Evidence tables III
Prognostic and economic evaluation
Hans de Beer, Robin Harbour, Rob Cook
Najoua Mlika-Cabanne, Sara Twaddle, Andreas Gerber, Ton Kuijpers

Why work on evidence tables?

- Need for a common definition
- Provides a real opportunity for joint working between guideline agencies and between GIN and other international groups
- Potentially could save significant duplication of effort across all guideline development agencies
Work so far...

1. WG agreed definition of ETs at Lyon Conference 2005
   - Evidence tables are methodological and outcome summaries that present data from a number of related studies. These answer a well defined question in a consistent format and aim to demonstrate overall trends in the evidence and enable the process of making recommendations.

2. Development of a minimum data set for summarising studies that evaluate an intervention and a definitive template for describing them
   - Presented in a workshop at the Toronto conference in August 2007.
   - Now accepted for publication by Quality & Safety in Health Care

3. Development of a template for summarising studies addressing a diagnostic question
   - The results of the evaluation study were presented at the Helsinki Conference in October 2008

4. Agreement of the specification for the registry of summarised studies to enable G-I-N members to share their work with others
   - Discussed at the Lisbon Conference 2009
   - G-I-N Board approved funding 2010
What we are doing now...

- Developing templates for:
  - summarising economic evaluation studies
  - summarising prognostic studies.

Members of the Core Group 2009-10

- Najoua Mlika Cabanne*
- Sara Twaddle
- Hans de Beer
- Rob Cook
- Markos Dintsios
- Andreas Gerber
- Robin Harbour
- Kelvin Hill
- Carif Whittington
- Magali Remy Stockinger
Other members of the ETWG

- Samar Aboulsoud-Hassona
- Lorne Becker
- Bernard Burnand
- Michel Laurence
- Thomas Kaiser
- Eeva Ketola
- Ton Kuijpers
- Regina Kunz
- Jorma Komulainen
- Stefan Lange
- Alric Ruether
- Rick Shiffman
- Sheamini Sivasampu
- Jean Slutsky

Draft template for prognostic studies

Ton Kuijpers
Hans de Beer
Introduction

- Prognosis: foreseeing, predicting, or estimating the probability or risk of future conditions

- In medicine, prognosis commonly relates to the probability or risk of an individual developing a particular state of health (an outcome) over a specific time, based on his or her clinical and non-clinical profile

- Outcomes are often specific events, such as death or complications, but they may also be quantities, such as disease progression, (changes in) pain, or quality of life
Introduction

Explanatory studies
• Studies investigating whether a single variable (such as a tumour or other biomarker) may be prognostic.

Prediction rules
• Studies aimed at predicting outcomes from multiple variables.

Examples of prediction rules
• the Apgar score to determine the prognosis of newborns
• cardiovascular risk profiles to predict heart disease in the general population
• prenatal testing to assess the risk that a pregnant woman will give birth to a baby with Down’s syndrome
Introduction

Consecutive phases in multivariable prognostic research
- Development studies
- Validation studies
- Impact studies

Prediction rules: development studies
- Development of a multivariable prognostic model, including identification of the important predictors, assigning relative weights to each predictor, and estimating the model's predictive performance through calibration and discrimination and its potential for optimism using internal validation techniques, and, if necessary, adjusting the model for overfitting.
Introduction

Prediction rules: validation studies
• Validating or testing the model’s predictive performance (eg, calibration and discrimination) in new participants. This can be narrow (in participants from the same institution measured in the same manner by the same researchers though at a later time, or in another single institution by different researchers using perhaps slightly different definitions and data collection methods) or broad (participants obtained from various other institutions or using wider inclusion criteria).

Prediction rules: impact studies
• Quantifying whether the use of a prognostic model by practising doctors truly improves their decision making and ultimately patient outcome, which can again be done narrowly or broadly.
Introduction

References


Finding existing templates

- Literature search carried out to identify existing templates for summarising prognostic studies
- Conducted by Robin Harbour and colleagues at the Scottish Intercollegiate Guidelines Network (SIGN), Edinburgh
Finding existing templates

- Asking G-I-N member organisations for prognostic templates they are currently using
- Contacting Cochrane Prognosis Methods Group by CBO (Ton Kuijpers / Hans de Beer)

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Background information

<table>
<thead>
<tr>
<th>Bibliographic citation</th>
<th>Use Vancouver style (Authors. Title. Journal name. Publication Date; Volume (Issue):Page Numbers) Insert the link to the publication.</th>
</tr>
</thead>
</table>
| Sources of funding and competing interest | Report:  
- The source of funding cited in the paper: 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 |
| Setting | Multicenter, Location/Country(ies), Healthcare 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 |
## Background information

<table>
<thead>
<tr>
<th>Questions addressed</th>
<th>Mention the questions really addressed (e.g. include all questions even if only one is relevant for you at the moment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of prognostic study</td>
<td>Specify whether the study relates to what prognostic factors are associated with outcome (explanatory study), or to what groups of prognostic factors best predicted outcome (outcome prediction study)</td>
</tr>
</tbody>
</table>

## Methods

<table>
<thead>
<tr>
<th>Study design (cited by author or actual)</th>
<th>Specify the study design: cross sectional study, cohort study, case control study, other (give details). Precise if it’s the design cited by author(s).</th>
</tr>
</thead>
</table>
| Eligibility criteria                   | Describe the:  
|                                       | - Eligibility criteria i.e. inclusion-exclusion criteria,  
|                                       | - Methods of selection of participants |
| Follow-up                              | Specify the follow-up moments, periods of recruitment, and data collection if applicable |
| Outcome events                         | Describe the outcome events identified by author(s), both primary and secondary ones |
| Prognostic factors and potential confounders | Describe the potential prognostic factors (in case of an outcome prediction study) or the central prognostic factor, potential confounders and effect modifiers (in case of an explanatory study) |
## Results

### Numbers

Report numbers of individuals at each stage of study:
- numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
- number of patients excluded and reasons (i.e., give reasons for non-participation at each stage)

### Patients characteristics

Describe the actual population involved in the study:
- Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders
- Indicate number of participants with missing data for each variable of interest
- Report follow-up time: average, median, and range if applicable
- Highlight discrepancies between groups

### Outcome events data

Report all available figures with 95% confidence intervals when available:
- Report numbers of outcome events or summary measures

## Results

### Effect size - outcomes events

**Explanatory**

Report all available figures with 95% confidence intervals when available:
- Report unadjusted univariate estimates and their precision
- Report adjusted multivariate estimates and their precision
- Specify category boundaries when continuous variables were categorized

**Outcome prediction studies**

- Development of the model
  - Report unadjusted univariate estimates and their precision
  - Report adjusted multivariate estimates and their precision
  - Report performance statistics of the model (AUC, expected / observed probability plots, Hosmer-Lemeshow goodness-of-fit tests, or other statistics, negative / positive predicted values.)
## Results

(continued)

<table>
<thead>
<tr>
<th>Effect size - outcomes events</th>
<th>validation of the model</th>
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<tbody>
<tr>
<td></td>
<td>• Report performance statistics of the model (e.g. AUC, expected / observed probability plots, Hosmer-Lemeshow goodness-of-fit H- or Ĉ-statistics, negative / positive predicted values.</td>
</tr>
</tbody>
</table>

| Authors conclusion | Report the authors’ conclusion |

## Critical appraisal

<table>
<thead>
<tr>
<th>Results validity</th>
<th>Discuss the validity of the results and potential bias present</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>• Internal validity: study design appropriateness, sources of potential bias, use of inappropriate statistical analysis, interpretation of the results (taking into account the study hypotheses), multiplicity of analyses, comment on patients lost to follow-up (if applicable), etc.</td>
</tr>
<tr>
<td></td>
<td>• External validity: discuss the generalisability of the study results (e.g. setting, population involved, test used, etc.)</td>
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<td></td>
<td>General comments, including own conclusion of the reviewer, if possible.</td>
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<tr>
<th>Other / Addendum</th>
<th>Optional</th>
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<tbody>
<tr>
<td></td>
<td>Further calculations made by the reviewer</td>
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</tbody>
</table>
Draft template for economics studies

Rob Cook

Finding existing templates

- Literature search carried out to identify existing economic templates
- Conducted by Andreas Gerber and colleagues at the Institute for Quality and Efficiency in Health Care (IQWiG), Cologne
Literature search strategies

PubMed

cost-effectiveness* [ti] OR economic evaluation* [ti] OR cost-utility-analy* [ti] OR cost-benefit* [ti] OR decision-making model* [ti]) AND (data extraction sheet* OR data extraction template)

The Cochrane Library (Wiley), including partial data banks

Search strategy: data extraction sheet* OR data extraction template*
Literature search strategies

Hand search (Web-sites)
• HTA-Institutions
• HTA-Handbooks/ Methods manuals
• HTA-reports containing “economic evaluation OR cost-effectiveness” in the title

All: Full text screening
• Institutes with focus on health economic evaluation
• WHO
• EUnetHTA Core model

Google

Internet portals:
Karlsruher Virtueller Katalog

Evidence tables used by member organisations

CADTH
CCOHTA
CDR
HTA (Germany)
KCE (Belgium)
Ludwig Boltzman Institut
NCCHTA (UK)
Background information

<table>
<thead>
<tr>
<th>Name of person completing template</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Date of completion</td>
<td></td>
</tr>
<tr>
<td>Bibliographic citation</td>
<td>Use Vancouver style (Authors. Title. Journal name. Publication Date; Volume (Issue):Page (Numbers) Hyperlink to publication</td>
</tr>
<tr>
<td>Sources of funding and competing interests</td>
<td>Quote the source of funding if mentioned in the paper. If possible, specify the source type (public research funds, Government, NGO, academic/university, healthcare industry, other). Quote any declared competing interests, or write “None stated”</td>
</tr>
</tbody>
</table>

Methods

<table>
<thead>
<tr>
<th>Study design</th>
<th>Specify the form of economic evaluation being used (CUA, CEA, CBA, etc).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viewpoint</td>
<td>State the viewpoint of the analysis.</td>
</tr>
<tr>
<td>Country/Countries</td>
<td>List the country/countries for economic evaluation</td>
</tr>
<tr>
<td>Time horizon</td>
<td>State the time horizon for both costs and benefits</td>
</tr>
<tr>
<td>Population</td>
<td>Describe the eligible population and the population used for effect/cost data</td>
</tr>
<tr>
<td>Interventions</td>
<td>Describe the alternatives being compared</td>
</tr>
<tr>
<td>Primary outcome measure(s)</td>
<td>State the primary outcome measure(s)</td>
</tr>
<tr>
<td>Source of effectiveness estimates</td>
<td>Identify the source (meta analysis, RCT, etc)</td>
</tr>
<tr>
<td>Methods used to value benefits</td>
<td>Identify the methods used (stated WTP, revealed WTP, conjoint analysis etc)</td>
</tr>
<tr>
<td>Utilities and benefits</td>
<td>Specify where utilities or benefits came from (literature values, elicited in the study etc).</td>
</tr>
</tbody>
</table>
## Methods continued

<table>
<thead>
<tr>
<th>Source of estimates of quantities of resources used</th>
<th>Describe the methods used to identify relevant resource use (survey, lit values, expert consultation, formal consensus methods etc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods used to estimate unit costs</td>
<td>Describe the methods used to identify relevant unit costs (survey, lit values etc) Include cost year</td>
</tr>
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<td>Describe the methods used to identify relevant unit costs (survey, lit values etc) Include cost year</td>
</tr>
<tr>
<td>Adjustment for inflation</td>
<td>Was adjustment for inflation performed if unit costs stemmed from different years?</td>
</tr>
<tr>
<td>Discounting</td>
<td>Was discounting performed? Were effects and cost discounted with the same rate(s)?</td>
</tr>
<tr>
<td>Approach to sensitivity analysis</td>
<td>Describe the methods used for sensitivity analysis (one way, two way, probabilistic etc)</td>
</tr>
<tr>
<td>Modelling and analysis</td>
<td>Detail any model used (Markov, Discrete Event Simulation etc)</td>
</tr>
</tbody>
</table>

## Results

<table>
<thead>
<tr>
<th>Costs and outcomes</th>
<th>Presented relevant costs and outcomes in both disaggregated and aggregated form</th>
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</thead>
<tbody>
<tr>
<td>Subgroup analyses</td>
<td>Were subgroup analyses performed? Are the based on the results of RCTs etc.?</td>
</tr>
<tr>
<td>Incremental analysis results</td>
<td>Present the results of IA</td>
</tr>
<tr>
<td>Sensitivity analysis results</td>
<td>Present the results of SA</td>
</tr>
</tbody>
</table>
## Critical appraisal

<table>
<thead>
<tr>
<th>Authors conclusion</th>
<th>Report authors’ conclusions verbatim</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validity of results</td>
<td>Comment on the strengths and weaknesses of the study. If weaknesses were identified were these likely to have made a difference to the results of the economic evaluation?</td>
</tr>
<tr>
<td>Other / addendum (optional)</td>
<td></td>
</tr>
</tbody>
</table>