Formulating recommendations in the absence of evidence

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Evidence-based guidelines

- Development process is to translate research findings into trusted recommendations that guide clinical decision making
- Often involve complex balancing of trade offs between benefits and harms of any given intervention – even where there is 'good' evidence
- Overall objective is to minimise 'bias' and allow transparency
- But it is an inherently subjective process
- Proliferation of formal systems to grade the evidence and formulate recommendations since 2000

Background

The National Health and Medical Research Council (NHMRC):

- Health and medical research funder
- Ethics advice for health care and research
- Provision of health advice
  - Approves guidelines
  - Sets 'Standard' for guidelines
  - Develops guidelines

To improve the quality of guidelines

- Access to Australian guidelines
  - National portal and guidelines register

Background

- 2011 NHMRC standard for clinical practice guidelines

To meet the NHMRC standard, CPG must:

1. Provide guidance on a clearly defined clinical problem based on an identified need
2. Be developed by a multidisciplinary group that includes relevant experts, end users and consumers affected by the guideline
3. Include a transparent process for declaration and management of potential conflict of interest by each member of the guideline development group
4. Be based on the systematic identification and synthesis of the best available scientific evidence
5. Make clear and actionable recommendations in plain English for health professionals practising in an Australian healthcare setting
6. Be easy to navigate for end-users
7. Undergo a process of public consultation and independent external clinical expert review
8. Incorporate a plan for dissemination including issues for consideration in implementation

For more information, go to: www.nhmrc.gov.au

Outline of presentation

How are recommendations formulated in the 'absence' of evidence?

- **Reviewed recommended methods in 15 current international Handbooks (exclude rating of evidence)**
- **Audited 10 clinical practice guidelines recently developed or approved by NHMRC in Australia**
- **Identified gaps and issues with current methods**
- **Developed a proposal for using a consistent and transparent approach**

International guidance

Review of 15 handbooks:

National (n=13)		International (n=2)
US	**Institute of Medicine** **Institute for Clinical Systems Improvement** **SORT** **USPSTF** **ACCP** **AAP** **ACCF/AHA**	**GRADE** **WHO**
UK	**NICE** **CEBM - Oxford**	
Scotland	**SIGN**	
New Zealand	**NZGG**	
Canada	**CMA**	
Australia	**NHMRC**	

Results of review

Handbook	Grading scheme	No evidence	Comment
GRADE	Strong / weak	No specific guidance (balance)	Consider trade-offs
WHO	Use GRADE	No specific guidance (balance)	Consider trade-offs
NICE	Use of must, should, could	Use 'consensus' to identify best practice when no evidence found	Formal or informal
SIGN	Use ABCD and GPP	Use GPP – mark with green check	Considered judgement
CEBM	Use ABCD	D = expert opinion, with no SR or evidence from bench research	Use D for 'troubling inconsistent findings'
NHMRC	Use ABCD, CBR, PP	CBR = low / no evidence from SR; PP = no SR, but deemed useful	PP used to support recommendations
NZGG	Use ABC, I	C=expert opinion (published); I=evidence to make rec insufficient	Consensus can be formal or informal
CMA	Use GRADE, SIGN or SORT	No specific guidance	

Results of review (cont.)

US	Grading scheme	No evidence	Comment
IOM	Multiple outlined	Not specified	Current schemes not adequate
ICSI	Grade I, II, III	III=limited evidence	Not assignable = no evidence
SORT	Use ABC	B=inconsistent evidence; C=consensus, usual practice, opinion or other evidence	Other evidence = bench, low level, prognostic etc. Consensus guidelines = no SR conducted
USPSTF	Use ABCD and I	A&B = for an intervention; C&D = against an intervention; I= insufficient evidence	Reflect balance of benefit and harm
ACCP	Use 1ABC; 2ABC	1C&2C=low or very low evidence	Reflect balance of benefit and harm
AAP	Use strong rec / recommendation / option	No specific guidance	Decision is based on aggregate evidence and balance of benefit / harm
ACCF/AHA	Use Class I, II, III	Class II a or b = conflicting evidence or opinion	Class III = evidence against intervention

NHMRC "Levels and Grades"

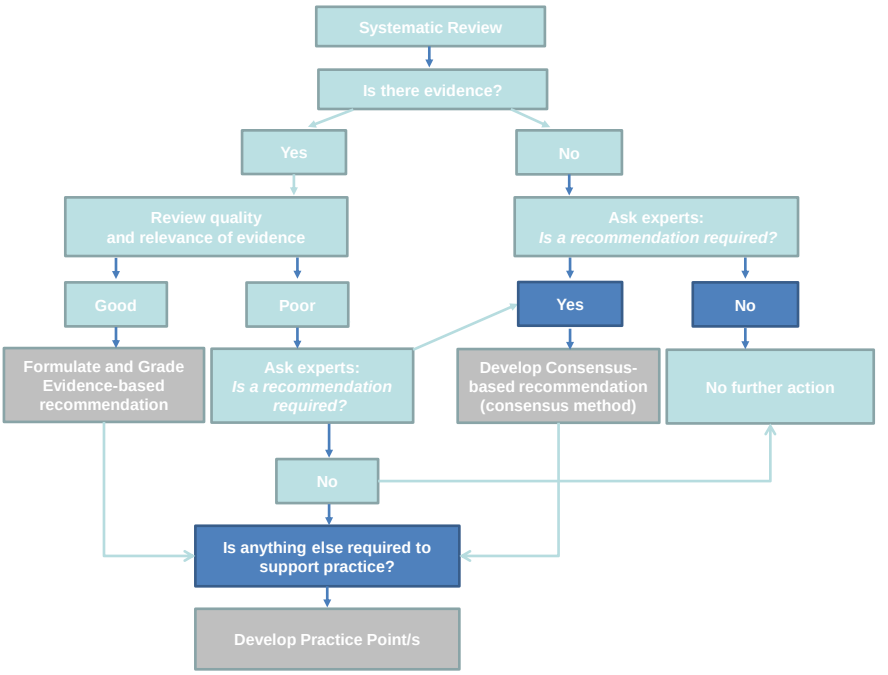
- **NHMRC levels of evidence and grades for recommendations for developers of clinical practice guidelines (www.nhmrc.gov.au/guidelines/resources-guideline-developers)**
- **Levels of evidence: hierarchy based on study design (not quality) and type of research question (intervention, diagnosis, prognosis, aetiology and screening)**
- **Grades based on assessment of 5 components of body of evidence: evidence base, consistency, clinical impact, generalisability, applicability**
- **Overall grade determined:**
  - **A: body of evidence can be trusted to guide practice**
  - **B: body of evidence can be trusted to guide practice in most situations**
  - **C: body of evidence provides some support for recommendation(s) but care should be taken in its application**
  - **D: body of evidence is weak and recommendation must be applied with caution**

Results of Audit of Australian guidelines

Guideline	Method used
Prevention of VTE in hospitals (2009)	When no high level evidence (I or II) is identified – used 'good practice points' (GPP), reached by consensus.
Glaucoma management (2010)	Unexplained, but used GPP for ungraded recommendations.
Stroke management (2010)	When no robust (I to IV) evidence is identified – used GPP, reached by consensus.
Use of antenatal magnesium sulphate (2010)	No recommendations when evidence is absent. However, GPP (outside scope) supplement graded recommendations
Depression in young people (2011)	When no high level evidence (I or II) is identified – used GPP, reached by consensus
Depression in the perinatal period (2011)	When no high level evidence (I or II) is identified – used GPP, reached by consensus
Foot problems in diabetes (2011)	When no/low level evidence or outside scope – used 'expert opinion'
Venous leg ulcers (2011)	When no/low evidence used 'consensus recommendations'; when outside scope of SR used 'practice points'.
Management of problem gambling (2011)	When no/low evidence used 'consensus recommendations'; when outside scope of SR used 'practice points'.
Management of polycystic ovary syndrome (2011)	When no/low evidence used 'consensus recommendations'; when outside scope of SR used 'practice points'.

Issues / gaps identified

- Hierarchies of grading often not intuitive
- Lack of agreed definitions of ‘low level’ or ‘no’ evidence
- Uncertainty regarding whether ‘no’ evidence means lack of evidence found, or not searched, or research not feasible
- Multiple schemes are used, even within one country
- Inconsistent use of an identified scheme
- Lack of guidance on decision making process of GDGs to make a recommendation when there is low level or no evidence
- Lack of agreed process for reaching consensus



Proposal for using a consistent and transparent approach

- Develop international consensus on what constitutes 'sufficient' evidence for a graded recommendation
- Develop international consensus on the use of three categories of recommendations:
  - Evidence based (EBR) – where systematic review identifies sufficient evidence for grading of recommendation
  - Consensus based (CBR) – where systematic review identifies no, low level or inconsistent evidence
  - Practice point (PP) – where systematic review was not conducted, but clinical guidance is deemed important to supplement a EBR or CBR for implementation
- Pilot a process for decision making in formulating CBR and practice points

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