Automating network meta-analysis

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Context: my research

- Development of ADDIS
  - Aggregate Data Drug Information System
- Decision support for evidence-based health policy decisions
  - So far focussed on drug benefit-risk assessment

ADDIS: core idea

[van Valkenhoef et al., 2012c]

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Database of Clinical Trials

[van Valkenhoef et al., 2012c]

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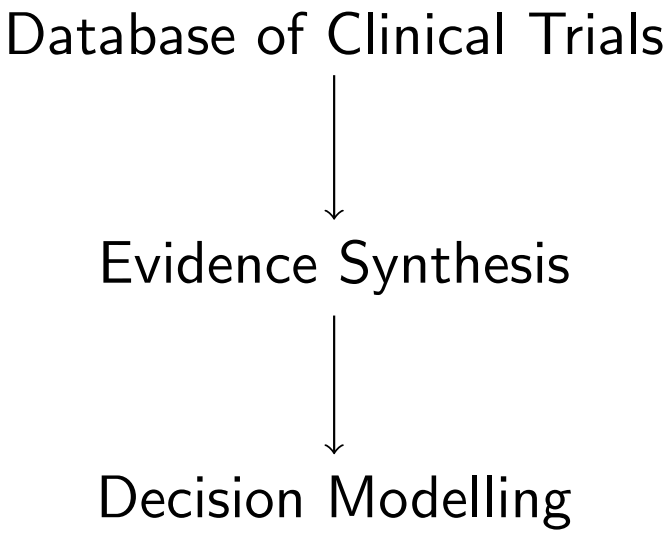
Evidence Synthesis

[van Valkenhoef et al., 2012c]

ADDIS: core idea



[van Valkenhoef et al., 2012c]

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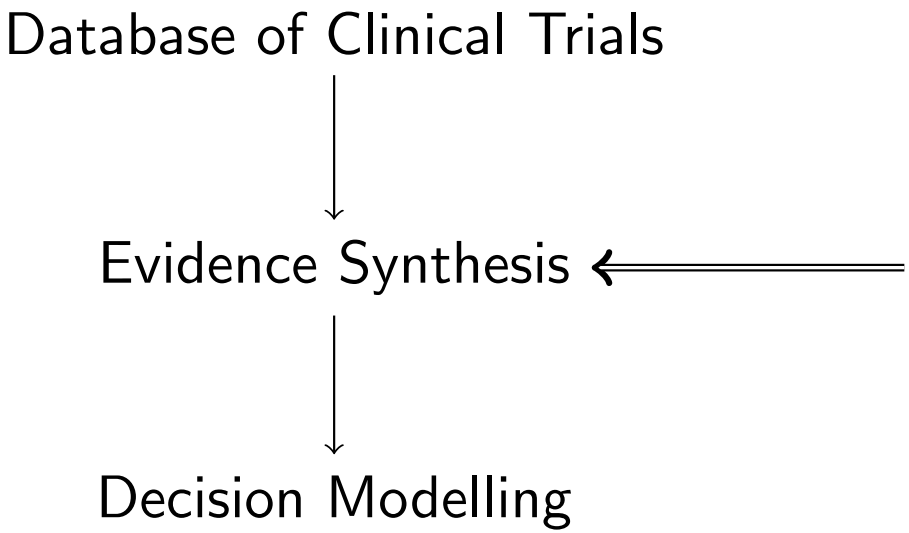

[van Valkenhoef et al., 2012c]

Network meta-analysis in ADDIS

- Pair-wise meta-analysis not suited for decision modelling
  - Often > 2 alternatives to be considered
  - *Consistent* use must be made of evidence
- Network meta-analysis solves this
  - Compare > 2 alternatives using network of trials
  - A.K.A.:
    - MTC: Mixed/Multiple treatment comparison
    - MTM: Mixed/Multiple treatment model/meta-analysis
- [van Valkenhoef et al., 2012b]

Consistency in network meta-analysis

- *Consistency* is the basic assumption:
  - $d_{x,z} = d_{x,y} + d_{y,z}$
- Intuitively: direct and indirect evidence 'compatible'
- Fundamentally: all studies are exchangeable
  - Inconsistency related to heterogeneity
- **Without consistency, there is no basis for decision!**

Testing for inconsistency

- Node-splitting [Dias et al., 2010]
  - Assess comparisons one-by-one
  - Comparing direct and indirect estimates
- Inconsistency models [Lu and Ades, 2006]
  - Identify sufficient set of 'inconsistency factors'
  - Under consistency, inconsistency factors $= 0$

Why automate?

- Writing BUGS code by hand: tedious, time-consuming, difficult, error-prone
- Most issues irrelevant to analysis
  - Exception: prior distributions
- Specialized frontend for network meta-analysis
  - Can save a lot of time
  - Prevents mistakes in BUGS code
  - Can draw attention to the *important* issues

Interest in automation

Lots of interest recently:

- My work with Tony Ades' group (Bristol U.)
- Alex Sutton / Nicola Cooper (U. of Leicester)
- Chris Schmidt (Tufts U.)
- Ian White – mvmeta (Cambridge)
- Petros Pechlivanoglou (next pres.)

The automation problem

For network meta-analysis in a Bayesian / MCMC framework:

- Generate model structure
- Choose prior distributions
- Specify data
- Generate starting values (for MCMC estimation)

[van Valkenhoef et al., 2012a]

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[van Valkenhoef et al., 2012a]

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  - Should be 'over-dispersed' relative to posterior

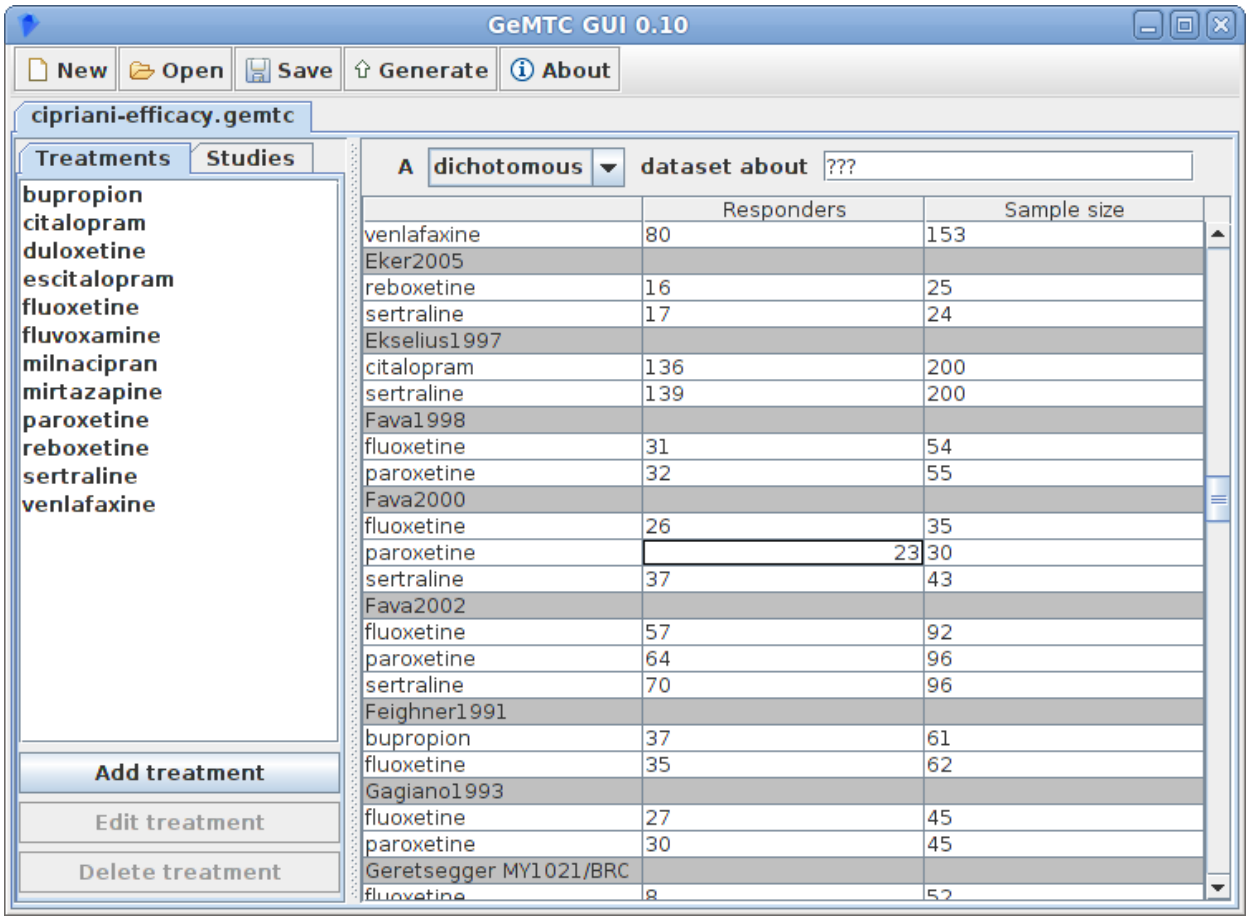
[van Valkenhoef et al., 2012a]

GeMTC: generate MTC models

- GUI for data entry / management
- Generates models for WinBUGS or JAGS
  - Consistency models: 100% implemented
  - Inconsistency models: works, but needs theoretical work
  - Node-split models: next version (0.12)
- Limited to (absolute) data on continuous / dichotomous scale
  - Relative effect data planned (0.14)
  - Other scales unplanned future work

[van Valkenhoef et al., 2011, 2012a]

Screenshots!



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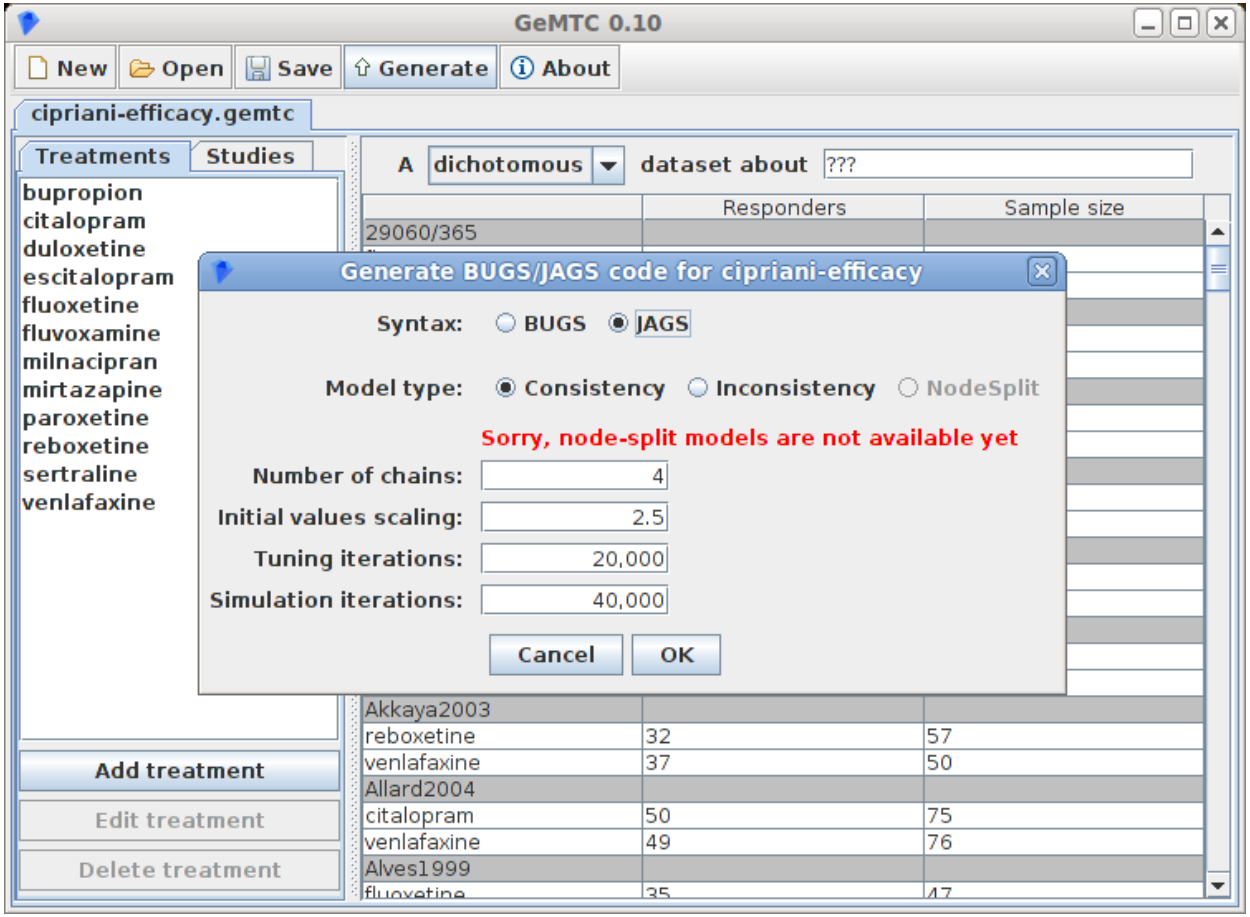

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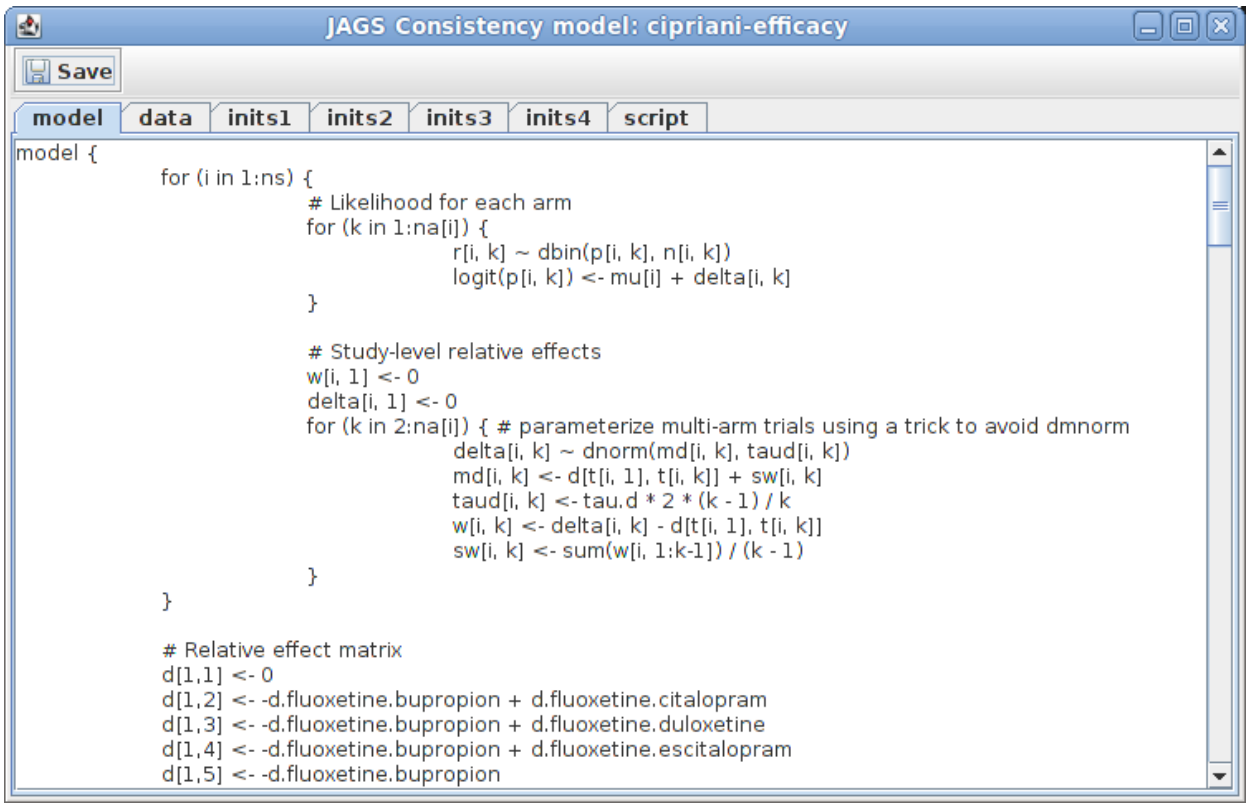

Other software

- ADDIS: also runs the MTC and makes graphs, tables
  - But: less flexible, transparent
- GeMTC CLI (command-line interface)
  - Good if you have *lots* of MTC to run
  - Or in 'reproducible research'
- GeMTC R package
  - Ties GeMTC model generation and JAGS together
  - Still work-in-progress / experimental

Discussion

- GeMTC generates MTC models
  - In very general, theoretically sound way
  - Free / open source: `http://drugis.org/`
- There is still much work to do
  - Implement additional methods
  - Improvements to GUI (e.g. customize priors)
  - Integrate analysis into GUI
  - Better / more complete R package
- Automating reveals interesting theoretical questions
  - E.g. how should inconsistency be defined?

S. Dias, N. J. Welton, D. M. Caldwell, and A. E. Ades. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med*, 29(7-8, Sp. Iss. SI): 932–944, 2010. doi: 10.1002/sim.3767.

G. Lu and A. E. Ades. Assessing evidence inconsistency in mixed treatment comparisons. *J Am Stat Assoc*, 101(474):447–459, 2006. doi: 10.1198/016214505000001302.

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