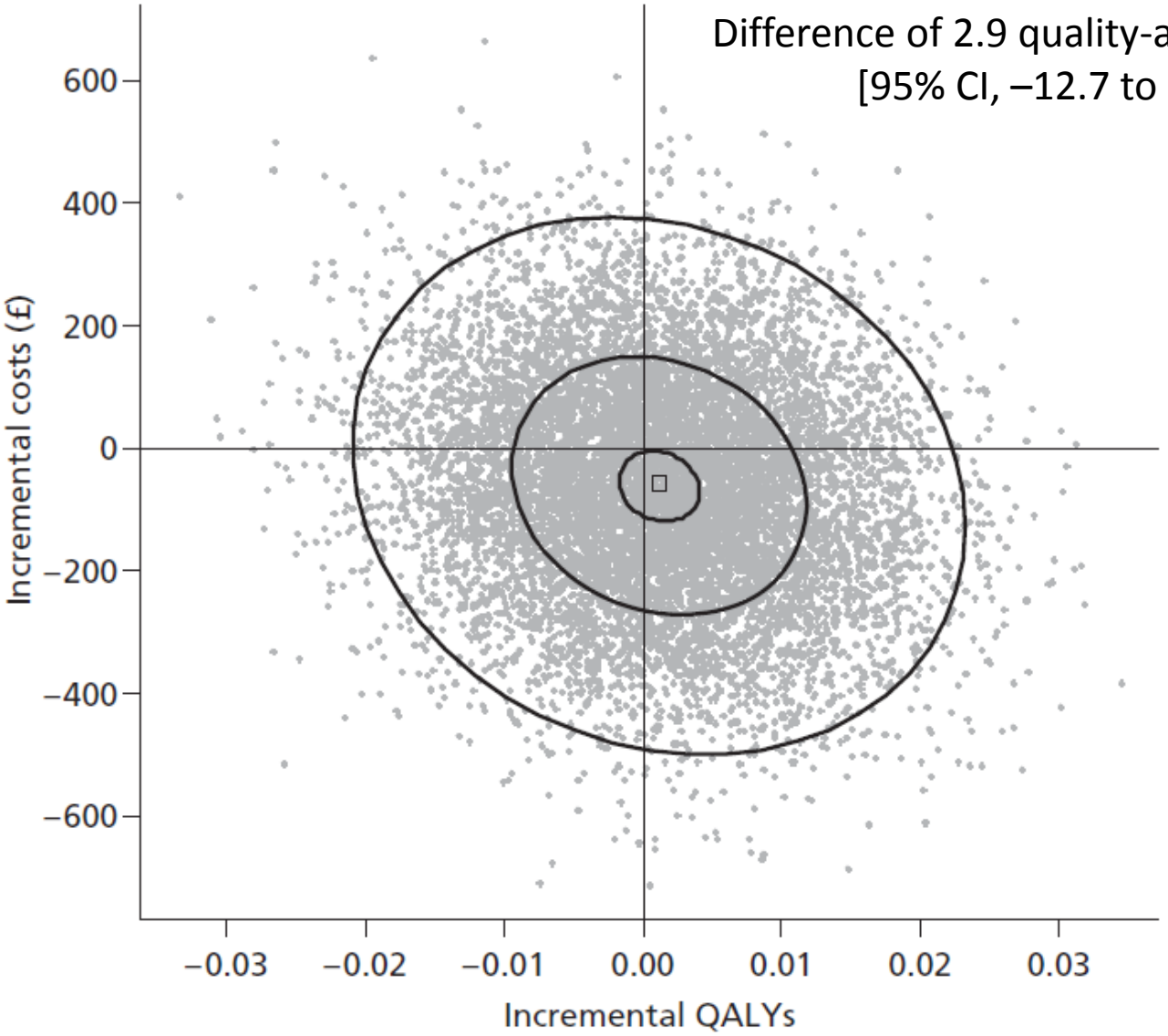
- For a drug which costs 3p per day with no benefits in depression, but with a potential to increase cancer risk and mask B_{12} deficiency, I would argue that an economic evaluation was unnecessary
- This would justify a deviation from the HEAP
- But… we had to deliver on our funding obligations!

Costs

Type of cost	Folate Mean (95% CI)	Placebo Mean (95% CI)	Difference (folate minus placebo) Mean (95% CI)
GP costs	164.20 (144.72 to 185.02)	186.46 (163.60 to 210.61)	–22.26 (–53.61 to 8.64)
Social care costs	148.46 (84.63 to 233.98)	324.86 (144.51 to 569.11)	–176.40 (–428.14 to 19.63)
Psychiatric hospital and community services costs	797.37 (562.94 to 1090.52)	886.40 (712.65 to 1089.37)	–89.03 (–404.23 to 249.42)
Antidepressant drug costs	72.93 (62.39 to 84.47)	75.30 (63.84 to 88.44)	–2.37 (–19.37 to 13.96)
All medication costs	239.95 (206.94 to 275.14)	256.79 (201.15 to 324.42)	–16.84 (–91.66 to 49.17)
Other costs	60.72 (44.60 to 78.85)	66.44 (48.50 to 86.49)	–5.72 (–31.42 to 19.50)
Total cost	1410.21 (1147.28 to 1729.31)	1719.12 (1398.10 to 2088.25)	–308.94 (–764.14 to 155.18)

Cost effectiveness

Difference of 2.9 quality-adjusted life-days
[95% CI, –12.7 to 7.0 days]



Experience from

- Assess whether heparin- or antibiotic-impregnated central venous catheters are better than standard CVCs at reducing incidence of bloodstream infections in children in ICU
- Determine the cost-effectiveness of each CVC type

HTA Health Technology Assessment

HEAP

- Aim
- Data
  - Healthcare resource utilisation
  - Unit costs
- Analysis
  - Cost analysis
  - Analysis of health outcomes
  - Incremental analysis
  - Analysis of uncertainty
  - Scenario analysis
  - Secondary analysis

Economic outcomes

- Costs
  - NHS perspective
  - Main cost driver is days in ICU
- Outcomes
  - Utility measurement not feasible
  - Economic health outcome was the same as the primary clinical outcome of bloodstream infection (BSI)
- Incremental cost per BSI averted

Pragmatist's view

- Trial-based economic evaluations must be informed by the clinical findings
- This would necessitate deviations from the HEAP under certain circumstances

Acknowledgements

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- MRC NWHTMR


THANKS
HEAPS