Part Two: Searches, assessing risk of bias and methodological quality, data collection and analysis
Learning objectives - Part Two

- Formulate a protocol for a search strategy for health economic studies
- Identify tools for assessment of risk-of-bias and methodological quality in health economic studies
- Formulate a protocol for collection of data on resource use, costs and cost-effectiveness
- Formulate a protocol for analysis and presentation of results
Preliminary points

- Advisory support from a health economist useful
  - Check with CRG - health economist advisor?
  - Contact Economics Methods Group janice.legge@newcastle.ac.uk

- Focus on how to prepare protocol for a critical review of health economics studies
Chapter 15: Incorporating economics evidence


Key points

- Economics is the study of the optimal allocation of limited resources for the production of benefit to society and is therefore relevant to any healthcare decision;
- Optimal decisions also require best evidence of effectiveness;
- This chapter describes methods for incorporating economics perspectives and evidence into Cochrane reviews, with a focus on critical review of health economics studies;
- Incorporating economics perspectives and evidence into Cochrane reviews can enhance their usefulness and applicability for healthcare decision making and new economic analyses.

15.1 The role and relevance of economics evidence in Cochrane reviews
15.2 Planning the economics component of a Cochrane review
15.3 Locating studies
15.4 Selecting studies and collecting data
15.5 Addressing risk of bias
15.6 Analysing and presenting results
15.7 Addressing reporting biases
15.8 Interpreting results

http://www.cochrane-handbook.org
Search methods for identification of studies

The methods used to identify studies should be summarized. The following headings are recommended. Before starting to develop this section, authors should contact their Cochrane Review Group (CRG) for guidance.

See also
- Search methods are discussed in detail in Chapter 6 (Sections 6.3).

Electronic searches

The bibliographic databases searched, the dates and periods searched and any constraints, such as language should be stated. The full search strategies for each database should be listed in an appendix to the review. If a CRG has developed a specialized register of studies and this is searched for the review, a standard description of this register can be referred to but information should be included on when and how the specialized register was most recently searched for the current version of the review and the search terms used should be listed.

See also
- Search strategies are discussed in detail in Chapter 6 (Section 6.4).

Searching other resources

List grey literature sources, such as internal reports and conference proceedings. If journals are specifically hand-searched for the review, this should be noted but hand-searching done by the authors to help build the specialized register of the CRG should not be listed because this is covered in the standardized description of the register. List people (e.g. trialists or topic specialists) and organizations who were contacted. List any other sources used, which may include, for example, reference lists, the World Wide Web or personal collections of articles.

The following optional headings may be used, either in place of ‘Searching other resources‘ (in which case they would be level 3 headings) or as subheadings (level 4).

Grey literature
Search methods for identification of studies

The methods used to identify studies should be summarized. The following headings are recommended. Before starting to develop this section, authors should contact their Cochrane Review Group (CRG) for guidance.

See also
- Search methods are discussed in detail in Chapter 6 (Sections 6.3).

Electronic searches

The bibliographic databases searched, the dates and periods searched and any constraints, such as language should be stated. The full search strategies for each database should be listed in an appendix to the review. If a CRG has developed a specialized register of studies and this is searched for the review, a standard description of this register can be referred to but information should be included on when and how the specialized register was most recently searched for the current version of the review and the search terms used should be listed.

See also
- Search strategies are discussed in detail in Chapter 6 (Section 6.4).

Searching other resources

List grey literature sources, such as internal reports and conference proceedings. If journals are specifically handsearched for the review, this should be noted but handsearching done by the authors to help build the specialized register of the CRG should not be listed because this is covered in the standardized description of the register. List people (e.g. trialists or topic specialists) and organizations who were contacted. List any other sources used, which may include, for example, reference lists, the World Wide Web or personal collections of articles.

The following optional headings may be used, either in place of ‘Searching other resources’ (in which case they would be level 3 headings) or as subheadings (level 4).

Grey literature
Searches: Electronic searches for health economics studies

- Electronic searches of MEDLINE, EMBASE, CINAHL etc. (alongside searches for studies of effects)
  - Further information on methods and tools (e.g. search filters for health economics studies) in Chapter 15 of Cochrane Interventions Handbook

- Electronic searches of specialist health economics literature databases
Searches: Electronic searches for health economics studies

- NHS Economic Evaluation Database (NHS EED)
  - Over 7,000 quality assessed structured abstracts of full economic evaluations, plus bibliographic records of partial economic evaluations
The Cochrane Library Evidence for healthcare decision-making

BROWSE
Cochrane Reviews: By Topics | New Reviews | Updated Reviews | A-Z | By Review Group
Other Resources: Other Reviews | Clinical Trials | Methods Studies | Technology Assessments | Economic Evaluations

SEARCH
Enter search term | Title, Abstract or Keywords
Advanced Search | MeSH Search | Search History | Saved Searches

BROWSE THE NHS ECONOMIC EVALUATION DATABASE
Critically Appraised Economic Evaluations | Other Economic Studies: Bibliographic Details | All Studies
ABCDEFGHIJKLMNOPQRSTUVWXYZ
AAOHM advisory: cost benefit and cost effectiveness analyses (Brief record)
An ABCD program to increase access to dental care for children enrolled in Medicaid in a rural county (Structured abstract)
Abcibimab: a pharmacoeconomic review of its use in percutaneous coronary revascularisation (Brief record)
Abcibimab: cost-effective survival advantage in clinical trials and clinical practice (Brief record)
Abcibimab provides cost-effective survival advantage in high-volume international practice (Structured abstract)
Abcibimab therapy in percutaneous intervention: economic issues in the United States (Brief record)
Abdominal adhesiolysis: inpatient care and expenditures in the United States in 1994 (Provisional record)
Abdominal aortic aneurysm (AAA): cost-effectiveness of screening, surveillance of intermediate-sized AAA, and management of symptomatic AAA (Brief record)
Abdominal aortic aneurysm: costs and long-term results after operative repair (Provisional record)
Abdominal aortic aneurysm: postoperative 10-year follow-up with cost analysis (Provisional record)
Abdominal aortic aneurysm screening: an epidemiological point of view (Brief record)
Abdominal aortic aneurysms: comparing costs of screening (Provisional record)
Abdominal aortic aneurysms: cost-effectiveness of elective endovascular and open surgical repair (Structured abstract)
Abdominal CT scanning in reproductive-age women with right lower quadrant abdominal pain: does its use reduce negative appendectomy rates and healthcare costs? (Provisional record)
Abdominal hysterectomy: complications, hospital stay and cost (Brief record)
Abdominal sacral colpopexy or vaginal sacrospinous colpopexy for vaginal vault prolapse: a prospective randomized study (Structured abstract)
The ability of managed care to control health care costs: how much is enough? (Provisional record)
The abnormal outpatient chemistry panel serum alkaline phosphatase: analysis of physician response, outcome, cost and health effectiveness (Structured abstract)
The Aboriginal and Torres Strait Islander casemix study (Provisional record)
ARBS housing screening for high risk infants (Provisional record)

http://www.thecochranelibrary.com
**NHS Economic Evaluation Database (NHS EED)**

*NHS Economic Evaluation Database (NHS EED)* contains over 7000 abstracts of quality assessed economic evaluations. The database aims to assist decision-makers by systematically identifying and describing economic evaluations, appraising their quality and highlighting their relative strengths and weaknesses.

More information about NHS EED can be found in the Help section.

Request 'last tracking' of a provisional abstract

http://www.crd.york.ac.uk/crdweb/
Searches: Electronic searches for health economics studies

- Health Economic Evaluations Database (HEED)
  - Published on Wiley InterScience
  - Free to Cochrane contributors via Cochrane.org intranet (Archie user name and password)
Welcome to the Cochrane intranet!

Discussion Forums

- For user testers: Beta 1 webinar now available 4 days 21 hours ago
- For user testers: Formal Beta testing CRS version 1 (searching) 5 days 22 hours ago (19)
- Comments welcome! Websites Development Report to CSG for Split, March 2011 1 week 5 days ago

Policy Manual

- 2.2.7 Copyright [Licence for Publication forms] 2 days 15 hours ago
- 2.2.7.2 Permission to republish Cochrane material in print 2 days 15 hours ago
- 2.2.6.3 Responding to feedback 2 days 23 hours ago
- 2.3 Commercial
Searches: Electronic searches for health economics studies

- Health Economic Evaluations Database (HEED)
  - c. 30,000 enriched abstract records (1994-), plus many more bibliographic records, of full and partial economic evaluations
  - International perspective: over 1500 non-English evaluations
  - Over 70 searchable fields (e.g. ICD-9 disease classifications; ATC drug classifications; Type of economic evaluation)
Searches: Electronic searches for health economics studies

- The CEA Registry
- Econlit
- COonnaissances et Décision en EConomie de la Santé (CODECS)
- Paediatric Economic Database Evaluation (PEDE)

http://www.york.ac.uk/inst/crd/econ4.htm
### Special Queries

**Directory of Topic-Specific PubMed Queries**

**Queries Targeted for Clinicians and Health Services Researchers**

<table>
<thead>
<tr>
<th><strong>Clinical Queries</strong></th>
<th>A search interface to find citations in the areas of:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Clinical Study Categories</strong>: Find citations corresponding to a specific clinical study category.</td>
</tr>
<tr>
<td></td>
<td><strong>Systematic Reviews</strong>: Find citations for systematic reviews, meta-analyses, reviews of clinical trials, evidence-based medicine, consensus development conferences, and guidelines.</td>
</tr>
<tr>
<td></td>
<td><strong>Medical Genetics</strong>: Find citations related to various topics in medical genetics.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Electronic Health Records</strong></th>
<th>PubMed search and links to other electronic health records information resources</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>Health Services Research (HSR) Queries</strong></th>
<th>A search interface to find PubMed citations relating to health care quality or to health care costs</th>
</tr>
</thead>
</table>

<table>
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<tr>
<th><strong>Cancer Topic Searches</strong></th>
<th>A search interface to retrieve PubMed citations on more than 100 major cancer topics</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>Healthy People 2010</strong></th>
<th>A search interface providing searches for published literature related to the Healthy People 2010 focus areas of the HP2010 Information Access Project.</th>
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</table>

<table>
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<tr>
<th><strong>Subjects</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>AIDS</strong></td>
<td>Limits search to the PubMed AIDS subset</td>
</tr>
</tbody>
</table>

PubMed Health Services Research (HSR) Queries

This page provides specialized PubMed searches on healthcare quality and costs.

After running one of these searches, you may further refine your results using PubMed’s Limits feature.

Results of searches on this page are limited to specific health services research areas (see definitions). For comprehensive searches, use PubMed directly.

Additional PubMed search filters are available, including a filter for Systematic Reviews.

Search by HSR Study Category

This search finds citations that correspond to a specific health services research study category. The search may be either broad and sensitive or narrow and specific. The search filters are based on the work of Haynes RI et al. See the filter table for details.

Searches: Electronic searches for health economics studies

Cochrane review (protocol) - *Chest physiotherapy for reducing respiratory morbidity in infants requiring ventilatory support*

Electronic searches
Cochrane Neonatal Review Group (see: Cochrane Neonatal Review Group, search strategy for Specialised Register in *The Cochrane Library*).

The Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library*)

MEDLINE (1966 to present)
EMBASE (1988 to present)
CINAHL (1982 to present)
PEDro (1929 to present)
NHS Economic Evaluation Database (1992 to present)
Health Economic Evaluations Database (1994 to present)
CEA Registry (1976 to present)
Paediatric Economic Database Evaluation (1980 to present)
PubMed (1966 to present)
Electronic searches

[recommended, level 3 heading]

The bibliographic databases searched, the dates and periods searched and any constraints, such as language should be stated. The full search strategies for each database should be listed in an appendix to the review. If a CRG has developed a specialized register of studies and this is searched for the review, a standard description of this register can be referred to but information should be included on when and how the specialized register was most recently searched for the current version of the review and the search terms used should be listed.

See also

- Search strategies are discussed in detail in Chapter 6 (Section 6.4).

Searching other resources

[recommended, level 3 heading]

List grey literature sources, such as internal reports and conference proceedings. If journals are specifically handsearched for the review, this should be noted but handsearching done by the authors to help build the specialized register of the CRG should not be listed because this is covered in the standardized description of the register. List people (e.g. trialists or topic specialists) and organizations who were contacted. List any other sources used, which may include, for example, reference lists, the World Wide Web or personal collections of articles.

The following optional headings may be used, either in place of 'Searching other resources' (in which case they would be level 3 headings) or as subheadings (level 4).

- Grey literature
- Handsearching
- Reference lists
- Correspondence

See also

- Other search resources are discussed in Chapter 6 (Section 6.2).
Searches: Searching other sources for health economics studies

Grey literature

- Sources of grey literature for studies of effects
- Online sources including coverage of economics grey literature
Grey literature

- Agency for Healthcare Research and Quality (AHRQ) http://www.ahrq.gov/
- Research Papers in Economics (RePEc) http://econpapers.repec.org/
- IDEAS http://ideas.repec.org/
- Quality Improvement Scotland http://www.nhshealthquality.org/nhsqis/CCC_FirstPage.jsp
- Euroscan http://www.euroscan.org.uk (new and emerging techs)

Searches: Searching other sources for health economics studies

Grey literature

- Sources of grey literature for studies of effects
- Online sources including significant coverage of economics grey literature
- Working papers and reports from specialist health economics research centres
  http://www.crd.york.ac.uk/crdweb/html/help.htm
Searches: Searching other sources for health economics studies

Handsearching?

- Handsearch specialist health economics journals
  (e.g. ‘Cost-Effectiveness and Resource Allocation’, ‘Health Economics’, ‘Journal of Health Economics’, ‘Pharmacoeconomics’, ‘Value in Health’)

- http://www.york.ac.uk/res/herc/resources/journals.htm
- http://www.crd.york.ac.uk/crdweb/html/help.htm
Searches: Searching other sources for health economics studies

Reference lists

- ...of identified studies of effects
- ...of identified health economic studies

In Revman:

Reference lists

Reference lists of identified studies will be searched to identify further potentially eligible RCTs and economic evaluations.
Searches: Searching other sources for health economics studies

Correspondence

- Contact CCEMG for help contacting health economist topic specialists? janice.legge@newcastle.ac.uk
- Final stage of search process
- No details of personal contacts required in protocol
Assessment of risk of bias in included studies

The method used to assess risk of bias (or methodological quality). Whether methods are applied independently by more than one author should be stated, along with how any disagreements are resolved. The tool(s) used should be described or referenced, with an indication of how the results are incorporated into the interpretation of the results.

See also

- The recommended tool for doing so is described in Chapter 8 (Section 8.5).

Measures of treatment effect

The effect measures of choice should be stated. For example, odds ratio (OR), risk ratio (RR) or risk difference (RD) for dichotomous data; difference in means (MD) or standardized difference in means (SMD) for continuous data. The following optional headings may be used, either in place of ‘Measures of treatment effect’ (in which case they would be level 3 headings) or as subheadings (level 4):

  - Dichotomous data
  - Continuous data
  - Time-to-event data

See also

- Types of data and effect measures are discussed in Chapter 9 (Section 9.2).

Unit of analysis issues

Special issues in the analysis of studies with non-standard designs, such as cross-over trials and cluster-randomized trials, should be described. Alternatively, optional (level 3) headings specific to the types of studies may be used, such as:
Assessment of risk-of-bias in health economics studies

Stage 1

Assess risk-of-bias in study generating the effects data used in each included full economic evaluation based on single, empirical primary studies of effects

- Use ‘The Cochrane Collaboration’s tool for assessing risk of bias’ (see Chapter 8 of Cochrane Handbook)

Stage 2

Assess overall methodological quality of each included full or partial economic evaluation
Assessment of risk-of-bias in health economics studies

Stage 2

Assess overall methodological quality of each included full or partial economic evaluation

- Economic evaluations conducted alongside single, empirical primary studies of effects
  - British Medical Journal Checklist (Drummond 1996)
  - CHEC Criteria list (Evers 2005)
- Model-based economic evaluations
  - Phillips checklist (Phillips 2004)
Assessment of risk-of-bias in health economics studies

Assessment of risk of bias in included studies

Risk-of-bias in single, empirical studies providing clinical data utilised in included economic evaluations will be assessed using the Cochrane Collaboration’s tool for assessing risk of bias (Higgins 2008)

Assessment of the overall methodological quality of included economic evaluations based on single, empirical studies will be informed by application of guidelines for authors and peer reviewers of economic submissions to the British Medical Journal (Drummond 1996) [and the CHEC Criteria list (Evers 2005)].

Assessment of the overall methodological quality of model-based economic evaluations will be informed by application of a recognised checklist for quality assessment in economic decision-analytic models (Phillips 2004).
Data extraction and management
[recommended, level 3 heading]

The method used to extract or obtain data from published reports or from the original researchers (for example, using a data collection form). Whether data are extracted independently by more than one author should be stated, along with how any disagreements are resolved. If relevant, methods for processing data in preparation for analysis should be described.

See also

- Data collection is discussed in Chapter 7, including which data to collect (Section 7.3), sources of data (Section 7.4), data collection forms (Section 7.5) and extracting data from reports (Section 7.6).

Assessment of risk of bias in included studies
[recommended, level 3 heading]

The method used to assess risk of bias (or methodological quality). Whether methods are applied independently by more than one author should be stated, along with how any disagreements are resolved. The tool(s) used should be described or referenced, with an indication of how the results are incorporated into the interpretation of the results.

See also

- The recommended tool for doing so is described in Chapter 8 (Section 8.5).

Measures of treatment effect
[recommended, level 3 heading]

The effect measures of choice should be stated. For example, odds ratio (OR), risk ratio (RR) or risk difference (RD) for dichotomous data; difference in means (MD) or standardized difference in means (SMD) for continuous data. The following optional headings may be used, either in place of 'Measures of treatment effect' (in which case they would be level 3 headings) or as subheadings (level 4):

- Dichotomous data
- Continuous data
Data extraction and management for health economics studies

- Precise data collection requirements for the economics components of reviews will need to be determined for each individual review.

- Depends on measures of resource use, costs and/or cost-effectiveness included in ‘Types of outcome measures’.

- Develop data collection form based on NHS EED template for structured abstracts
  [Link](http://www.york.ac.uk/inst/crd/pdf/nhseed-handb07.pdf)
Data extraction and management for health economics studies

Data extraction and management

The data extraction form for economic evaluations will be adapted from the format and guidelines used to produce structured abstracts of full economic evaluations for inclusion in the NHS Economic Evaluation Database (Craig 2007).

http://www.york.ac.uk/inst/crd/pdf/nhseed-handb07.pdf
Measures of treatment effect
[recommended, level 3 heading]

The effect measures of choice should be stated. For example, odds ratio (OR), risk ratio (RR) or risk difference (RD) for dichotomous data; difference in means (MD) or standardized difference in means (SMD) for continuous data. The following optional headings may be used, either in place of ‘Measures of treatment effect’ (in which case they would be level 3 headings) or as subheadings (level 4):

- Dichotomous data
- Continuous data
- Time-to-event data

See also
- Types of data and effect measures are discussed in Chapter 9 (Section 9.2).

Unit of analysis issues
[recommended, level 3 heading]

Special issues in the analysis of studies with non-standard designs, such as cross-over trials and cluster-randomized trials, should be described. Alternatively, optional (level 3) headings specific to the types of studies may be used, such as:

- Cluster-randomised trials
- Cross-over trials
- Studies with multiple treatment groups

See also
- Unit of analysis issues are discussed in Chapter 9 (Section 9.3).
- Some non-standard designs are discussed in detail in Chapter 16, including cluster-randomized trials (Section 16.3), cross-over trials (Section 16.4), and studies with multiple intervention groups (Section 16.5). Non-randomized studies are discussed in Chapter 13.
Dealing with missing data
[recommended, level 3 heading]

Strategies for dealing with missing data should be described. This will principally include missing participants due to drop-out (and whether an intention-to-treat analysis will be conducted), and missing statistics (such as standard deviations or correlation coefficients).

See also
- Issues relevant to missing data are discussed in Chapter 16 (Sections 16.1) and intention-to-treat issues in Chapter 16 (Section 16.2).

Assessment of heterogeneity
[recommended, level 3 heading]

Approaches to addressing clinical heterogeneity should be described, along with how the authors will determine whether a meta-analysis is considered appropriate. Methods for identifying statistical heterogeneity should be stated (e.g. visually, using I², using a chi-squared test).

See also
- Assessment of heterogeneity is discussed in Chapter 9 (Section 9.5).

Assessment of reporting biases
[recommended, level 3 heading]

This section should describe how publication bias and other reporting biases are addressed (for example, funnel plots, statistical tests, imputation). Authors should remember that asymmetric funnel plots are not necessarily caused by publication bias (and that publication bias does not necessarily cause asymmetry in a funnel plot).

See also
- Reporting biases are discussed in Chapter 10.

Data synthesis
See also
- Reporting biases are discussed in Chapter 10.

Data synthesis
[recommended, level 3 heading]
The choice of meta-analysis method should be stated, including whether a fixed-effect or a random-effects model is used. If meta-analyses are not undertaken, systematic approaches to synthesizing the findings of multiple studies should be described.
See also
- Meta-analysis and data synthesis are discussed in Chapter 9 (Section 9.4).

Subgroup analysis and investigation of heterogeneity
[recommended, level 3 heading]
All planned subgroup analyses should be listed (or independent variables for meta-regression). Any other methods for investigating heterogeneity of effects should be described.
See also
- Investigating heterogeneity is discussed in Chapter 9 (Section 9.6).

Sensitivity analysis
[recommended, level 3 heading]
This should describe analyses aimed at determining whether conclusions are robust to decisions made during the review process, such as inclusion/exclusion of particular studies from a meta-analysis, imputing missing data or choice of a method for analysis.
See also
- Sensitivity analysis is discussed in Chapter 9 (Section 9.7).
Subgroup analysis and investigation of heterogeneity
[recommended, level 3 heading]
All planned subgroup analyses should be listed (or independent variables for meta-regression). Any other methods for investigating heterogeneity of effects should be described.

See also
- Investigating heterogeneity is discussed in Chapter 9 (Section 9.6).

Sensitivity analysis
[recommended, level 3 heading]
This should describe analyses aimed at determining whether conclusions are robust to decisions made during the review process, such as inclusion/exclusion of particular studies from a meta-analysis, imputing missing data or choice of a method for analysis.

See also
- Sensitivity analysis is discussed in Chapter 9 (Section 9.7).

The following further, optional (level 3) headings for the Methods section may be helpful:

Economics issues

Methods for future updates
Authors seeking to cover economics aspects of interventions in a review will need to consider economics issues from the earliest stages of developing a protocol.

See also
- Economics issues are discussed in Chapter 15.
- Issues in updating reviews are discussed in Chapter 3.
Analysis and presentation of results of health economics studies

- Use of tables
- Use of a narrative summary
Analysis and presentation of results of health economics studies

Economics issues

Characteristics and results of included economic evaluations will be summarised using additional tables, supplemented by a narrative summary that will compare and evaluate methods used and principal results between studies.

Unit cost data will also be tabulated, when available.
Analysis and presentation of results of health economics studies

Economics issues

The currency and price year applicable to measures of costs in each original study will be reported alongside measures of costs, incremental costs and incremental cost-effectiveness, by study.

Where details of currency and price year are available in original studies, measures of costs, incremental costs and cost-effectiveness will be converted to [2011] International Dollars using implicit price deflators for GDP and GDP Purchasing Power Parities (http://eppi.ioe.ac.uk/costconversion/default.aspx ; Shemilt 2010).
Analysis and presentation of results of health economics studies

Economics issues

Details of the methodological characteristics of individual included health economics studies will be summarised in ‘Characteristics of included studies’ tables.

All elements of the economics component of this review will be conducted according to current guidance on the use of economics methods in the preparation and maintenance of Cochrane reviews (Shemilt 2008).
EVIDENCE-BASED DECISIONS AND ECONOMICS

HEALTH CARE, SOCIAL WELFARE, EDUCATION AND CRIMINAL JUSTICE

Edited by
Ian Shemilt
Miranda Mugford
Luke Vale
Kevin Marsh
Cam Donaldson

WILEY-BLACKWELL BMJ BOOKS