Template[1] for summarising studies addressing prognostic questions

Instructions to fill the table:

- When no element can be added under one or more heading, include the mention:
  - "Not applicable" when an item is not to be informed (according to the type of study);
  - "Not described" when an item must be informed but no information is given in the publication.
- Describe all the results given in the manuscript even if those are not relevant to the study aim or main reason for data-extraction.
- Refer to the addendum for added results calculated or reconstructed by the reviewer.

Name of person completing template:
Date of completion:

HEADINGS	DESCRIPTION
Bibliographic citation	Use Vancouver style (Authors[2]. Title. Journal name. Publication Date; Volume (Issue):Page Numbers) Insert the link to the publication.
Sources of funding and competing interest	Report: ➢ The source of funding cited in the paper: Write "Stated" or "Not Stated" and specify if any give name(s) of organisation or corporation. Specify if possible the source type (public research funds, NGO, government, Academic/university healthcare industry or other) ➢ Competing interests: Write "Stated" or "Not Stated" and specify if any

[1] Minimum data abstracted from a single study to allow consistent comparison across studies and to inform a group process in evidence synthesis.

[2] Limit to the first 6 authors and then add *et al.* If there is a society, it counts as an author.

Competing interest	Competing interests: write "stated" or "not stated" and specify if any
Setting	Multicentre, location/country(ies), healthcare setting (primary, secondary, tertiary), workplace setting
Objective(s) of the study	Report, as cited by author(s), the objective(s) of the study including both primary and secondary aims, if applicable
Type of prognostic study	Specify whether the study is a prognostic course study, a prognostic factor (explanatory) study, or an outcome prediction (risk group) study). The addendum at the end of document explains and illustrates the types of prognostic studies
METHODS	
Study design	Specify what you think is the actual study design: cross sectional study, cohort study, case control study, other (give details) Optional: if you think the actual study design differs from the one cited by the author(s), you could mention this
Sampling method	Methods of selecting study participants: convenience sample, consecutive patients, population based random sample.
Eligibility criteria	Describe the eligibility criteria (i.e. Inclusion-exclusion criteria)
Follow-up moments	Report periods of recruitment and follow-up moments
Outcome measures	Describe the primary outcome measures identified by author(s). Description of secondary outcome measures is optional. Example (see also study of Schellingerhout et al in addendum): Outcome measure is global perceived recovery, dichotomized into "recovered or much improved" and "persistent complaints")
Prognostic factors and potential confounders (applies to a prognostic factor	*In case of a prognostic factor study*: Describe potential prognostic factors mentioned in the paper. In case of a central prognostic factor, describe the central prognostic factor, all potential confounders and effect modifiers mentioned in the paper

study, or an outcome prediction study.)	*In case of an outcome prediction study*: Describe all potential prognostic factors mentioned in the paper
RESULTS	
Numbers	Report numbers of participants: 1. Numbers of potentially eligible participants, 2. Number of participants Included in the study, 3. Number of participants completing follow-up and median as well as frequency distribution for follow-up time 4. Optional: if available copy and paste flowchart from the paper
Patients characteristics	Describe the actual population involved in the study by giving characteristics of study participants: 1. Demographic characteristics (age, sex, ethnicity, socio-economic status) 2. Relevant context-sensitive (e.g. Stage of disease) characteristics
Outcome measures data	Report outcomes measures data and include all available figures with 95% confidence intervals or other measures of dispersion such as standard errors (if confidence intervals aren't reported) Example (see also study of schellingerhout et al in addendum): Persistent complaints were reported by 43% of the patients in the development population after 6 months of follow-up
Effect size of prognostic factors (applies to a prognostic factor study, or an outcome prediction study.)	*In case of a prognostic factor study*: Report all available figures with p values and 95% confidence intervals or other measures of dispersion such as standard errors (if CIs aren't reported): Report statistically significant unadjusted univariable estimates and their precision Report statistically significant adjusted multivariable estimates and their precision (reporting of statistically insignificant factors is optional) Specify category boundaries when continuous variables were categorized
Effect size of prognostic factors (applies to a prognostic factor study, or an outcome prediction study.)	*In case of an outcome prediction study:* - development of the model Report statistically significant unadjusted univariable estimates and their precision Report statistically significant adjusted multivariable estimates and their precision (R^2) Report performance statistics of the model (see addendum for relevant statistics)

	(reporting of statistically insignificant factors is optional) - validation of the model Report performance statistics of the model (see addendum for relevant statistics)
Authors conclusion	Report the authors' conclusion

ADDENDUM

Introduction prognostic studies
Prognosis refers to the possible outcomes of a disease and the expected probability with which they can occur (e.g. death in a liver cancer patient). Another definition is: prognosis should be considered as occurrence relations between predictors and outcomes in defined populations of people with disease.

Important to prognosis is consideration and assessment of characteristics or factors that are associated with or determine the course of a condition. Health-care professionals may use prognostic information to educate or inform the management of their patients.

There are three main types of prognosis questions: 'What is the most likely course?', 'What factors are associated with, or determine, outcome?' and 'Can we identify risk groups who are likely to have different outcomes'? Studies investigating the course of a disease are called: Prognostic course studies. Studies investigating prognostic factors associated with outcome of a disease are called Prognostic factor (Explanatory) studies, while studies developing a model/tool (testing combinations of variables) that best predict outcome of a disease according to risk groups, are called Outcome prediction (Risk group) studies. Although the label Prognostic factor study suggests a single prognostic factor is studied, often multiple prognostic factors are studied.

It should be noticed that studies will be found that have a mixed character. For example a combination of a prognostic course study and a prognostic factor study.

Example of a prognostic course study
Cassidy JD, Côté P, Carroll LJ, Kristman V. Incidence and course of low back pain episodes in the general population. Spine (Phila Pa 1976). 2005 Dec 15;30(24):2817-23.

OBJECTIVES. To estimate incidence and course of severity-graded low back pain (LBP) episodes in adults.

STUDY DESIGN. Population-based, prospective cohort.

METHODS. An incidence cohort of 318 subjects free of LBP and a course cohort of 792 prevalent cases was formed from respondents to a mailed survey. Incident, recurrent, persistent, aggravated, improved, and resolved episodes were defined by the Chronic Pain Questionnaire. The follow-up at 6 and 12 months was 74% and 62%, respectfully. Annual estimates were age and sex standardized.

RESULTS. The cumulative incidence was 18.6% (95% confidence interval [CI], 14.2%–23.0%). Most LBP episodes were mild. Only 1.0% (95% CI, 0.0%–2.2%) developed intense and 0.4% (95% CI, 0.0%–1.0%) developed disabling LBP. Resolution occurred in 26.8% (95% CI, 23.7%–30.0%), and 40.2% (95% CI, 36.7%–43.8%) of episodes persisted. The severity of LBP increased for 14.2% (95% CI, 11.5%–16.8%) and improved for 36.1% (95% CI, 29.7%–42.2%). Of those that recovered, 28.7% (95% CI, 21.2%–36.2%) had a recurrence within 6 months, and 82.4% of it was mild LBP. Younger subjects were less likely

to have persistent LBP (incidence rate ratio, 0.88; 95% CI, 0.80–0.97) and more likely to have resolution (incidence rate ratio, 1.26; 95% CI, 1.02–1.56).

CONCLUSIONS. Most new and recurrent LBP episodes are mild. Less than one third of cases resolve annually, and more than 20% recur within 6 months. LBP episodes are more recurrent and persistent in older adults.

Example of prognostic factor study
Fransen M, Woodward M, Norton R, Coggan C, Dawe M, Sheridan N. Risk factors associated with the transition from acute to chronic occupational back pain. Spine (Phila Pa 1976). 2002 Jan 1;27(1):92-8.

Objective. To identify individual, psychosocial, and workplace risk factors associated with the transition from acute to chronic occupational back pain.

Study Design. A prospective cohort study was conducted on workers claiming earnings-related compensation for low back pain. Information obtained at the time of the initial claim was linked to compensation status (still claiming or not claiming) 3 months later.

Methods. At the time of the initial compensation claim, a self-administered questionnaire was used to gather information on a wide range of risk factors. Then 3 months later, chronicity was determined from claimants' computerized records.

Results. The findings showed that 3 months after the initial assessment, 204 of the recruited 854 claimants (23.9%) still were receiving compensation payments. A combined multiple regression model of individual, psychosocial, and workplace risk factors demonstrated that severe leg pain (odds ratio [OR], 1.9), obesity (OR, 1.7), all three Oswestry Disability Index categories above minimal disability (OR, 3.1– 4), a General Health Questionnaire score of at least 6 (OR, 1.9), unavailability of light duties on return to work (OR, 1.7), and a job requirement of lifting for three fourths of the day or more all were significant, independent determinants of chronicity ($P < 0.05$).

Conclusions. Simple self-report measures of individual, psychosocial, and workplace factors administered when earnings-related compensation for back pain is claimed initially can identify individuals with increased odds for development of chronic occupational disability.

Example of outcome prediction study
Schellingerhout et al (2010), Prognosis of Patients With Non-specific Neck Pain. Development and External Validation of a Prediction Rule for Persistence of Complaints

Objective. Development and validation of a prediction rule that estimates the probability of complaints persisting for at least 6 months in patients presenting with non-specific neck pain in primary care.

Study Design. Reanalysis of data from 3 randomized controlled trials.

Methods. The study population consisted of a sample (n = 468) from the adult primary care population (18–70 years) in The Netherlands presenting with non-specific neck pain. The primary outcome measure was global perceived recovery measured at 6 months of follow-up. Seventeen baseline characteristics of the patients were included in the analysis. Significant predictors were identified by multivariable backward stepwise logistic regression

analysis. A score chart was constructed by using the regression coefficient estimates. The score chart was externally validated in a cohort of patients with non-specific neck pain (n = 315), who participated in a randomized controlled trial in the United Kingdom (PANTHERtrial).

Results. The multivariable analysis resulted in a set of 9 predictors. The score chart has a discriminative ability of 0.66. External validation of the score chart showed a discriminative ability of 0.65, an adequate calibration, a good fit, and a low explained variation.

Conclusion. We developed a score chart, estimating the probability of persistent complaints at 6 months follow-up for patients with non-specific neck pain. This chart performed well in the study population and external validation population. The prediction which patients are more likely to develop persistent complaints is significantly improved by the score chart.

A note on statistics in outcome prediction (Risk group) studies

To understand whether a particular prognostic model or prognostic index provides a useful tool to inform patient treatment, the accuracy of the model predictions need to be reported, both in terms of

1) how well the model separates individuals who develop the outcome from those that do not (**discrimination**), and
2) how close the predicted risks are to the actual observed risks (**calibration**).

Currently several measures of model performance are used, although there is no consensus on which are the most clinically useful given the range of different clinical decisions directed from prognostic models.

Several measures of discrimination have been developed including:

- R squared
- c-index (equivalent to the area under the ROC curve).
- SEP (for survival data SEP is the weighted geometric mean of ‘absolute' relative risks between strata and baseline, ‘absolute' meaning that 1/RR replaces RR for relative risks RR(<1)
- D statistic (a measure of prognostic separation)
- K (a measure of the probability of concordance)
- NRI (the net reclassification improvement)
- IDI (integrated discrimination improvement)
- decision curve analysis.

Calibration in Cox models can be presented at a specific time point, as a plot of observed proportions of events against predicted probabilities in a new dataset often based on 10ths of risk groups. In logistic regression models the Hosmer-Lemeshow test can be used.

(Sources: Mallett et al. BMC Medicine 2010, 8:2, http://www.biomedcentral.com/1741-7015/8/21; Royston et al in: BMJ 2009;338:b604 doi: 10.1136/bmj.b604)