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Foreword

This short book provides the skills and tools to empower the reader to make better sense of clinical evidence. Present-day journal articles reflect ever-increasing complexity in research design, methods and analyses, and this welcome addition to the field will help readers to get the most from such papers.

With a little practice the book will indeed make it easier to understand the evidence related to healthcare interventions; it provides a clear and accessible account across the whole subject area. The authors avoid unnecessary jargon and have designed the book to be flexible in its use – it can be read from cover to cover or dipped into for specific topics.

Clinical Evidence Made Easy is helpfully structured into two main sections. The first provides the reader with the necessary skills underpinning evidence-based practice, the second gives invaluable tools for appraising different types of articles together with practical examples of their use. Moreover, the configuration within the sections makes for easy reading: common headings are used across chapters so that the reader quickly becomes familiar with the structure and the way ideas are presented.

This is a great book for busy clinicians who want to learn how to deliver evidence-based practice and have at their fingertips the tools to make sense of the burgeoning research literature. Indeed, it will also be valuable for those engaged in research, to aid the planning and delivery of their own projects.

Professor Paul Ewings,
Director of the Research Design Service South West
(National Institute for Health Research)

January 2014
Preface

This book is designed for healthcare professionals who need to know how to understand and appraise the clinical evidence that they come across every day.

We do not assume that you have any prior knowledge of research methodology, statistical analysis or how papers are written. However basic your knowledge, you will find that everything is clearly explained.

We have designed a clinical evidence appraisal tool for each of the main types of research method. These can be found in the second section of the book, ‘Clinical evidence at work’, and you can use them to help you evaluate research papers and other clinical literature, so that you can decide whether they should change your practice.

You can also test your understanding of what you have learnt by working through the extracts from original papers in the ‘Clinical evidence at work’ section.

Michael Harris, Gordon Taylor and Daniel Jackson

October 2013
About the authors

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Acknowledgements

We would like to thank everyone who has commented on our drafts, in particular Dr Fiona Fox, Lis Grey and Dr John Valentine.

Thanks also to our publisher, Dr Jonathan Ray, for his patience and helpful advice.
How to use this book

If you want a clinical evidence and critical appraisal skills course

• Work through the book from start to finish for a complete course in how to understand and appraise clinical evidence.
• The first page starts with the assumption that you want to go right back to first principles.
• Each chapter will build on what you have learnt in previous chapters.
• The chapters have simple examples that illustrate what you are reading.
• We have cut down on the jargon as much as possible. All new words are highlighted and explained.

If you are in a hurry

• Choose the chapters that are relevant to you. Each chapter is designed so that it can be read in isolation.

If you want a reference book

• You can use this as a reference book. The index is detailed enough for you to find what you want quickly.
• New concepts are highlighted in bold in the text so that you can find them and their explanations quickly and easily.

Applying your knowledge

• The appraisal tools in the ‘Clinical evidence at work’ section give you a system that you can use to evaluate any clinical evidence that you encounter.
Test your understanding

• See how the appraisal tools are used in extracts from real-life published papers in the ‘Clinical evidence at work’ section.

Study advice

• Go through difficult sections when you are fresh and try not to cover too much at once.
• You may need to read some sections a couple of times before the meaning sinks in. You will find that the examples help you to understand the principles.
Abbreviations

ARR  absolute risk reduction
CI   confidence interval
CONSORT  Consolidated Standards of Reporting Trials
EBHC  evidence-based healthcare
EBM  evidence-based medicine
EBP  evidence-based practice
HR  hazard ratio
ICER  incremental cost-effectiveness ratio
IQR  inter-quartile range
ITT  intention to treat
LR  likelihood ratio
NICE  National Institute for Health and Care Excellence
NNH  number needed to harm
NNT  number needed to treat
NPV  negative predictive value
OR  odds ratio
OTC  over the counter
PP  per protocol
PPV  positive predictive value
RCT  randomized controlled trial
RR  risk ratio
RRR  relative risk reduction
SD  standard deviation
SIGN  Scottish Intercollegiate Guidelines Network
Chapter 25

Research that summarizes other research

Appraisal tool

Systematic reviews and meta-analyses are at the top of the hierarchy of evidence. However, our confidence in them is misplaced if they have not been carried out rigorously.

The scope

1. What research question is the author trying to answer? How important is it?

   • Check that the ‘Background’ or ‘Introduction’ section explains the reasoning behind the paper and justifies the research question.

Finding the evidence

2. Did the authors use a comprehensive and systematic approach to identify papers?

   • Did the authors explain which databases they searched and the keywords that they used?
   • Have they looked for relevant references in the papers that they identified?
   • Was hand searching for relevant journals considered?
3. How did they look for literature that was not in the main bibliographic databases?

- How did they look for grey literature?
- Have they searched trials registers for unpublished work?
- Did they ask experts in the field and authors of relevant papers?

**Assessing the quality of papers identified**

4. How were the papers assessed for quality?

- The strategy should be clearly described.
- Reviewers need to use a validated scoring system.
- Was more than one assessor used, with a process for resolving disagreements?

5. Is there a list of the evidence that has been identified and included?

- Readers need to be able to check the evidence themselves if they wish.

6. How clear is the description of the findings?

- Where relevant, there needs to be a description of the patient groups, the interventions, outcomes and their timing.

**In a meta-analysis...**

7. Was it reasonable to bring the individual papers together in a meta-analysis?

- Studies not meeting the authors’ research design and quality criteria need to be excluded.
- Were the characteristics of the individual studies tabulated?
8. How were any missing data handled?
   - Did the researchers contact the original research authors to ask for further details?

9. What were the results?
   - Look for a Forest plot with the pooled relative risk or odds ratio estimate and its 95% CI.
   - Was any difference statistically significant? If so, was it clinically important?

10. Was the level of heterogeneity between papers considered?
    - Was heterogeneity assessed by either a Cochran’s Q test or an I² measure?
    - What modelling system was used? Expect to see fixed-effects modelling if there is no heterogeneity and random-effects modelling if there is some heterogeneity.

11. Did the funnel plot show evidence of publication bias?
    - This would be suggested by asymmetry in the plot.

12. Was there a sensitivity analysis?
    - Check how the different possible analyses affect the pooled result estimations. Are any very different, throwing the conclusions into doubt?

*In a meta-synthesis...*

7. Was it reasonable to bring the individual papers together in a meta-synthesis?
We need to check that the meta-synthesis is not trying to combine studies that have different underpinning approaches, for instance descriptive and inductive methodologies.

Studies not meeting the authors’ research design and quality criteria should be excluded.

The characteristics of the individual studies should be tabulated.

8. Do the findings offer more than summaries?

  • Look for a novel interpretation of the results.

*Putting it all together…*

The final questions for this appraisal tool are given in *Chapter 29.*
Research that summarizes other research – in practice

The following highlighted extracts are reproduced with permission from The BMJ Publishing Group.

A meta-analysis of cognitive-based behaviour change techniques as interventions to improve medication adherence

The scope

1. What research question are the authors trying to answer? How important is it?

The authors wanted to evaluate the use of cognitive-based behaviour change techniques (CBCTs) as interventions to improve medication adherence. No previous systematic reviews or meta-analyses had reported on the efficacy of motivational interviewing in facilitating medication adherence.

Estimates suggest that 30–50% of patients prescribed medications for chronic illnesses do not adhere to their prescribed medication regimen.

This non-adherence has been demonstrated to diminish treatment effect which can result in prolonged illness, additional investigations and prescriptions that may otherwise have been unnecessary.

Finding the evidence

2. Did the authors use a comprehensive and systematic approach to identify papers?

The databases were listed and, because keywords like ‘motivational interviewing’ were unlikely to have been used consistently in this field, a broad search strategy was taken. Identified papers were checked for relevant references.
There was no suggestion that relevant journals had been hand searched, or that there had been a search for grey literature.

We developed a search strategy to avoid restriction to predetermined terms such as “motivational interviewing” as many of the techniques of interest are not classified using specific or consistent terms.

Truncations (*), wild cards ($), hyphens and other relevant Boolean operators were used where permitted.

We applied the search strategy to the MEDLINE, EMBASE, PsychINFO, CINAHL and Cochrane databases in April 2013 without date or language restrictions.

The reference lists of all screened full-text articles were also used to identify further relevant articles.

3. How did they look for unpublished evidence?

The authors did not state that they had searched trials registers for unpublished work or asked experts in the field.

Assessing the quality of papers identified

4. How were the papers assessed for quality?

The strategy, including the use of a validated scoring system and a process for resolving disagreements, was clearly stated.

A quality assessment of all included studies was made using the Cochrane risk of bias tool.

The risk of bias was assessed in five domains deemed relevant to the included studies.

The quality assessment process was undertaken independently by two reviewers, with consensus on the final risk classifications reached through discussion.
5. Is there a list of the evidence that has been identified and included?

The 26 studies are listed, as are their references.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bailey et al</td>
<td>Hospital clinic, USA</td>
</tr>
<tr>
<td>Berger et al</td>
<td>Telephone calls to patients at home, USA</td>
</tr>
<tr>
<td>Brown et al</td>
<td>Hospital clinic, UK</td>
</tr>
<tr>
<td>Dilorio et al</td>
<td>Community clinic, USA</td>
</tr>
</tbody>
</table>

6. How clear is the description of the findings?

The table extract below shows how the authors tabulated summaries of the disease areas, interventions, outcomes and timings for each patient group.

<table>
<thead>
<tr>
<th>Study</th>
<th>Disease area</th>
<th>Intervention description</th>
<th>Components received by control group</th>
<th>Sample size</th>
<th>Intervention length (average)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Konkle-Parker et al</td>
<td>HIV</td>
<td>Adherence intervention guided by the Information-Motivation-Behavioural Skills model</td>
<td>Standard care; usual clinic appointments</td>
<td>36</td>
<td>8 sessions over 24 weeks. Average overall duration 1 h 30 min</td>
</tr>
<tr>
<td>Maneesriwongul et al</td>
<td>HIV</td>
<td>MI with counselling</td>
<td>Standard care; 60 education and provision of leaflets at point of prescribing</td>
<td>3 sessions approximately 30 min over a 4 week period</td>
<td></td>
</tr>
</tbody>
</table>
For the meta-analysis

7. Was it reasonable to bring the individual papers together in a meta-analysis?

The authors excluded studies not meeting their criteria. The characteristics of the individual studies were shown in a table.

Full-text articles excluded (n=58):

- Not a motivational interviewing or CBCT n=14
- Did not assess or report medication adherence n=8
- Not an RCT n=13...

Two researchers independently screened titles and abstracts against the inclusion and exclusion criteria using a piloted abstract screening tool.

8. How were any missing data handled?

The researchers contacted the original authors to ask for missing details.

For studies with missing data or ambiguities, the corresponding author was contacted for clarification.

9. What were the results?

The data were analysed with a statistic called “Hedges’ g”, a measure of effect size. A Hedges’ g value of zero would imply that there is no effect, i.e. no difference between the interventions.

The individual and overall values are shown with their 95% CIs.
Figure: Forest plot for studies included in meta-analysis.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Hedges’ g (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Es. (2001)</td>
<td>0.48 (0.00, 0.96)</td>
</tr>
<tr>
<td>Wagner (2006)</td>
<td>-0.08 (-0.35, 0.20)</td>
</tr>
<tr>
<td>Weber (2004)</td>
<td>0.69 (0.14, 1.24)</td>
</tr>
<tr>
<td>Williams (2012)</td>
<td>-0.32 (-0.77, 0.13)</td>
</tr>
<tr>
<td>Overall (I-squared = 67.9%, p = 0.000)</td>
<td>0.34 (0.23, 0.46)</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis

The meta-analysis suggested that receipt of a cognitive-based behavioural adherence intervention was associated with statistically significant improvements in medication adherence, but these were small and the clinical relevance is unknown.

We have established that receipt of a cognitive-based behavioural medication adherence intervention is likely to elicit small improvements in medication adherence, but the clinical relevance and impact of this improvement remain unknown.

10. Was the level of heterogeneity between papers considered?

The authors commented that there was notable heterogeneity, and they raised the question as to whether the studies were sufficiently comparable to warrant pooling in a meta-analysis.

Heterogeneity was high with an I² value of 68%.

A random effects model was employed...
11. Did the funnel plot show evidence of publication bias?

There was asymmetry in the funnel plot. This, as the authors point out, was indicative of publication bias. However, they used techniques to account for publication bias to provide a conservative effect size estimate.

**Figure:** Funnel plot for studies included in meta-analysis.

12. Was there a sensitivity analysis?

There was no sensitivity analysis.

**Putting it all together...**

The authors’ methodology has some limitations and they concede that the improvements in medication adherence are small, with unknown clinical relevance.

Because of this, some readers may feel that their conclusion that “CBCTs are effective interventions for improving medication adherence …” is overstated.