To systematically review the use of mathematical modelling to predict real world effectiveness from RCT efficacy data, range from statistical evidence synthesis to mathematical prediction models.

**OBJECTIVE**
- To systematically review the use of mathematical modelling to predict real world effectiveness from RCT efficacy data

**METHODS**

**In- and exclusion criteria**
- Description of a mathematical model in the field of comparative effectiveness research
- Studies with a methodological focus
- Applications for medical interventions
  - Infectious diseases
  - No prediction of effectiveness based on efficacy

**Data sources**
EMBASE, MEDLINE, JRSS, HTA websites, reference lists of eligible and other relevant papers found in the search

**RESULTS**

Four broad model types identified

   - Discrete health states, transition between states
   - Simulation on cohort level or on individual level (microsimulation models)
   - Markovian assumption often imposed

2. **Discrete event simulation models** (Guo et al. 2009)
   - Events instead of states
   - Not restricted to discrete states
   - Algorithmic procedure

3. **Mechanistic models** (Schultz et al. 2012)
   - Ordinary differential equations
   - Describe whole physiology of a patient

   - Survival analysis

Examples of predictive steps identified
- Across population characteristics
  - Prediction of occurrence of stroke and death for a trial-excluded patient population
  - Prediction of drug response in a genetically characterized patient subgroup
- Over time
  - Prediction of long-term survival outcomes of anti-diabetic treatment

**Disease areas**
- Cardiovascular disease (N=6)
- Oncology (N=1)
- Neurosciences (N=1)

**DISCUSSION**

- Limitations of identified models: lack of external validation, Markovian assumption
- Few included papers: mathematical models very common e.g. in disease progression modelling or for cost-effectiveness analysis, but rarely used to bridge efficacy-effectiveness gap
- This review complements existing literature reviews on specific modelling techniques by adding the focus on bridging the gap from efficacy to effectiveness via mathematical models

**REFERENCES**


Clarke, P.M. et al., 2004. A model to estimate the lifetime health outcomes of patients with type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS no. 68). Diabetologia 47, 1747–1759.


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