Provision of methodological knowledge for the quality assessment of primary studies

Training in evidence-based medicine and participation in methodological study

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Alfred Krupp von Bohlen und Halbach endowed chair
Prof. Dr. Jürgen Wasem
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Once only in winter semester 2011/12: training in evidence-based medicine and participation in a methodological study instead of exercises and homework (3 ETCS)

The examination attainment will be delivered in the last session, consisting of the quality assessment of studies by different instruments after being trained in evidence-based medicine.

Participation in all sessions is absolutely necessary for the data evaluation and analysis, the success of the study, and therefore highly desirable and obligatory. In case of illness, a medical certificate is required.
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23.11.2011: 14.00-16.00 o‘clock SE005
Theoretical provision of essential terms of EbM and quality criteria, validity assessment of 1 study

18.01.2012: 12.00-16.00 o‘clock SM205
Deepening of the knowledge by simulation of quality aspects, poster presentation, quizz, introduction of assessment instruments, application training

25.01.2012: 14.00-16.00 o‘clock SE005
Execution of the methodological study
Structure of the first session I/III

The concept of evidence-based medicine: the five steps

1. Formulating a well-built question
   - PICO-scheme, example patient from everyday clinical practice

2. Literature research
   - Types of primary and secondary studies, MeSH-terms/Boolean operators, example study as a research result

3. Critical appraisal
   - Validity (internal, external), classification of evidence (G-BA*, AHRQ**), single aspects, assessment of example study

4. Application of results in practice
   - example patient, example study

5. Evaluation

* Gemeinsamer Bundesausschuss = Federal Joint Committee
** Agency for Healthcare Research & Quality
Structure of the first session II/III

Criteria for the quality assessment
- Randomisation (single, permuted, cluster, inadequate)
- Concealment
- Blinding


The authors: double blinded versus single blinded. Lancet 2002; 359: 696–700

- Drop-out/loss to follow-up
- ITT (mnemonic: „Once randomised, always analysed“)
- Sample size calculation (outcome criterion, effect size expected, statistical power, type I-error/level of significance, sample size determined)
Structure of the first session III/III

- Criteria for the quality assessment
  - Sponsoring
  - Bias and its prevention: Selection (Reporting, Publication), Performance, Detection, Attrition, Language, Recall, Citation, Healthy-user, Confirmation

- Assessment of example study

- Limits of evidence-based medicine and criticism
Structure of the second session

- Introduction: Stratification, Reliability/Validity
- Poster presentation
  - Randomisation; concealment; blinding; drop-out, loss to follow-up; ITT- and per-protocol analysis; sample size calculation, confidence intervals, p-values; types of bias
- Simulation of randomisation, blinding, concealment, drop-out, loss to follow-up, ITT
- Introduction of assessment instruments
- Application training
- Verbal quiz between two teams with hangman
Simulation of Randomisation, Blinding, Concealment, Drop-out, ITT

- Random number table in a sealed, opaque envelope
- Prepared dextrose cubes with numbers written on: Blinding of treatment allocation

- Stratification
  - By sex
  - By age groups < 25 years and ≥ 25 years
### Unblinding (sealed opaque envelope with random number table)

<table>
<thead>
<tr>
<th>Participant</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<td>1</td>
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<td>5</td>
<td>2</td>
<td>8</td>
</tr>
</tbody>
</table>

#### Intervention: 0-4

#### Control: 5-9
# Participants in the study course

|   | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  | 11  | 12  | 13  | 14  | 15  | 16  | 17  | 18  | 19  | 20  | 21  | 22  | 23  | 24  | 25  | 26  | 27  | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38  | 39  | 40  | 41  | 42  | 43  | 44  | 45  | 46  | 47  | 48  | 49  | 50  |
|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 1 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 6 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 11|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 16|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 21|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 26|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 31|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 36|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 41|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 46|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

- **Crossover**
- **Drop-out**
- **Loss to follow-up**
- **Intervention**
- **Control**

Barbara Buchberger, Taormina, 1st November 2013
Populations for analyses

- **Intention-to-treat population: n=47**
  - Intervention: n= 27
  - vs. control: n= 20

- **Per-protocol population**
  - Intervention: n= 14 (-8 crossover- 4 drop-out- 1 loss to follow-up)
  - vs. control: n= 14 (-2 drop-out- 4 loss to follow-up)

- **As-treated population**
  - Intervention: n= 14 (-8 crossover- 4 drop-out- 1 loss to follow-up)
  - vs. control: n= 22 (+8 crossover- 2 drop-out- 4 loss to follow-up)
Quality assessment instruments

Julian Higgins

Helen Thomas

Catherine L. Hill

Peter Jüni

Jürgen Windeler


Hill CL, La Valley MP, Felson DT. Arthritis and Rheumatism 2002; 46(3): 779-84.


# Cochrane risk of bias tool

<table>
<thead>
<tr>
<th>No</th>
<th>Criterion</th>
<th>Judgement</th>
<th>Support for judgement</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>Quote:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low risk</td>
<td>Comment:</td>
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<td>Unclear risk</td>
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<tr>
<td></td>
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<td></td>
<td>Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.</td>
</tr>
<tr>
<td>2</td>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Quote:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low risk</td>
<td>Comment:</td>
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<td></td>
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<td>Unclear risk</td>
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<td>Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.</td>
</tr>
<tr>
<td>3</td>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Quote:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low risk</td>
<td>Comment</td>
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<td>Unclear risk</td>
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<td>Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.</td>
</tr>
</tbody>
</table>
Thank you for your attention

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