

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)
 - Framinham Wilson (23 validations)
- Extensions to IPD meta-analysis underway
 - Internal-external cross-validation
 - Ensuring more consistent calibration performance
- Implemented in the R package "metamisc"

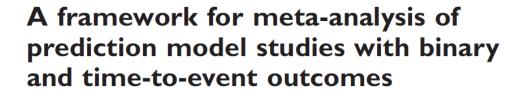






Guidance paper (in press)

Article



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A selection of key references

- Debray et al. JCE 2015. <u>10.1016/j.jclinepi.2014.06.018</u>
- Debray et al. BMJ 2017. <u>10.1136/bmj.i6460</u>
- Moons et al. PLOS MED 2014. <u>10.1371/journal.pmed.1001744</u>
- Snell et al. SMMR 2017. <u>10.1177/0962280217705678</u>
- Wolff et al. *Under review 2018*. (PROBAST)





