EDITORIAL

# Implementing systematic reviews of prognosis studies in Cochrane

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Over the last 30 years Cochrane has strived to advance the importance of conducting systematic reviews of therapeutic strategies, diagnostic tests, and risk factors. Now, the Cochrane community embarks on systematic reviews of prognosis studies in the *Cochrane Database of Systematic Reviews*.

Prognosis research has escalated in the last two decades. Today, frequently echoed terms are 'personalized medicine', 'precision medicine', or 'risk-based medicine', often used as synonyms. Almost all healthcare research programmes, medical journals, and even private companies (such as Google, IBM, and Philips) adopt these terms, across all medical domains and settings. Personalized or precision medicine does not just address effectiveness of treatments or preventive strategies, but rather addresses how to use an individual's prognostic information to make personally tailored choices about the best suited treatment or preventive management. Likely due to this worldwide focus on personalized or precision medicine, studies on prognostic and predictive factors (markers) and models have become abundant in the medical literature. Consequently, Cochrane needs to respond to this and produce systematic reviews that summarize the huge amount of data and evidence emerging from these primary prognosis studies, to enable stakeholders to make appropriate healthcare decisions.

The Prognosis Methods Group (methods.cochrane.org/prognosis), with funding support from Cochrane (Methods Innovation Fund and Strategic Methods Fund) and supportive academic institutions, has dedicated time and resources to the development and testing of novel methods and tools for the design, conduct, quantitative synthesis, interpretation, and reporting of systematic reviews of prognosis studies. This work includes strategies and tools for defining the review question, the PICOTS (population; index prognostic factor or model; comparative factor or model; outcomes to be predicted; timing of the prediction horizon and of the moment of prognosis; setting), search strategies, data extraction, critical appraisal, risk of bias assessment, quantitative synthesis, interpretation, reporting, and grading the certainty of summarized evidence, which can all be found on the Prognosis Methods Group website.[1]

For specific implementation within Cochrane the Prognosis Methods Group has developed review proposal and protocol writing templates, which provide detailed guidance.[2] Review templates will follow soon. All the Group's methods and tools will support systematic reviews of the four main types of prognosis research: [3][4][5][6]

1. Overall prognosis: studies aimed at quantifying the (overall) incidence of certain outcomes (e.g. comorbidity, complication, death, quality of life), occurring in a certain time period (hours, days, weeks, months, years, lifetime) in individuals within a certain health state (e.g. diagnosed with a certain disease, undergoing some type of surgery, being pregnant, or simply being a healthy citizen in the general population).
2. Prognostic factors: studies aimed at investigating which factors predict (the occurrence of) certain outcomes occurring in a certain time period in individuals within a certain health state. Ideally, these studies address the independent prognostic ability of a factor, i.e. (multivariably) adjusted for other prognostic factors, rather than the univariable association of a prognostic factor.
3. Prognostic models: studies aimed at developing, validating, and adjusting (e.g. extending) multivariable prognostic models that include multiple prognostic factors combined, and are to be used for making predictions in individuals.
4. Treatment selection factors/models: studies aimed at investigating which factors or combination of factors (models) are predictive for the outcome or effects of some treatments and not for the outcome or effects of other treatments.

The Prognosis Methods Group will develop guidance for the conduct of systematic reviews for all these four types of prognosis studies. To date, development of methodological guidance has focused mostly on types 2 and 3, although most guidance aimed at these types can also be applied directly to systematic reviews of types 1 and 4, as we indicate in the review proposal and protocol templates.[2]

The Group also provides training for Cochrane Review authors and


 

editors, including five face-to-face workshops given each year at the Cochrane Colloquium. These 90-minute workshops cover a general introduction to reviews of prognosis studies, data extraction, risk of bias assessment, meta-analysis and interpretation (using both aggregate and individual participant data), and grading of summarized review results. In 2018 we ran a half-day pre-Colloquium workshop, which will be extended to a full-day workshop from 2019 onwards. Advanced face-to-face courses at several locations provide more comprehensive topics on the synthesis of systematic reviews of prognosis studies. Finally, there will be online courses - both introductory and advanced courses - where all the steps of performing a review can be followed, anywhere in the world.

Since January 2018, when active implementation of systematic reviews of prognosis studies started within Cochrane, the Prognosis Methods Group has worked with many Cochrane Review Groups and Networks on 17 Cochrane Reviews of prognosis studies. These reviews cover a wide range of clinical problems and all four types of prognosis questions and studies. In September 2018, the first of these systematic reviews was published.[7] This review, published by Cochrane Wounds, assesses whether protease activity really is useful in the prediction of wound healing in people with venous leg ulcers. Another review, nearing completion by Cochrane Metabolic and Endocrine Disorders, and funded by the World Health Organization, determines the average risk to develop type 2 diabetes mellitus over different time horizons for people with intermediate hyperglycaemia.[8] Both these Cochrane Reviews address a frequent and large problem in their fields and provide a summary of all existing evidence. In addition to these two reviews, as of September 2018, 15 more reviews are underway, eight of them with already published protocols.

Finally, it is important that the Cochrane community produces systematic reviews of prognosis studies that address relevant clinical questions and problems. Therefore, we will shortly undertake a survey of Cochrane editors to scope and prioritize the prognosis questions in their domains. This will enable us to optimally spend time and resources to provide the summarized evidence on the problems that matter.

We look forward to taking up this challenge and rolling out this new type of review across Cochrane.

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### Declarations of interest

The authors have completed the ICMJE form for disclosure of potential conflicts of interest (forms available on request). The authors are the co-ordinator (JAAGD) and convenors (other authors) of the Cochrane Prognosis Methods Group (methods.cochrane.org/prognosis). KGMM is Director of Research of a large (around 500 employees) research and teaching institute within Utrecht University Medical Center. The institute conducts both investigator- and industry-driven research projects with a number of pharmaceutical and diagnostic companies. In addition, some of the members of staff receive unrestricted grants for research projects from a number of companies. It is the institute's explicit policy to work with several companies and not to focus on one or two industrial partners. KGMM receives no personal payment from any industrial partner. JH reports funding from the Cochrane Strategic Methods Fund and the Cochrane Methods Innovation Fund in relation to the work described in this Editorial. RDR also receives funding from HHR and other sources to conduct prognosis research in general but received no funding for this Editorial. The authors have no other disclosures.

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## References

1. Cochrane Prognosis Methods Group. Prognosis systematic review methods. methods.cochrane.org/prognosis/review-tools/publications-and-resources/prognosis-systematic-review-methods (accessed 23 July 2018).

2. Cochrane Prognosis Methods Group. Review tools. methods.cochrane.org/prognosis/our-publications (accessed 23 July 2018).

3. Hemingway H, Croft P, Perel P, Hayden JA, Abrams K, Timmis A, et al. Prognosis research strategy (PROGRESS) 1: a framework for researching clinical outcomes. *BMJ* 2013;346:e5595. https://doi.org/10.1136/bmj.e5595

4. Riley RD, Hayden JA, Steyerberg EW, Moons KGM, Abrams K, Kyzas PA, et al. Prognosis research strategy (PROGRESS) 2: prognostic factor research. *PLOS Medicine* 2013;10(2):e1001380. https://doi.org/10.1371/journal.pmed.1001380

5. Steyerberg EW, Moons KGM, Van der Windt DA, Hayden JA, Perel P, Schroter S, et al. Prognosis research strategy (PROGRESS) 3: prognostic


 https://doi.org/10.1002/14651858.ED000129

model research. *PLOS Medicine* 2013;10(2):e1001381. https://doi.org/10.1371/journal.pmed.1001381

6. Hingorani AD, Van der Windt DA, Riley RD, Abrams K, Moons KGM, Steyerberg EW, et al. Prognosis research strategy (PROGRESS) 4: stratified medicine research. *BMJ* 2013;346:e5793. https://doi.org/10.1136/bmj.e5793

7. Westby MJ, Dumville JC, Stubbs N, Norman G, Wong JKF, Cullum N, et al. Protease activity as a prognostic factor for wound healing in venous leg ulcers. *Cochrane Database of Systematic Reviews* 2018;(9):CD012841. https://doi.org/10.1002/14651858.CD012841.pub2

8. Richter B, Hemmingsen B, Metzendorf M-I, Takwoingi Y. Intermediate hyperglycaemia as a predictor for the development of type 2 diabetes: prognostic factor exemplar review. *Cochrane Database of Systematic Reviews* 2017;(5):CD012661. https://doi.org/10.1002/14651858.CD012661


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