TRANSLATING RESEARCH FOR POLICY IMPACT AND PRACTICE

DEVELOPING CLINICAL GUIDELINES:AN EVIDENCE BASED APPROACH

Peter Tugwell

[with help from Luis Gabriel Cuervo, Jeremy Grimshaw, Gordon Guyatt, Annette O'Connor, Andy Oxman, Jordi Pardo, Tamara Rader, Nancy Santesso, Holger Schunemann, Dawn Stacey, Vivian Welch and my Ottawa group.]

Clinical practice guidelines

'Systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances'.

Institute of Medicine (1992). *Guidelines for clinical practice: from development to use.*

International CPG Activities

Many countries have established clinical practice guideline programs including:

- US and Canadian Preventive Task Force
- Canadian provincial guidelines programs
- Dutch College of General Practitioners
- National Institute for Clinical Effectiveness
- Scottish Intercollegiate Guidelines Network
- New Zealand Guidelines Group
- National Health and Medical Research Council Australia
- US Agency for Health Care Policy and Research

? Caribbean Countries

In
Get Connected

Guidelines for Guidelines

Jamaica
http://www.moh.gov.jm/legislation/guidelinesforms-a-lists
http://www.moh.gov.jm/general/publication

Tools   Help

age ▾   Safety ▾   Tools ▾   ❓▾   🔳 🔳 ⓢ ⓑ

Ministry of Health

Government of Jamaica 🇯🇲

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◀   June 2013   ▶

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"*Modernized, appropriately equipped division efficiently contributing to the provision of quality health care service delivery.*"

STANDARDS & REGULATIONS

1 2 ▲ 3

Registration/Assessment Guidelines, Forms & Lists   📄 🖨 ✉

Written by Administrator

Friday, 15 January 2010 15:38

Registration of Drugs and other Items

Registration of drugs and other products/items are major regulatory functions executed through the Pharmaceutical & Regulatory Affairs Department. It involves in-depth scientific evaluation of the technical documentation submitted in support of registration resulting in licensing of a drug or other related product. It is one of the primary mechanisms through which the quality, safety and efficacy of drugs, and other products mentioned in the Food and Drugs Act and Regulations are ensured.

'Drug' refers to any substance that conforms to the definition prescribed by the Act. Such substances generally require registration and include drugs, herbal preparations and some vitamins and supplements. Registration may also be required for any cosmetic, food or device making therapeutic claims.

In instances where products are deemed safe enough to be placed on the market without formal

Question for you -the audience! Please discuss with your neighbour Identify 1 of each of the following:

Think of

 A] *Patients*: one benefit and one harm of guidelines to Patients

B]*Clinicians* : one benefit and one harm of guidelines to Clinicians.

Potential benefits and harms for <u>patients</u> ?

Potential benefits <u>for patients</u>

- improve health outcomes

- improve consistency of care

- summarise benefits and harms of treatment options (consumer guidelines)

- empower patients to make informed treatment choices

- help patients to influence policy

Woolf et al (1999). *British Medical Journal.*

Potential harms for patients

- flawed guidelines may result in sub optimal, ineffective or harmful practices

- inflexible guidelines may result in inappropriate care for individual patients

- consumer versions of guidelines may be inaccurate

- distort policy decisions

Woolf et al (1999). *British Medical Journal.*

Potential benefits and harms for <u>healthcare professionals?</u>

- .

Potential benefits for <u>healthcare professionals</u>

- summarise and synthesise evidence

- improve quality of clinical decisions

- support quality improvement activities

- identify future research needs

Woolf et al (1999). *British Medical Journal.*

Guidelines :Potential <u>harms</u> for healthcare professionals

- provide inaccurate summaries and syntheses of evidence
- reduce professionalism (cookbook medicine)
- medico-legal concerns
- economic impact
- discourage research

Woolf et al (1999). *British Medical Journal.*

Who here from the Caribbean has experience with guideline development ?

- Please tell us about :
- Composition of guideline development group
- Methods of identifying and synthesising evidence
- Methods of developing guidelines

2 of my recent guideline experiences using Cochrane Systematic Reviews

1. Primary Care for Immigrants and Refugees to Canada

2. Osteoarthritis management in Primary Care

After reviewing all the Guideline systems where we could use Cochrane SRs, we decided to use the 'GRADE' approach

GRADE (*G*rades of Recommendation, Assessment, Development and Evaluation)

CANADIAN GUIDELINES FOR IMMIGRANT HEALTH

Evaluation of evidence-based literature and formulation of recommendations for the clinical preventive guidelines for immigrants and refugees in Canada

Peter Tugwell MD MSc, Kevin Pottie MD MClSc, Vivian Welch MSc PhD, Erin Ueffing BHSc MHSc, Andrea Chambers MSc, John Feightner MD MSc; for the Canadian Collaboration for Immigrant and Refugee Health (CCIRH)

ABSTRACT

Background: This article describes the evidence review and guideline development method developed for the Clinical Preventive Guidelines for Immigrants and Refugees in Canada by the Canadian Collaboration for Immigrant and Refugee Health Guideline Committee.

Methods: The Appraisal of Guidelines for Research and Evaluation (AGREE) best-practice framework was combined with the recently developed Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to produce evidence-based clinical guidelines for immigrants and refugees in Canada.

Results: A systematic approach was designed to produce the evidence reviews and apply the GRADE approach, including building on evidence from previous systematic reviews, searching for and comparing evidence between general and specific immigrant populations, and applying the GRADE criteria for making recommendations. This method was used for priority health conditions that had been selected by practitioners caring for immigrants and refugees in Canada.

Interpretation: This article outlines the 14-step method that was defined to standardize the guideline development process for each priority health condition.

Key points

- We combined the AGREE best-practice framework with the recently developed GRADE approach to develop evidence-based clinical preventive guidelines for immigrants and refugees to Canada.
- This methods paper documents the systematic approach used to produce the evidence reviews and apply the GRADE approach.
- The 14-step approach included building on evidence from previous systematic reviews, searching for and comparing evidence between general and specific immigrant populations, and applying the GRADE criteria for making recommendations.
- For each recommendation, the basis (balance of benefit and harms, quality of evidence, and values) is stated explicitly to ensure transparency.

P rimary care practitioners who care for recently arrived immigrants and refugees have raised concerns over the lack of evidence-based guidelines for clinical prevention, noting that it is not always clear whether current recommendations made for the general population in Canada can be generalized to this population. In 2006, the Canadian Collaboration for Immigrant and Refugee Health (CCIRH) Guideline Committee was formed to address this issue by first identifying the top-priority health conditions for this population. The group of 20 health conditions identified was very diverse ranging from infectious disease to chronic conditions including depression. The challenge was creating a rigorous interdisciplinary process and then to generate pragmatic recommendations. This document outlines the systematic approach designed to produce the evidence reviews.

A variety of methods is used for developing clinical guidelines and practice recommendations.[1] We used the recently developed approach of moving away from recommendations classified by letters and numbers to the simplified classification system recommended by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group[2] and applied this to clinical preventive actions. Our guideline development process followed the Appraisal of Guidelines Research & Evaluation (AGREE) instrument (www.agreetrust.org), which is recognized internationally as providing best-practice criteria for evidence-based guideline development.

We developed the recommendations on the basis of a pre-specified process overseen by the CCIRH Guideline Committee. Defining a methods process ensured that each guideline was developed in a systematic, reproducible manner and was based on the best evidence available. This process was based

CMAJ Evidence Based Clinical Guidelines for Immigrants and Refugees

Infectious Diseases

- MMR/DPTP-HIB
- Varicella (Chicken Pox)
- Hepatitis B
- Tuberculosis
- HIV/ AIDS*
- Hepatitis C
- Intestinal Parasites
- Malaria

NCD

- Diabetes
- Dental disease
- Contraception
- Cervical Cervix/HPV
- Iron Deficiency Anemia
- Mental Health and Maltreatment
  - Depression
  - Post Traumatic Stress Disorder
  - Child Maltreatment
  - Intimate Partner Violence
- Pregnancy Care
- Vision Disorders

American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee

MARC C. HOCHBERG,ROY D. ALTMAN,KARINE TOUPIN APRIL,MARIA BENKHALTI,GORDON GUYATT,JESSIE MCGOWAN,TANVEER TOWHEED,VIVIAN WELCH,
GEORGE WELLS,AND PETER TUGWELL

ACR Proposal

- Pharmacologic and non-pharmacologic interventions for OA

Knee and Hip OA Treatments

NON-PHARMACOLOGIC

- Acupuncture
- Exercise
- Foot insole
- Knee brace
- Manual physio
- TENS
- Weight loss

PHARMACOLOGIC

- Acetaminophen
- Chondroitin Sulfate
- Cortico-steroid injection
- Glucosamine Sulfate
- Opioids
- Tramadol
- Oral NSAIDs
- Topical capsaicin
- Topical NSAIDs
- Hyaluronates injection

ACR Proposal

- Pharmacologic and non-pharmacologic interventions [incl weight loss, exercise, knee brace,foot insole]

- **Use of the 'GRADE' Method**
  - **to create Summary of Findings tables and to make recommendations**

Knee and Hip OA Treatments

NON-PHARMACOLOGIC

- Acupuncture
- Exercise
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- Knee brace
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- TENS
- Weight loss

PHARMACOLOGIC

- Acetaminophen
- Chondroitin Sulfate
- Cortico-steroid injection
- Glucosamine Sulfate
- Opioids
- Tramadol
- Oral NSAIDs
- Topical capsaicin
- **Topical NSAIDs**
- Hyaluronates injection

SUMMARY OF FINDINGS TABLE
SOF TABLE

E.g. Topical NSAIDs vs. placebo

Patient or population: patients with knee OA
Intervention: Topical NSAIDs
Comparison: placebo

Outcomes	Illustrative comparative risks		Absolute difference	Relative effect	No of Participants (studies)	Quality of the evidence (GRADE)	NNT
	Control group rate	Intervention rate					
	Placebo	**Topical NSAIDs**					
Benefits							
Pain WOMAC. Scale from: 0 to 100. (follow-up: 4 weeks)	35%	54% (47% to 60%)	19%	1.52	1378 (9)[2]	⊕⊕⊕⊕ **high**	5 (4 to 7)
Harms							
Dry skin number of patients with event (follow-up: 4 weeks)	1%	36% (5% to 258%)	35%	RR 30	168 (1)	⊕⊕⊕⊕ **high**	3 (0 to 26) (reflects benefit in placebo)
Rash number of patients with event (follow-up: 4 weeks)	4%	13% (4% to 46%)	9%	RR 3.67	168 (1)	⊕⊕⊕⊕ **high**	10 (2 to 463) (reflects benefit in placebo)

[1] The study reported a weighted mean difference of change over placebo. We calculated the SMD using Excel and RevMan 5.
[2] There is also another review done in 2008 by Ozguney. However, they did not pool results. The chosen meta-analysis (Biordal, 2006) includes more RCTs (from 1993 to 2004 including the studies by Bookman, 2004 and Roth, 2004 which were the newest studies in the Ozguney review).

ACR Proposal

- Pharmacologic and non-pharmacologic interventions [incl weight loss, exercise, knee brace,foot insole]

- Use of the 'GRADE' Method
  - to create Summary of Findings tables and to make recommendations

- **ACR Panel Experience**
  - **Apply evidence base to patient Scenarios using Decision Aids**

Case study: Paul, age 55, has Osteoarthritis of the knees.

- Shows good knowledge about the options.

- Is motivated to make a change.

- Had indicated pain relief is his objective.

- Decides to discuss NSAIDs with his doctor.

Stepped care Decision Aid

Based on Cochrane Reviews and GRADE –based Recommendations

What are my options for managing hip or knee osteoarthritis?
A stepped decision aid to discuss options with your practitioner

What is Osteoarthritis?

It breaks down the cartilage in a joint. This causes joint pain, stiffness and swelling. It limits people from doing what they want and need to do. Usually the symptoms come on slowly, but get worse over time. There is no cure but symptoms can be controlled.

How is osteoarthritis affecting you? (Check ☑ the answer that shows how you felt IN THE PAST WEEK)

In the past week…..	Not at all/ No Pain	Mildly	Moderately	Severely	Extremely
How intense has your joint pain been?	☐	☐	☐	☐	☐
How much has your joint pain affected your sleep?	☐	☐	☐	☐	☐
How much has your joint pain affected your overall quality of life?	☐	☐	☐	☐	☐
How much has your joint pain made it DIFFICULT to do your daily activities such as errands, chores, hobbies, socializing, travel, and being physically active.	☐	☐	☐	☐	☐

What are you doing now to manage your osteoarthritis? (Check ☑ those you use now)

The treatments are listed in levels ranging from simpler (0) to stronger (5). When simpler treatments no longer work, stronger ones with possible side effects are tried. Sometimes surgery is needed.

Level 0	☐ Nothing yet ☐ Chondroitin	☐ Hot pepper cream such as Capsaicin	☐ Glucosamine	☐ TENS- Electrical currents applied to skin
Level 1	☐ Exercise	☐ Healthy weight	☐ Acupuncture	☐ Acetaminophen such as Tylenol
Level 2	☐ Non-steroidal creams (NSAID) such as Pennsaid® lotion	☐ Insoles	☐ Joint injection with steroid or viscosupplement	
Level 3	☐ NSAID pills such as Advil			
Level 4	☐ Opioid (narcotic) painkillers such as oxycontin, oxycodone, morphine, demerol			
Level 5	☐ See a surgeon about joint replacement			

List other things you have tried:_____

How often have you followed your current plan during the past week? (Circle the best answer)

|						
I followed my exercise program	0 days	1-2 days	3-4 days	5-6 days	7 days	Does not apply
I did things to control my weight	0 days	1-2 days	3-4 days	5-6 days	7 days	Does not apply
I took my daily medicines	0 days	1-2 days	3-4 days	5-6 days	7 days	Does not apply

What are your options?
- **Make no change.** You continue as you are doing now.
- **Make a change.** You follow your plan more regularly or you try another option.

**Working through the 4 steps of this decision aid may help you decide**

Step 1: What are the benefits and harms of each treatment option?

Blocks of 100 faces show a "best estimate" of what happens to 100 people who choose different options for one to 6 months. Each face (☺) stands for one person. The shaded areas show the number of people who improve (have less pain) or are harmed. There is no way of knowing in advance if you will be the one who improves or is harmed. About 30 out of 100 people will improve on their own even if they take an inactive or fake treatment. This is called the "placebo effect".

Level	Options	Benefits	Serious Harms and Side Effects
Level 0 *** ** **** These options have the same benefits and harms as a placebo (fake treatment)	• Chondroitin • Hot pepper cream (capsaicin) • Glucosamine • Electrical treatment applied to the skin (TENS)	In 100 people: 30 improve on their own 0 improve due to treatment 70 don't improve	The chance of serious harm is the same for treatment or placebo (fake treatment). Capsaicin can cause discomfort when applied to the skin.
Level 1 *** ** **** These options work a bit better than a placebo and avoid serious harm	• Exercise • Healthy weight • Acupuncture • Acetaminophen (such as Tylenol)	In 100 people: 30 improve on their own 6 improve due to treatment 64 don't improve	The chance of serious harm is the same for treatment or placebo (fake treatment). Exercise can cause people to stop due to pain. Acupuncture can cause bruising.
Level 2 *** ** **** For patients who fall level 1, these options work better than a placebo and avoid serious harm	• NSAID creams (such as Pennsaid lotion) • Insoles • Joint injections with steroid or viscosupplement	In 100 people: 30 improve on their own 21 improve due to treatment 49 don't improve	The chance of serious harm is the same for treatment or placebo (fake treatment). NSAID creams can cause dry skin or rash. A common side effect from joint injection (viscosupplement) is a skin reaction at the joint site.
Level 3 **** These options work better than a placebo. More people are harmed by the treatment than in level 2.	• NSAID pills (such as Advil)	In 100 people: 30 improve on their own 21 improve due to treatment 49 don't improve	NSAID pills can cause nausea, stomach bleeding or ulcers, or heart attack. In 100 people under 60 years with no history of a heart disease: 99 are not harmed 1 gets a heart attack due to NSAID pills Number of heart attacks increase in older people or those with previous heart attacks
Level 4 **** These options work better than a placebo. More people are harmed by the treatment than level 3.	• Opioid (narcotic) painkillers such as opioids, oxycontin, oxycodone, morphine, demerol	In 100 people: 30 improve on their own 21 improve due to treatment 49 don't improve	Opioid painkillers can cause nausea, constipation, or withdrawal symptoms. 23 more people get withdrawal symptoms when their Opioid painkillers are reduced 77 people avoid withdrawal symptoms
Level 5	Surgery	See a surgeon about joint replacement surgery if other options have not worked.	

NOTE: The estimates of benefits and harms of most options are based on sound research. Level 2 and 3 options and most of Level 1 options are rated '4 plus (++++). This means that further research is very unlikely to change the estimates. Some options in Level 1 (healthy weight), Level 2 (insoles) and Level 0 (Chondroitin, Capsaicin) are rated '3 plus (+++). This means their estimates may change if further research is done. TENS in Level 0 is rated 'two plus (++), which means that estimates are very likely to change with further research.

Visual representation of what the research shows, includes the assessment of methodological quality of the evidence using GRADE

Step 1: What are the benefits and harms of each option?

Level 3 ++++ These options work better than a placebo. More people are harmed by the treatment than in level 2.	• NSAID pills (such as Advil)	In 100 people: **30** improve on their own **21** improve due to treatment **49** don't improve	NSAID pills can cause nausea, stomach bleeding or ulcers, or heart attack. In 100 people under 60 years with no history of a heart disease: **99** are not harmed **1** gets a heart attack due to NSAID pills Number of heart attacks increase in older people or those with previous heart attacks
Level 4 ++++ These options work better than a placebo. More people are harmed by the treatment than level 3.	• Opioid (narcotic) painkillers such as opioids, oxycontin, oxycodone, morphine, demerol	In 100 people: **30** improve on their own **21** improve due to treatment **49** don't improve	Opioid painkillers can cause nausea, constipation, or withdrawal symptoms. **23** more people get withdrawal symptoms when their Opioid painkillers are reduced **77** people avoid withdrawal symptoms
Level 5	Surgery	See a surgeon about joint replacement surgery if other options have not worked.	

100 faces illustrate the benefits of the intervention

Step 2: Which reasons to choose each option matter most to you?

- Common reasons to choose each option are listed below
- Show how much each reason matters to you by circling a number from 0 to 5
- '0' means it is **not** important to you. '5' means it is **very** important to you.
- If a reason is important to you, the options to consider are shown in the column on the right

How important is it to you …	Not Important					Very Important	Options to consider if this reason is important to you
To get better pain relief	0	1	2	3	4	5	Try other options in your current Level or move to the next Level.
To avoid taking pills?	0	1	2	3	4	5	Try options in Level 1 or 2.
To avoid needles?	0	1	2	3	4	5	Avoid acupuncture in Level 1 and joint injections in Level 2.
To avoid bleeding ulcers or heart attack?	0	1	2	3	4	5	Avoid NSAID pills in level 3.
To avoid withdrawal symptoms?	0	1	2	3	4	5	Avoid OPIOID painkillers in Level 4.
List other reasons _____	0	1	2	3	4	5	
_____	0	1	2	3	4	5	

Discussion of options with patients based on what is important to them

Step 3: What else do you need to prepare for decision making?

Find out how well this decision aid helped you to learn the key facts.
Check ☑ the best answer.

1. Which option has the highest chance of improving pain?	☐ Steroid joint injection	☐ Acetaminophen	☐ Chondroitin	☐ Don't Know
2. Which option has the highest chance of bleeding stomach ulcers or heart attack?	☐ Glucosamine	☐ NSAID pills	☐ Opioid painkillers	☐ Don't Know
3. Which option has the highest chance of withdrawal symptoms?	☐ Glucosamine	☐ NSAID pills	☐ Opioid painkillers	☐ Don't Know
4. If 100 people take NSAID pills for 1 to 6 months, how many <u>more</u> people with no history of heart disease will have a heart attack from taking them?	☐ 0	☐ 1	☐ 2-5	☐ Don't Know
5. Over time, the pain from osteoarthritis usually…	☐ Gets worse	☐ Stays the same	☐ Gets better	☐ Don't Know

Check your answers against those at the bottom of the page

Find out how comfortable you feel about deciding.*
Check ☑ the best answer

Do you know enough on the benefits and harms of each option to make a choice?	☐ Yes	☐ No
Are you clear about which benefits and harms matter most to you?	☐ Yes	☐ No
Do you have enough support and advice from others to make a choice?	☐ Yes	☐ No
Do you feel sure about the best choice for you?	☐ Yes	☐ No

If you answered 'No' to any of these, discuss with your practitioner.

Discuss of patient knowledge of the benefits and harms

Readiness to make a decision

Make a list of your next steps.

<div style="float:right">Next Steps</div>

_____

_____

_____

_____

_____

_____

Physician receives a one page clinical summary of the patients answers

Patient's Self Reported Outcomes during the week of _____

Average Pain Severity

Joint pain during activities

Functional Difficulty
due to joint pain

Patient's Perceptions of Current Plan

Level 0	☐ I have not tried anything yet	☐ Chondroitin	☐ TENS	☐ Capsaicin
Level 1	☐ Exercise program	☐ Maintain healthy weight	☐ Glucosamine	☐ Insoles
	☐ Acetaminophen	☐ Acupuncture		
Level 2	☐ Topical NSAIDs	☐ Joint injection: Corticosteroid	☐ Joint injection: Viscosupplementation	
Level 3	☐ NSAID pills	☐ Opioid painkillers		
Level 4	☐ See a surgeon about joint replacement			

Other things tried:

Adherence to daily regime (#days/week)	0	1-2	3-4	5-6	7	No plan

Exercise
Control weight
Take daily medicines

Patient's Preference & Decisional Needs

Certainty	Prefers to: **Change management plan: NSAIDS**
	✗ **Does not feel:** sure about best choice

Knowledge	**75%** correct answers	✔ **Knows:** Joint injection more effective than: chondroitin, acetaminophen
		✔ **Knows:** NSAIDs has highest chance: bleeding ulcer, heart attack
		✔ **Knows:** Opioids have highest chance: withdrawal symptoms
	✔ **Does feel:** knows enough	✗ **Does not know:** osteo pain gets worse over time

Values	✔ **Does feel:** clear re values		Not Important				Very Important
		Reasons to choose each option	1	2	3	4	5
		Get better pain relief					
		Avoid prescription pills					
		Avoid needles					
		Avoid serious harms such as bleeding ulcers and heart attack					
		Avoid withdrawal symptoms					
		Other:					

Support	✗ **Does not feel:** has enough support/advice						
Barriers to change			Not 1	2	3	4	Very 5
	Motivated to do this						
	Confident that can do this						
	Barriers to doing this	*None*					
	Facilitators to doing this	*Very organized taking pills*					

Questions	***What do you think about NSAIDs.?***

LETS LOOK AT 'GRADE'

Grades of **R**ecommendation, **A**ssessment, **D**evelopment and **E**valuation

Key features of GRADE
(*G*rades of Recommendation, Assessment, Development and Evaluation)

- Background on guidelines and GRADE
- Quality of evidence
- Going from evidence to recommendations

Key features of GRADE
(*G*rades of Recommendation, Assessment, Development and Evaluation)

- **Background on guidelines and GRADE**
- Quality of evidence
- Going from evidence to recommendations

Appraising evidence and developing recommendations

- To guide healthcare decision-making, a guideline (panel) should weight the desirable and undesirable consequences related to that decision for the relevant setting on the basis of the *best available* evidence and integrate values and preferences.

- Evidence = observations in the world

- Best available = implies hierarchy of evidence

Background

- WHO develops advice (recommendations) "all the time"
- Format differs, methods differ, much criticism
- May 2005 World Health Assembly resolution
    - WHO Director-General "to undertake an assessment of WHO's internal resources, expertise and activities in the area of health research, with a view to developing a position paper on WHO's role and responsibilities in the area of health research, and to report through the Executive Board to the next World Health Assembly."

WHO guidelines were considered

✓ not transparent

✓ not evidence based

Oxman et al, Lancet 2007;369:1883-9

In other words

- ✓ ↓ Systematic reviews
- ✓ ↓ Transparency about judgements
- ✓ ↑ Expert opinion confused with evidence
- ✓ ↑ Conflict of interest
- ✓ ↓ Adaptation of global guidelines to end users' needs
- ✓ ↔ Tension between time taken and when advice needed
- ✓ ↓ Resources

Which approach?

Recommendation for use of oral anticoagulation in patients with atrial fibrillation and rheumatic mitral valve disease

Evidence	Recommendation	Organization
• B	Class I	➢ AHA
• A	1	➢ ACCP
• IV	C	➢ SIGN

GRADE
Working Group
Grades of **R**ecommendation
Assessment, **D**evelopment and
Evaluation

- Aim: to develop (use and test) a common, transparent and sensible system for grading the quality of evidence and the strength of recommendations (over 100 systems)
- International group of guideline developers, epidemiologists, clinical researchers, public health officers, methodologists & clinicians from around the world (>300 contributors) – since 2000

GRADE Uptake

- World Health Organization
- Allergic Rhinitis in Asthma Guidelines (ARIA)
- American Thoracic Society
- American College of Physicians
- European Respiratory Society
- European Society of Thoracic Surgeons
- British Medical Journal
- Infectious Disease Society of America
- American College of Chest Physicians
- UpToDate®
- National Institutes of Health and Clinical Excellence (NICE)
- Scottish Intercollegiate Guideline Network (SIGN)
- Cochrane Collaboration
- Infectious Disease Society of America
- Clinical Evidence
- Agency for Health Care Research and Quality (AHRQ)
- Partner of GIN
- Over 60 major organizations

Getting from evidence to recommendations - GRADE

Recommendations are judgments:
- – Quality of evidence
- – Trade off between benefits and harms
- – Values and preferences
- – Resource use

But judgments need to be based on the best available evidence and transparent

GRADE Quality of Evidence

In the context of making recommendations:

- The quality of evidence reflects the extent of our confidence that the estimates of an effect are adequate to support a particular decision or recommendation.

GRADE: quality of (a body of) evidence & recommendations

Clear separation, but *judgments* required:

1) 4 categories of quality of evidence:
   – methodological quality of evidence

   – likelihood of **bias** related to recommendation

   – by outcome and across outcomes

2) Recommendation: 2 grades – weak (aka conditional) or strong (for or against an action)?
   – balance of benefits and downsides
   – values and preferences
   – resource use
   – quality of evidence

GRADE evidence profile

Author(s): YFY (update from CDSR version)
Date: 2009-10-09
Question: Should Antibiotics vs. no antibiotics be used for children with otitis media?
Settings: outpatient
Bibliography: Sanders S, Glasziou PP, DelMar C, Rovers M. Antibiotics for acute otitis media in children. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No.: CD000219. DOI: 10.1002/14651858.CD000219.pub2. (2008 version)

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotics	no antibiotics	Relative (95% CI)	Absolute		
Pain at 24 hours (follow-up 24 hours)												
5	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	223/624 (35.7%)	36.7%[1]	RR 0.9 (0.78 to 1.04)	37 fewer per 1000 (from 81 fewer to 15 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain at 2 to 7 days (follow-up 2-7 days)												
10	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	228/1425 (16%)	26%[1]	RR 0.72 (0.62 to 0.83)	73 fewer per 1000 (from 44 fewer to 99 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Hearing - 1 month (follow-up 1 months; as measured by tympanometry)												
4	randomized trials	no serious limitations	no serious inconsistency	serious[2]	serious[3]	none	153/467 (32.8%)	168/460 (36.5%)	RR 0.89 (0.75 to 1.07)	40 fewer per 1000 (from 91 fewer to 26 more)	⊕⊕OO LOW	CRITICAL
Hearing - 3 months (follow-up 3 months; as measured by tympanometry)												
3	randomized trials	no serious limitations	serious	serious[2]	no serious imprecision	none	96/410 (23.4%)	96/398 (24.1%)	RR 0.97 (0.76 to 1.24)	7 fewer per 1000 (from 58 fewer to 58 more)	⊕⊕OO LOW	CRITICAL
Vomiting, diarrhea, or rash												
5	randomized trials	no serious limitations	very serious[4]	no serious indirectness	no serious imprecision	none	110/690 (15.9%)	83/711 (11.7%)	RR 1.38 (1.09 to 1.76)	44 more per 1000 (from 11 more to 89 more)	⊕⊕OO LOW	CRITICAL

[1] This is the median event rate.
[2] Tympanometry surrogate for hearing
[3] 95 CI interval includes clear benefit as well as harm
[4] Relative study inconsistency is not present. However, the absolute rates of adverse effects ranged from 1 to 50% suggesting inconsistency.

Quality assessment

No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Pain at 24 hours (follow-up 24 hours)						
5	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none
Pain at 2 to 7 days (follow-up 2-7 days)						
10	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none
Hearing - 1 month (follow-up 1 months; as measured by tympanometry)						
4	randomized trials	no serious limitations	no serious inconsistency	serious[2]	serious[3]	none
Hearing - 3 months (follow-up 3 months; as measured by tympanometry)						
3	randomized trials	no serious limitations	serious	serious[2]	no serious imprecision	none
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GRADE evidence profile

Author(s): YFY (update from CDSR version)
Date: 2009-10-09
Question: Should Antibiotics vs. no antibiotics be used for children with otitis media?
Settings: outpatient
Bibliography: Sanders S, Glasziou PP, DelMar C, Rovers M. Antibiotics for acute otitis media in children. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No.: CD000219. DOI: 10.1002/14651858.CD000219.pub2. (2008 version)

No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotics	no antibiotics	Relative (95% CI)	Absolute	Quality	Importance
			Quality assessment				**No of patients**		**Effect**			
Pain at 24 hours (follow-up 24 hours)												
5	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	223/624 (35.7%)	36.7%[1]	RR 0.9 (0.78 to 1.04)	37 fewer per 1000 (from 81 fewer to 15 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain at 2 to 7 days (follow-up 2-7 days)												
10	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	228/1425 (16%)	26%[1]	RR 0.72 (0.62 to 0.83)	73 fewer per 1000 (from 44 fewer to 99 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Hearing - 1 month (follow-up 1 months; as measured by tympanometry)												
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No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotics	no antibiotics	Relative (95% CI)	Absolute	Quality	Importance
Quality assessment							**Summary of findings**					**Importance**
							No of patients		**Effect**		**Quality**	
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Determinants of confidence

- **RCTs** ⊕⊕⊕⊕
- **observational studies** ⊕⊕○○

- **5 factors that can lower quality**
  1. limitations in detailed study design and execution *(risk of bias criteria)*
  2. Inconsistency *(or heterogeneity)*
  3. Indirectness *(PICO and applicability)*
  4. Imprecision
  5. Publication bias

- **3 factors can increase quality**
  1. large magnitude of effect
  2. opposing plausible residual bias or confounding
  3. dose-response gradient
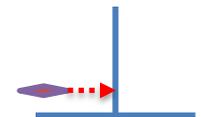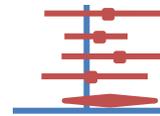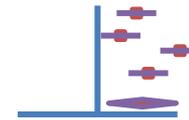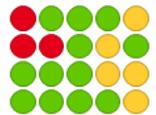
Strength of recommendation

"The strength of a recommendation reflects the extent to which we can, across the range of patients for whom the recommendations are intended, be confident that desirable effects of a management strategy outweigh undesirable effects."

• Strong or conditional

Implications of a *strong* recommendation

- Patients: Most people in this situation would want the recommended course of action and only a small proportion would not

- Clinicians: Most patients should receive the recommended course of action

- Policy makers: The recommendation can be adapted as a policy in most situations

Implications of a *conditional/weak* recommendation

- Patients: The majority of people in this situation would want the recommended course of action, but many would not

- Clinicians: Be more prepared to help patients to make a decision that is consistent with their own values/decision aids and shared decision making

- Policy makers: There is a need for substantial debate and involvement of stakeholders

Formulate question

Select outcomes   Rate importance

Outcomes across studies

Create evidence profile with GRADEpro

Rate quality of evidence for each outcome

P	Outcome	Critical
I	Outcome	Critical
C	Outcome	Important
O	Outcome	Not important

High ⊕⊕⊕⊕

Moderate ⊕⊕⊕◯

Low ⊕⊕◯◯

Very low ⊕◯◯◯

Grade down
1. Risk of bias
2. Inconsistency
3. Indirectness
4. Imprecision
5. Publication bias

Grade up
1. Large effect
2. Dose response
3. Opposing bias & Confounders

Summary of findings & estimate of effect for each outcome

Systematic review

Input?

Guideline development

Grade recommendations
- For or against (direction) ↓↑
- Strong or conditional/weak (strength)

By considering balance of:
- ❏ Quality of evidence
- ❏ Balance benefits/harms
- ❏ Values and preferences

Revise if necessary by considering:
- ❏ Resource use (cost)

Panel

Guideline

Grade overall quality of evidence
across outcomes based on lowest quality of *critical* outcomes
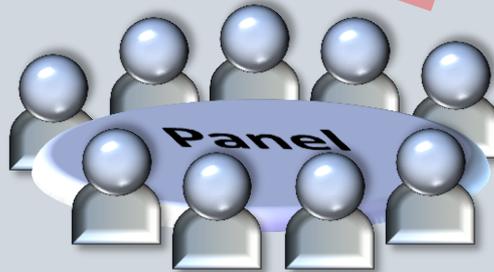
Formulate Recommendations (↓↑|⊕...)
- "We recommend using..." | "Clinicians should..."
- "We suggest using..." | "Clinicians might..."
- "We suggest <u>not</u> using..." | "Clinicians ... not..."
- "We recommend <u>not</u> using..." | "Clinicians should not..."

Conclusions

- Guidelines should be based on the **best available** evidence to be evidence based
- GRADE is the approach used by WHO and gaining acceptance internationally
  - combines what is known in health research methodology and provides a structured approach to improve communication
- Does not avoid judgments but provides framework
- Criteria for evidence assessment across questions and outcomes
- Criteria for moving from evidence to recommendations
- Transparent, systematic
  - four categories of quality of evidence
  - two grades for strength of recommendations
- Transparency in decision making and judgments is key

Thank you!

- Questions?

Desirable attributes of CPGs

- Validity
- Reliability
- Reproducibility
- Representative development
- Clinical applicability
- Clinical flexibility
- Clarity
- Meticulous documentation
- Scheduled review

Institute of Medicine (1992). *Guidelines for clinical practice: from development to use.*

Identifying evidence for guideline development

Possible methods include:

- Expert opinion

- Unsystematic reviews

- Systematic reviews.

Grimshaw, Russell (1993). *Quality in Health Care.*