

# A framework for meta-analysis of prediction model studies with binary and time-to-event outcomes

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# Prognostic modeling research

- Development of risk prediction models
  - Identification of high risk individuals
  - Tailoring of medical interventions
- Validation highly recommended and increasingly common
  - *"All models are wrong but some are useful"* (Box G. 1978)
  - Assess prediction model performance across different settings & populations



# Synthesis of validation study results

- Summarize prediction model performance
- Identify generalizability of model predictions
  - Temporal validity
  - Geographical validity
  - Domain validity
- Assess need for local adjustments or improvements
  - Model re-calibration
  - Model revision
  - Model extension (e.g. received treatment(s), line of care, ...)

# Methods for quantitative synthesis

- **Challenge #1:** data extraction
  - Standard errors commonly unavailable
  - Calibration often not (rigorously) assessed
- **Challenge #2:** meta-analysis
  - Limited number of validation studies
  - Normality assumptions generally untenable
  - Identifying and modeling between-study heterogeneity

# Methods for quantitative synthesis

- A new statistical framework
  - Frequentist and Bayesian meta-analysis methods
  - One- and two-stage meta-analysis methods
  - Weakly informative prior distributions (empirically based)
- Use commonly reported information to estimate
  - Concordance statistic
  - Total O:E ratio
  - Calibration slope

# Methods for quantitative synthesis

- Case studies
  - EuroSCORE II (23 validations)
  - Framingham Wilson (23 validations)
- Extensions to IPD meta-analysis underway
  - Internal-external cross-validation
  - Ensuring more consistent calibration performance
- Implemented in the R package "[metamisc](#)"

# Guidance paper (in press)

Article

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# A selection of key references

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