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Estonia WHO EHIF | Webinar | November 28, 2016

Adaptation, Adoption and de novo development of Recommendations using GRADE Evidence to Decision Frameworks

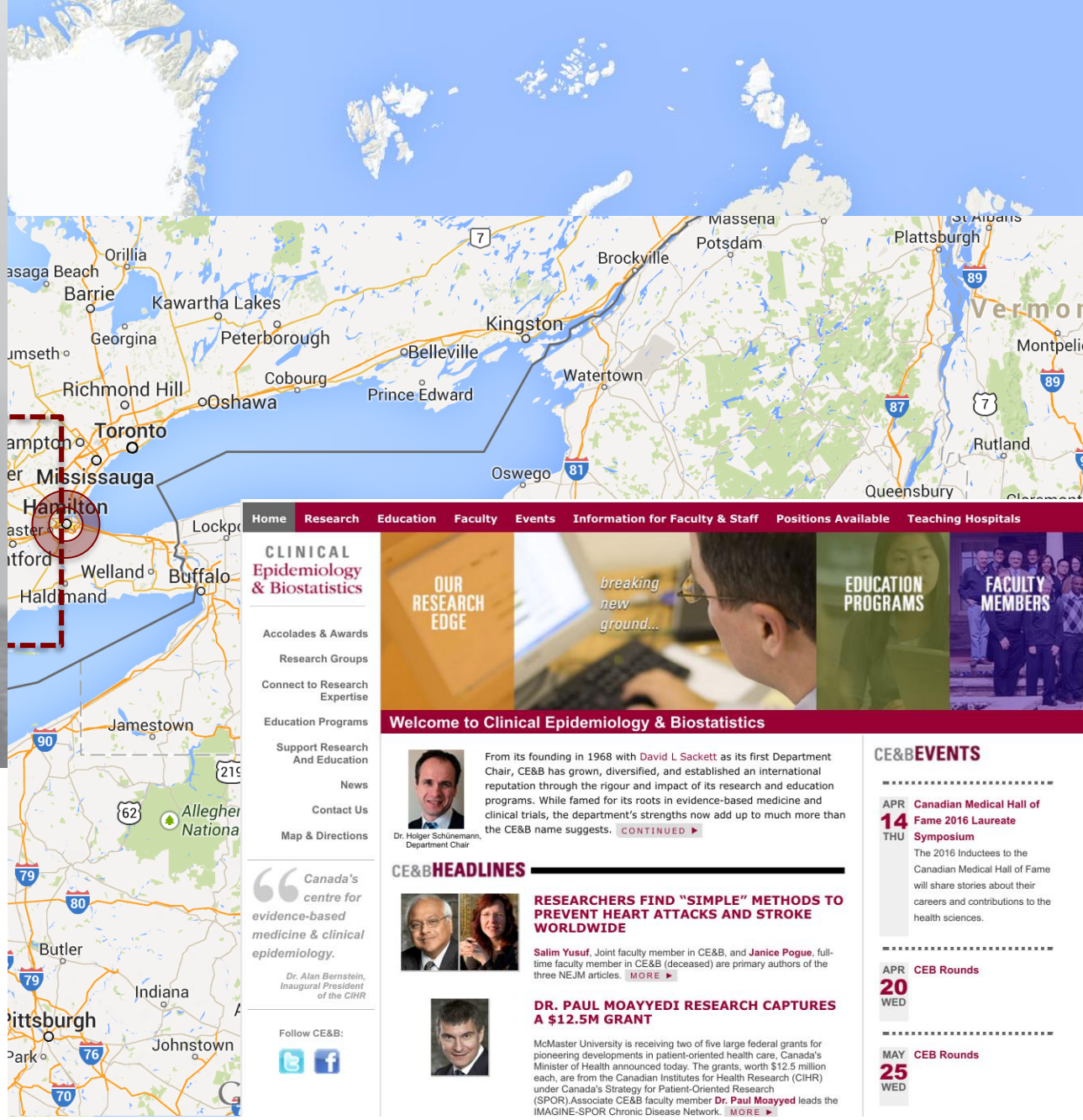
McMaster University
CLINICAL EPIDEMIOLOGY AND BIOSTATISTICS

Mac GRADE Centre | McMaster University

Cochrane Canada

Guidelines International Network

“Birthplace of evidence-based medicine and problem based learning”



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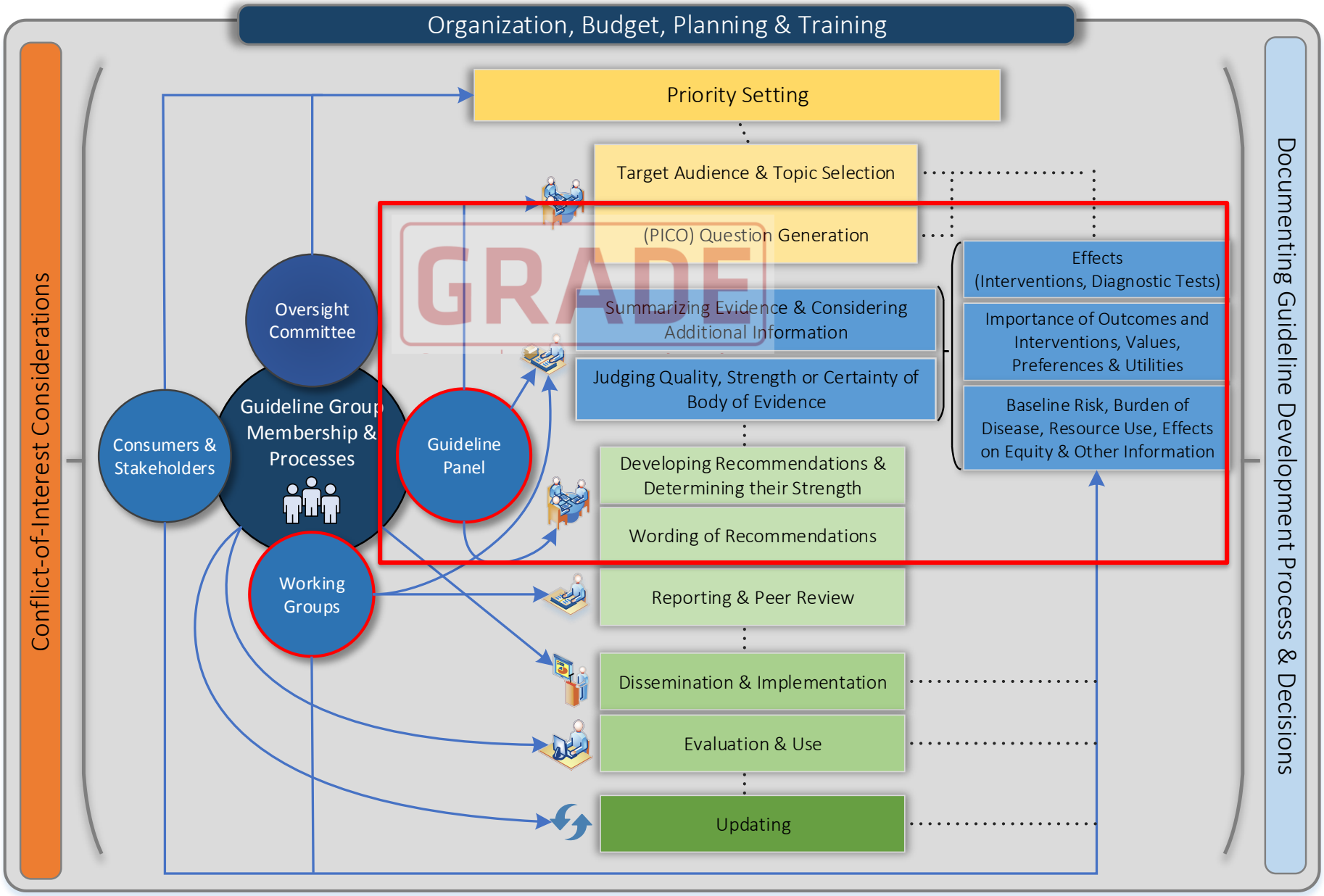
Disclosure

- Co-chair GRADE working group
- World Health Organization: various guideline committees
  - Co-director, WHO collaborating center on evidence informed policy making
- Cochrane – Cochrane Canada Director
- GIN – Board of Directors
- No direct financial COI

Today's presentation

- Guidelines and context of GRADE EtDs
- EtD Background and Development
- Use and application of EtDs
- Using GRADE EtDs for Adolopment
  - Adoption, adaptation and de novo creation of recommendations



Schünemann et al. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. CMAJ. 2014 Feb 18;186(3):E123-42.

http://cebgrade.mcmaster.ca/guidecheck.html

GRADE working group

- Developed a unifying, transparent and sensible system for grading the quality of evidence and developing recommendations
- For systematic reviews, HTA and guidelines
- International contributors (>500) with diversity in background beginning in the year 2000
- First articles in 2003 & 2004
- 2008 BMJ series; 2011 JCE series – over 20,000 cites
- Various other publications (incl. GRADE Handbook)
- IT applications GRADEpro GDT
- 11 Centers and networks on all continents

CMAJ 2003, BMJ 2004, BMC 2004, BMC 2005, AJRCCM 2006, Chest 2006, BMJ 2008, JCE 2011-2012

GRADE working group

- Over 100 organizations adopted or use GRADE
- Open membership – free: www.gradeworkinggroup.org

GRADE

2 principles

- **Certainty of evidence**
  - Involves assessing evidence transparently
  - Confidence in an estimate of effect, e.g. screening?
  - Starts with single research studies
  - Ends with a body of evidence by health outcome
    - high, moderate, low, very low certainty
- **Recommendations**
  - Involves making judgments and decisions transparent
  - Evidence to Decision (EtD) frameworks
    - Comprehensive list of criteria that influence a recommendation
  - Clearly developed & formulated action message
    - Strong or conditional recommendations for or against an option

GRADE working group

Formulate question

Select outcomes

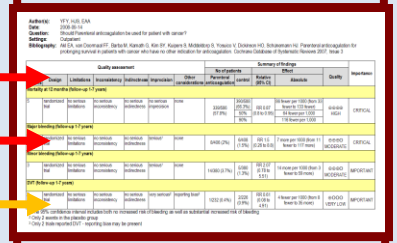
Rate importance

Outcomes across studies

P
I
C
O

Outcome Critical
Outcome Critical
Outcome Important
Outcome Not important

Create **evidence profile/SoF** Table with GRADEpro



Summary of findings & estimate of effect for each outcome

Rate quality of evidence for each outcome

High
Moderate
Low
Very low

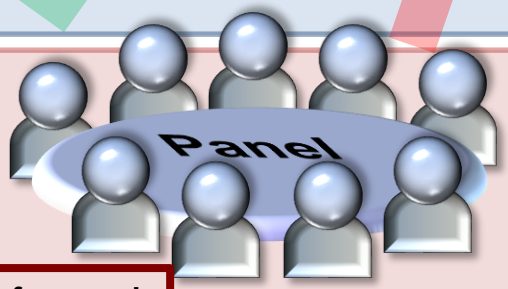
Randomization raises initial quality
RCTs: high
Observational: low

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

Evidence synthesis (systematic review/HTA)

Input?



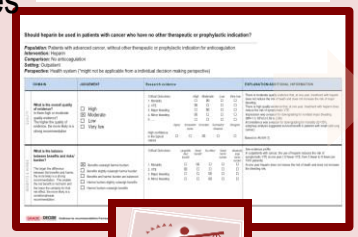
Recommendation/Decision

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

By considering balance of consequences (evidence to recommendations):
- ❑ Quality of evidence
- ❑ Balance benefits/harms
- ❑ Values and preferences (equity)
- ❑ Resource use (cost, feasibility)
- ❑ Acceptability

EtD framwork

GRADEpro GDT



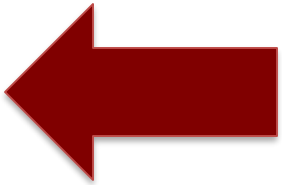
Guideline

Grade overall quality of evidence across outcomes based on lowest quality of ***critical*** outcomes

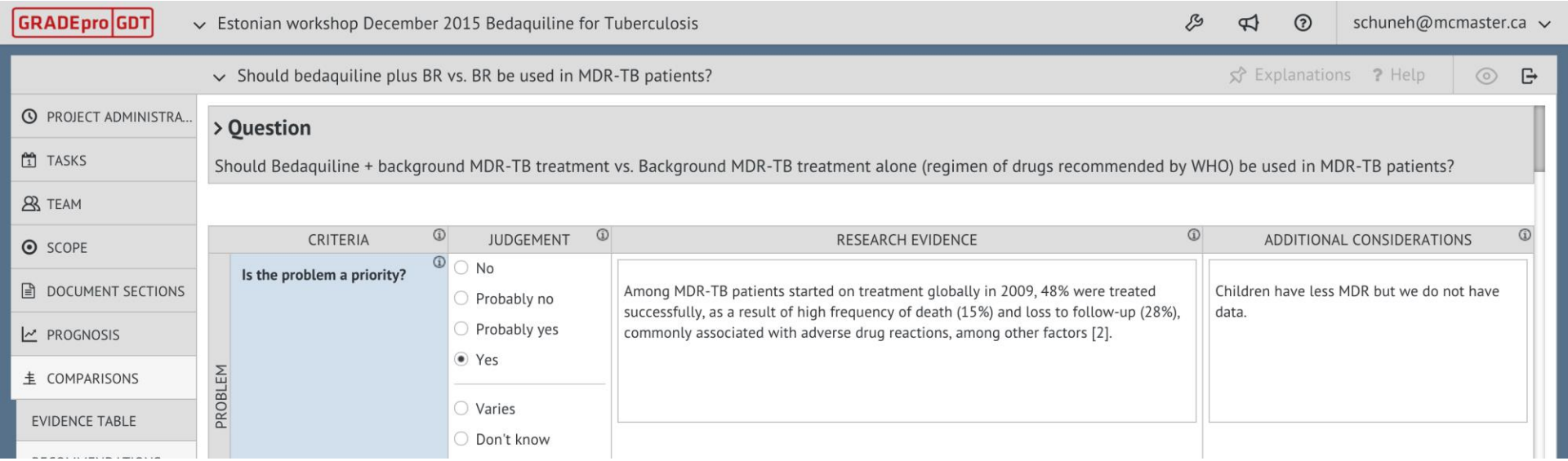
Formulate Recommendations (↓↑ | ⊕…)
"The panel recommends that ….should..."
"The panel suggests that ….should..."
"The panel suggests to **not** ..."
"The panel recommends to **not**..."
Transparency, clear, actionable

For groups making recommendations

- Question
  - Details
  - Subgroups
  - Background
- Assessment
  - Criteria
  - Judgements
  - Research evidence
  - Additional considerations
- Conclusions
  - Type of recommendation
  - Recommendation
  - Justification
  - Implementation considerations
  - Monitoring and evaluation
  - Research considerations



EtD frameworks



- ***Criteria*** on which a recommendation is based
- ***Judgements*** that must be made in relation to each criterion
- ***Research evidence*** to inform each judgement
- ***Additional considerations*** that inform or explain each judgement

GRADE Evidence to Decision (EtD) framework

Can help guideline panels (and decision makers) move from evidence to a recommendation or decision by

- Informing judgements about the pros and cons of each option (intervention)
- Considering each important factor that determine a decision (criteria)
- Providing a concise summary of the best available research evidence to inform judgements
- Helping to structure discussion and identify reasons for disagreements
- **Making the basis for decisions transparent and adaptable for target audiences**

What are we doing as a guideline panel?

Discuss evidence

Question

Should Acyclovir vs. Placebo be used for treatment of first clinical episodes of Herpes Simplex Virus 2?

	CRITERIA	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
PROBLEM	**Is the problem a priority?**	○ No ○ Probably no ○ Probably yes ◉ Yes ○ Varies ○ Don't know Detailed judgements	Globally, it is estimated that XXXXXXX people are newly infected with HSV2 each year. When symptoms of genital herpes occur, there are generally one or more genital or anal blisters called ulcers. First-episode infections of genital herpes are more extensive and primary lesions last two to six weeks versus approximately one week for lesions in recurrent disease. Infection with HSV2 also may increase the risk of acquiring HIV infection. Moreover, HSV2 can be transmitted to neonates from an infected pregnant mother.	
DESIRABLE EFFECTS	**How substantial are the desirable anticipated effects?**	○ Trivial ○ Small ○ Moderate ◉ Large ○ Varies ○ Don't know Detailed judgements	We found 5 randomised controlled trials comparing acyclovir in different doses compared to placebo. See Table below for the summary of the evidence.	

Acyclovir compared to Placebo for treatment of first clinical episodes of Herpes Simplex Virus 2

Outcomes	№ of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Acyclovir
Duration of symptoms from onset of treatment assessed with: time to resolution	238 (5 RCTs) [1]	⨁⨁◯◯ LOW [2,3]	-	The mean duration of symptoms from onset of treatment was **0** days	MD **3.2 days fewer** (4.94 fewer to 1.46 fewer)
Pain	129 (3 RCTs) [4]	⨁⨁◯◯ LOW [2,3]	-	The mean pain was **0** days	MD **2.1 days fewer** (2.95 fewer to 1.25 fewer)

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Add relevant considerations

Question

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PROBLEM	**Is the problem a priority?**	○ No ○ Probably no ○ Probably yes ◉ Yes ○ Varies ○ Don't know Detailed judgements	Globally, it is estimated that XXXXXXX people are newly infected with HSV2 each year. When symptoms of genital herpes occur, there are generally one or more genital or anal blisters called ulcers. First-episode infections of genital herpes are more extensive and primary lesions last two to six weeks versus approximately one week for lesions in recurrent disease. Infection with HSV2 also may increase the risk of acquiring HIV infection. Moreover, HSV2 can be transmitted to neonates from an infected pregnant mother.	
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Make judgments
(when research evidence complete) – w/o COI

Question

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PROBLEM	**Is the problem a priority?**	○ No ○ Probably no ○ Probably yes ◉ Yes ○ Varies ○ Don't know Detailed judgements	Globally, it is estimated that XXXXXXX people are newly infected with HSV2 each year. When symptoms of genital herpes occur, there are generally one or more genital or anal blisters called ulcers. First-episode infections of genital herpes are more extensive and primary lesions last two to six weeks versus approximately one week for lesions in recurrent disease. Infection with HSV2 also may increase the risk of acquiring HIV infection. Moreover, HSV2 can be transmitted to neonates from an infected pregnant mother.	
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Presentation and use of criteria can be tailored

- Interactive EtDs (iEtD)
- Lets us choose the criteria
- If obvious or not considered omit
- Available in GRADEpro (www.gradepro.org)

SETTINGS
ETD TEMPLATES
TASKS
TEAM
SCOPE
PROGNOSIS
COMPARISONS
PANEL VOICE
DOCUMENT SECTIONS
DISSEMINATION

Assessment

- ☑ Problem
  Is the problem a priority?
- ☑ Desirable Effects
  How substantial are the desirable anticipated effects?
- ☑ Undesirable Effects
  How substantial are the undesirable anticipated effects?
- ☑ Certainty of evidence
  What is the overall certainty of the evidence of effects?
- ☑ Values
  Is there important uncertainty about or variability in how much people value the main outcomes?
- ☑ Balance of effects
  Does the balance between desirable and undesirable effects favor the intervention or the comparison?
- ☑ Resources required
  How large are the resource requirements (costs)?
- ☑ Certainty of evidence of required resources
  What is the certainty of the evidence of resource requirements (costs)?
- ☑ Cost effectiveness
  Does the cost-effectiveness of the intervention favor the intervention or the comparison?
- ☑ Equity
  What would be the impact on health equity?
- ☑ Acceptability
  Is the intervention acceptable to key stakeholders?
- ☑ Feasibility
  Is the intervention feasible to implement?

Live use of iEtDs

EtDs are shared with panel members before the meeting and online:

- Clarify the process
- During the preparation for input on the evidence (all members including conflicted members could be involved)
- For initial agreement on the included evidence and additional considerations
- If possible, feasible and appropriate for agreement on judgments for specific decision criteria (but may all happen at an in-person meeting)
- Final draft EtDs before a final meeting

Guideline Development To

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gdt.guidelinedevelopment.org/central_prod/_design/client/index.html#projects/p_klegault_eed7a557-b2f7-453f-8f05-3a804a5e742a/evidence-syntheses/6C42B90...

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Should plasma exchange vs. no plasma exchange be used for CAPS? | Explanations | Help

- ADMINISTRATION
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- DOCUMENT SECTIONS
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Recommendations preview

Assessment

	CRITERIA	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
PROBLEM	**Is the problem a priority?**	○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ◉ Don't know Detailed judgements	In the most recently published full series of CAPS Registry patients, mortality in the 280 patient cohort was 44% (Cervera 2009). Specific therapies, or combinations of therapies, may reduce mortality in CAPS (Cervera 2009). The problem may be of particular concern in patients with systemic lupus erythematous (SLE). In a study analyzing 262 patients enrolled in the CAPS Registry up to September 2005, SLE patients made up 39% of the cohort (103 patients). In this subset, mortality appears to be significantly higher than in patients with primary CAPS: 58% versus 35% (Bayraktar 2007).	
	How substantial are the desirable anticipated effects?	○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ◉ Don't know Detailed judgements	A systematic review was performed using the Cochrane Highly Sensitive Search strategy to retrieve articles pertaining to use of plasma exchange compared to no plasma exchange in CAPS. The search yielded 598 abstracts, and two researchers (KL & CH) performed abstract screen in duplicate, identifying 55 abstracts for full text screen. Screening of full texts was performed in duplicate, and 6 relevant studies were identified. Data was extracted pertaining to the outcomes of death, permanent organ dysfunction, permanent neurologic deficit, complete recovery, major bleeding, amputation and thrombosis. See below for the evidence profile. **Harms of plasma exchange:** There are no studies specifically evaluating harms of plasma exchange in CAPS. Several studies have evaluated the adverse events of plasma exchange (Shemin 2007, Basic-Jukic 2005, Mokrzycki 1994). The Shemin et al, study in 2007 was a prospective study of 1,727 TPE treatments in 174 patients over 66 months showed that the most common adverse effects were fever (7.7%), urticaria (7.4%), and hypocalcemic effects, e.g. parasthesias, nausea and vomiting, chest pain, hypotension, cardiac arrhythmia (7.3%). Adverse events occurred in 36% of all patients. TPE was discontinued in 3 (0.2%) of patients for adverse events and 2 (0.1%) required transfer to a higher level of acuity. No deaths occurred. Albumin-saline was used as the replacement solution in 57% of treatments and 43% used fresh-frozen plasma (FFP). FFP was associated with significantly higher risk of adverse effects compared	In a study utilizing the CAPS registry data up to 2005 (262 patients), patients with SLE (SLE-CAPS) (n=103) were compared to patients with primary CAPS (P-CAPS) (n=127). In a multivariate analysis of the SLE-CAPS and P-CAPS populations combined, plasma exchange was significantly associated with reduced mortality [0.36 (95% CI 0.14-0.92)]. (Bayraktar 2007)

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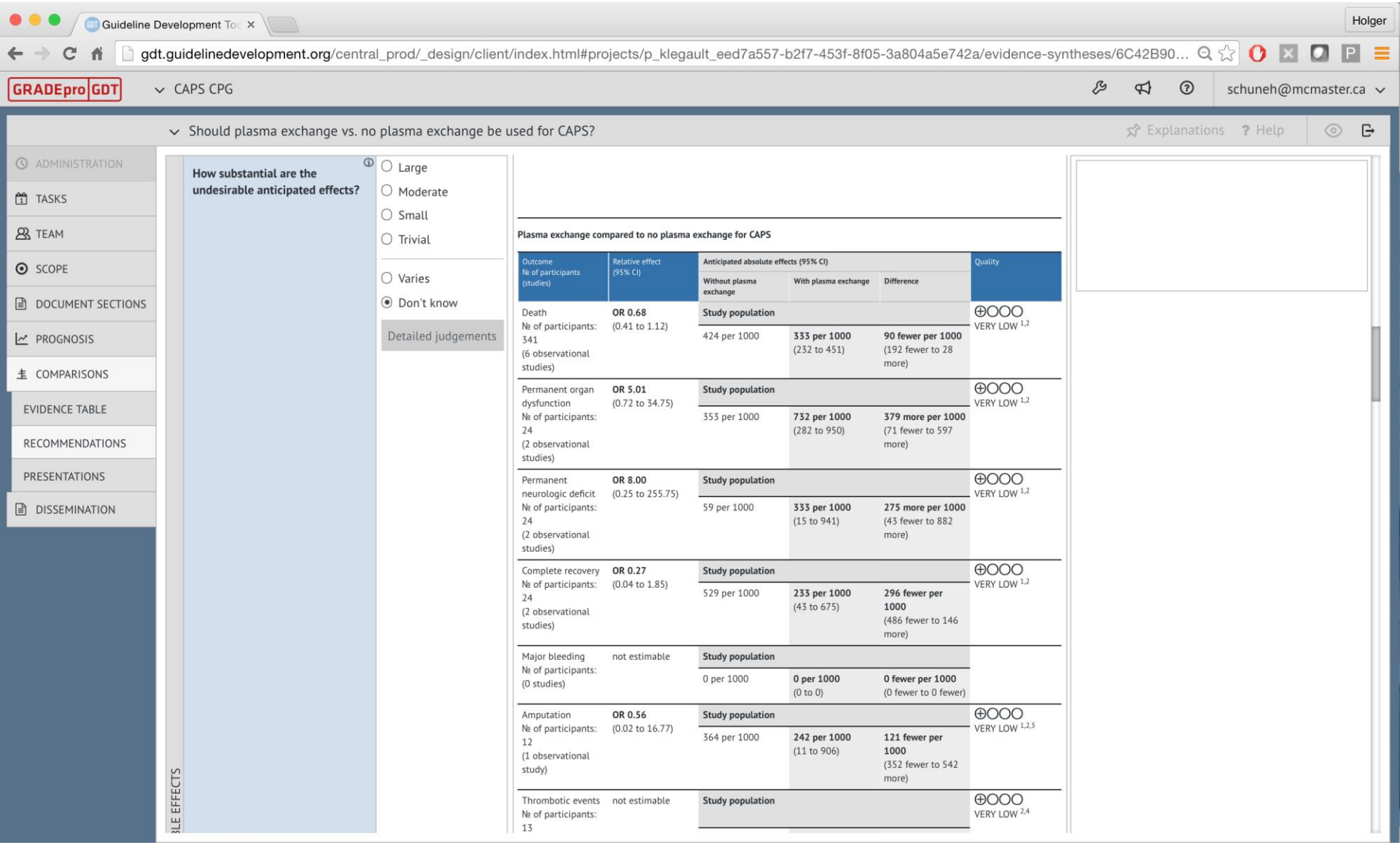

RESOURCES REQUIRED

How large are the resource requirements (costs)?	○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ◉ Don't know Detailed judgements	A systematic literature search was performed using the Medline and Embase databases to retrieve economic analyses pertaining to CAPS patients. The databases were searched to March 2016. There were 7 citations identified, however no published studies evaluated resource requirements in CAPS. Thus there are no published studies evaluating cost of TPE in CAPS. The cost of TPE has been outlined in studies in other conditions, in several countries. **United States:** A 2012 study of TPE vs IVIG in myasthenia graves (MG) described the estimated costs of TPE in the United States, as follows: 1 exchange: $2980, 1 dose albumin: $1119, Catheter: $520, Catheter placement: $859, Catheter removal: $353 (Heatwole 2012) A lower estimate of TPE costs was described in a 2011 study by Winters et al: $4,638.16 for 5 treatments (Winters 2011). **France:** In the French Cooperative Group randomized controlled trial on the use of TPE in Guillain-Barré syndrome (GBS) the cost of TPE was collected: Unit cost for TPE, including acquisition, amortization and residual value of the machine, maintenance costs, and operating costs, related to the number of PEs per year over 500 PEs per year on average): €500 (Espérou 2000) **Canada:** A cost-minimization analysis of plasma exchange in MG patients stated that the cost of a 5 treatment course of TPE cost CAN$6,271 overall (Hospital costs $4,628, blood products $1,455, physician fees $187) (Furlan 2015) **India:** In a 2013 study of TPE for GBS in Western India, one cycle of TPE, including the cost of PE Kit and replacement fluid: Rs 30,000 ($445 US) (Gajjar 2013). **Brazil:** For a treatment course for GBS, mean direct cost of TPE treatment (5 sessions) was US$6,059 ± 1,701 per patient (de Britto, 2011)	
What is the certainty of the evidence of resource requirements (costs)?	○ Very low ○ Low ○ Moderate ○ High ◉ No included studies Detailed judgements	The certainty of the evidence of resource requirements is very low, as the studies presented only describe costs of TPE itself in other conditions. The data presented are not necessarily representative of costs for CAPS patients. Furthermore the studies do not present data regarding any cost-benefit or similar type analysis, thus there is no analysis relating to the implications of resource use in this population.	

Guideline Development Tool

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gdt.guidelinedevelopment.org/central_prod/_design/client/index.html#projects/p_klegault_eed7a557-b2f7-453f-8f05-3a804a5e742a/evidence-syntheses/6C42B90…

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Should plasma exchange vs. no plasma exchange be used for CAPS? | Explanations | Help

- ADMINISTRATION
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Conclusions

Should plasma exchange vs. no plasma exchange be used for CAPS?

Type of recommendation	Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
	○	○	○	○	○
Recommendation	For treatment of patients with CAPS, the CAPS guideline panel suggests/recommends using/not using plasma exchange (conditional/strong recommendation, xx certainty in the evidence).				
Justification					
Subgroup considerations					
Implementation considerations					

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GRADEpro GDT | Estonian workshop December 2015 Bedaquiline for Tuberculosis | schuneh@mcmaster.ca

Should Bedaquiline + background MDR-TB treatment vs. Background MDR-TB treatment alone (regimen of drugs recommended by WHO) be used in MDR-T | Explanations | Help

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Recommendations preview

Assessment

PROBLEM

CRITERIA	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Is the problem a priority?	○ No ○ Probably no ○ Probably yes ◉ Yes ○ Varies ○ Don't know Detailed judgements	Among MDR-TB patients started on treatment globally in 2009, 48% were treated successfully, as a result of high frequency of death (15%) and loss to follow-up (28%), commonly associated with adverse drug reactions, among other factors [2].	Children have less MDR but we do not have data.

EFFECTS

CRITERIA	JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
How substantial are the desirable anticipated effects?	○ Trivial ○ Small ○ Moderate ◉ Large ○ Varies ○ Don't know Detailed judgements	Summary of findings: Bedaquiline for multidrug-resistant tuberculosis	Consensus this is a large effect. It is unkown if HIV medication interacts with bedaquiline. Alcohol use may influence pharmacokinetics of the drug.

Bedaquiline + background MDR-TB treatment compared to Background MDR-TB treatment alone (regimen of drugs recommended by WHO) in MDR-TB patients

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)
	Risk with Background MDR-TB treatment alone (regimen of drugs recommended by WHO)	Risk with Bedaquiline + background MDR-TB treatment			
Subjects cured by end of study: 120 weeks (C208 Stage 2: mITT) [1,2]	**Study population** 32 per 100 [1]	**58 per 100** (40 to 74) [1]	**RR 1.81** (1.26 to 2.31) [3,6]	132 (1 RCT) [1,3]	⨁⨁◯◯ LOW [4,5]
Serious Adverse Events during investigational 24 week treatment phase (C208 Stages	**Study population** 2 per 100	**7 per 100**	**RR 3.60** (0.77 to 14.00)	207 (2 RCTs) [7,9]	⨁◯◯◯ VERY LOW [5,8]

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Should Bedaquiline + background MDR-TB treatment vs. Background MDR-TB treatment alone (regimen of drugs recommended by WHO) be used in MDR-T | Explanations | Help

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Summary of judgements

Conclusions

Should Bedaquiline + background MDR-TB treatment vs. Background MDR-TB treatment alone (regimen of drugs recommended by WHO) be used in MDR-TB patients?

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	◉	○

Recommendation

The panel suggests suggests adding bedaquiline to a WHO recommended regimen in MDR-TB adult patients under the following conditions (conditional recommendation, very low certainty of the evidence).

In addition:

- A duly informed decision making-process by patients should be followed. Patient should know the risk.
- What dose? Lower dose to lower the risk of bedaquiline
- If patient is already on QT prolongating drugs then possible avoid use. E.g. PLHIV. Need to monitor ECG in these patients.
- Do not apply to children - risk are too high.

Cancel | Apply

Justification

Overall justification

Detailed justification

Desirable Effects
2.5 x higher probability of being cured than dying with the intervention (for different reasons).

Undesirable Effects

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	with a potential increase in mortality, serious adverse effects, and very low certainty of the evidence. For patients with extensively drug-resistant (XDR) tuberculosis and limited, if any other options, the desirable effects probably outweigh the undesirable effects.
Subgroup considerations	Bedaquiline is only suggested for patients with extensively drug-resistant MDR TB under the specified conditions.
Implementation considerations	• A process to ensure informed decision-making by patients should be established. • Equipment for baseline testing and monitoring for QT prolongation and development of arrhythmia should be available. • Monitoring of cardiac and liver disease should be available.
Monitoring and evaluation	• Spontaneous reporting of adverse drug reactions should be reinforced at country level and active pharmacovigilance should be established among patient groups treated with the drug. • Resistance to bedaquiline should be monitored. • Resistance to other anti-TB drugs should be monitored following WHO recommendations.
Research priorities	• Phase 3 clinical trial(s) of safety and efficacy of bedaquiline, with particular attention to mortality (including causes of death), in the treatment of MDRTB should be accelerated • Pharmacokinetics, safety and efficacy studies in specific populations (paediatrics, HIV patients, alcohol and drug users, elderly, pregnant women, extrapulmonary TB, persons with diabetes) • Safety studies, including type, frequency and severity of adverse events (short term and long term) • Drug-drug interactions, including with other existing and newly developed TB drugs and ARVs • Impact on mortality (including cause of death) • Acquisition of resistance to bedaquiline and to other TB drugs • Duration and dosing of treatment • Patients' values • Further research on the validity of culture conversion as a surrogate marker of treatment outcome

thebmj | BMJ 2016;353:i2016 | doi: 10.1136/bmj.i2016

GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction

Pablo Alonso-Coello,[1,2] Holger J Schünemann,[2,3] Jenny Moberg,[4] Romina Brignardello-Petersen,[2,5] Elie A Akl,[2,6] Marina Davoli,[7] Shaun Treweek,[8] Reem A Mustafa,[2,9] Gabriel Rada,[10,11,12] Sarah Rosenbaum,[4] Angela Morelli,[4] Gordon H Guyatt,[2,3] Andrew D Oxman[4] the GRADE Working Group

GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines

Pablo Alonso-Coello,[1,2] Andrew D Oxman,[3] Jenny Moberg,[3] Romina Brignardello-Petersen,[2,4] Elie A Akl,[2,5] Marina Davoli,[6] Shaun Treweek,[7] Reem A Mustafa,[2,8] Per O Vandvik,[3] Joerg Meerpohl,[9] Gordon H Guyatt,[2,10] Holger J Schünemann,[2,10] the GRADE Working Group

ELSEVIER

Journal of Clinical Epidemiology ■ (2016) ■

ORIGINAL ARTICLE

GRADE Guidelines: 16. GRADE evidence to decision frameworks for tests in clinical practice and public health

Holger J. Schünemann[a,b,c,*], Reem Mustafa[a,c,d], Jan Brozek[a,b,c], Nancy Santesso[a,c], Pablo Alonso-Coello[a,c,e], Gordon Guyatt[a,b,c], Rob Scholten[f], Miranda Langendam[c,g], Mariska M. Leeflang[g], Elie A. Akl[a,c,h], Jasvinder A. Singh[c,i], Joerg Meerpohl[c,j],

Neumann et al. Implementation Science (2016) 11:93
DOI 10.1186/s13012-016-0462-y

Implementation Science

RESEARCH Open Access

The GRADE evidence-to-decision framework: a report of its testing and application in 15 international guideline panels

Ignacio Neumann[1,2], Romina Brignardello-Petersen[1,3], Wojtek Wiercioch[1], Alonso Carrasco-Labra[1,3], Carlos Cuello[1], Elie Akl[4], Reem A. Mustafa[1,5], Waleed Al-Hazzani[1], Itziar Etxeandia-Ikobaltzeta[1,7], Maria Ximena Rojas[8], Maicon Falavigna[9], Nancy Santesso[1], Jan Brozek[1,6], Alfonso Iorio[1], Pablo Alonso-Coello[1,10] and Holger J. Schünemann[1,6*]

OPEN ACCESS Freely available online

PLoS MEDICINE

Health in Action

Transparent Development of the WHO Rapid Advice Guidelines

Holger J. Schünemann*, Suzanne R. Hill, Meetali Kakad, Gunn E. Vist, Richard Bellamy, Lauren Stockman, Torbjørn Fosen Wisløff, Chris Del Mar, Frederick Hayden, Timothy M. Uyeki, Jeremy Farrar, Yazdan Yazdanpanah, Howard Zucker, John Beigel, Tawee Chotpitayasunondh, Tran Tinh Hien, Bülent Özbay, Norio Sugaya, Andrew D. Oxman

ADOLOPMENT

Use guidelines in your context

- Adoption – use the recommendation as is
- Adaptation – modify to fit your needs
- De novo – new recommendation
  - Can be based on existing evidence summaries

Adoption

- Use of existing, trustworthy recommendations without modification of the original recommendation and providing information on how to implement them
- In ideal case, based on review and agreement with judgments that influenced the original recommendation

Adoption

- The adopted recommendation would have the same specific population, intervention and comparators as the original recommendation, and the same certainty in the evidence rating.
- Choice of the guideline scope and the individual recommendations follows from their availability.
- Cheapest and quickest way of developing a guideline.

Adaptation

- Involves identifying the pertinent health questions, searching for existing guidelines that address those questions and performing critical appraisal, and deciding to accept or modify whole guidelines or their specific recommendations by considering whether they are up to date, acceptable and applicable given the cultural and organizational context.

Adaptation

- Credible, up to date, acceptable, applicable and feasible to implement given the cultural and organizational context?
- The adapted recommendation may have a change in the specific population, intervention, comparator than the original recommendation, and a different certainty in the evidence.
- The adapted recommendation will provide additional information on “conditions”, monitoring, implementation, and implications for research.

Adoption and Adaptation

Serve two primary purposes:

1) investing limited resources by building on existing efforts to provide local, regional or national guidance; and
2) considering factors that are specific to these settings to enhance usability for the intended target groups. Using this approach, guideline developers must choose which recommendations to adapt.

- ☺ Transparently laying out the judgments that a guideline panel makes when formulating recommendations would facilitate their later adaptation.
- ☹ Existing guidelines often do not provide the necessary details about this process and other decisions necessary to work on their adaptation and adoption.

De novo development

- New questions and seeking to answer them in new guidelines
- Can be based on existing evidence synthesis such as systematic reviews or health technology assessments that are relevant

Choice of approach

- Availability of monetary and non-monetary resources, credibility, maximization of uptake, the benefits of sharing information widely
- Avoidance of duplication of efforts
- Organizations will need to decide on the best approaches
  - develop detailed strategies and build capacity to implement them

World Health Organization

REGIONAL OFFICE FOR Europe

Developing and implementing guidelines for health policy and clinical practice in Estonia:

By: Paul Garner
Suzanne Hill
Holger Schünemann

McMaster University
Inspiring Innovation and Discovery

Example Projects

Objective: To develop health care guidelines on 22 clinical topics (project 1) and one separate guideline in different project (project 2).

Timeline: June 2013 through June 2015 (project 1)
May 2016 (project 2)

Focus on ***'ad-o-lopment"*** of recommendations

Groups and Roles

McMaster Guideline Working Group

Saudi Centre for EBHC:

- Project coordination
- Recruiting panel members
- Facilitating communication with panels
- Dissemination of guidelines

Saudi Expert Guideline Panels

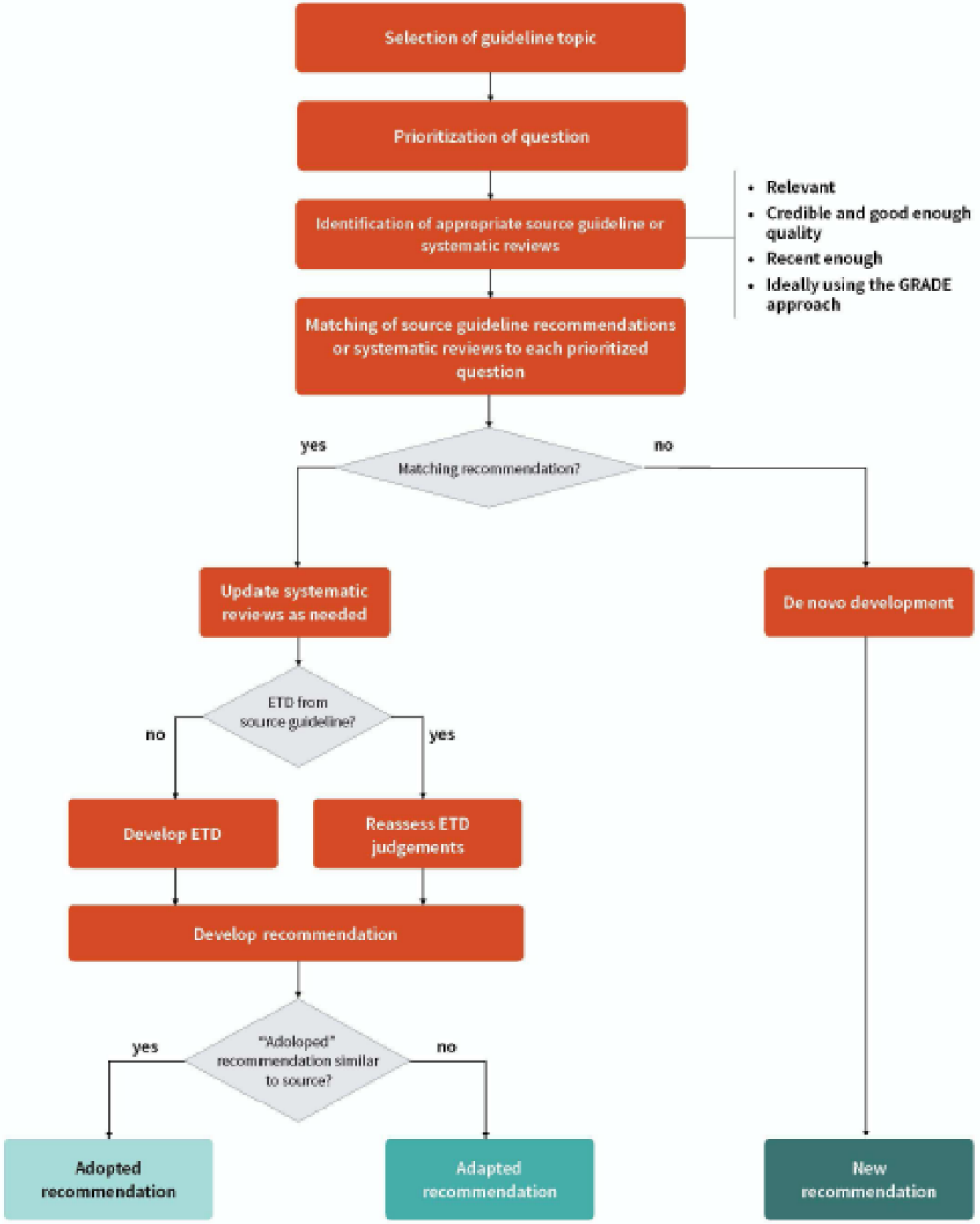
Groups and Roles

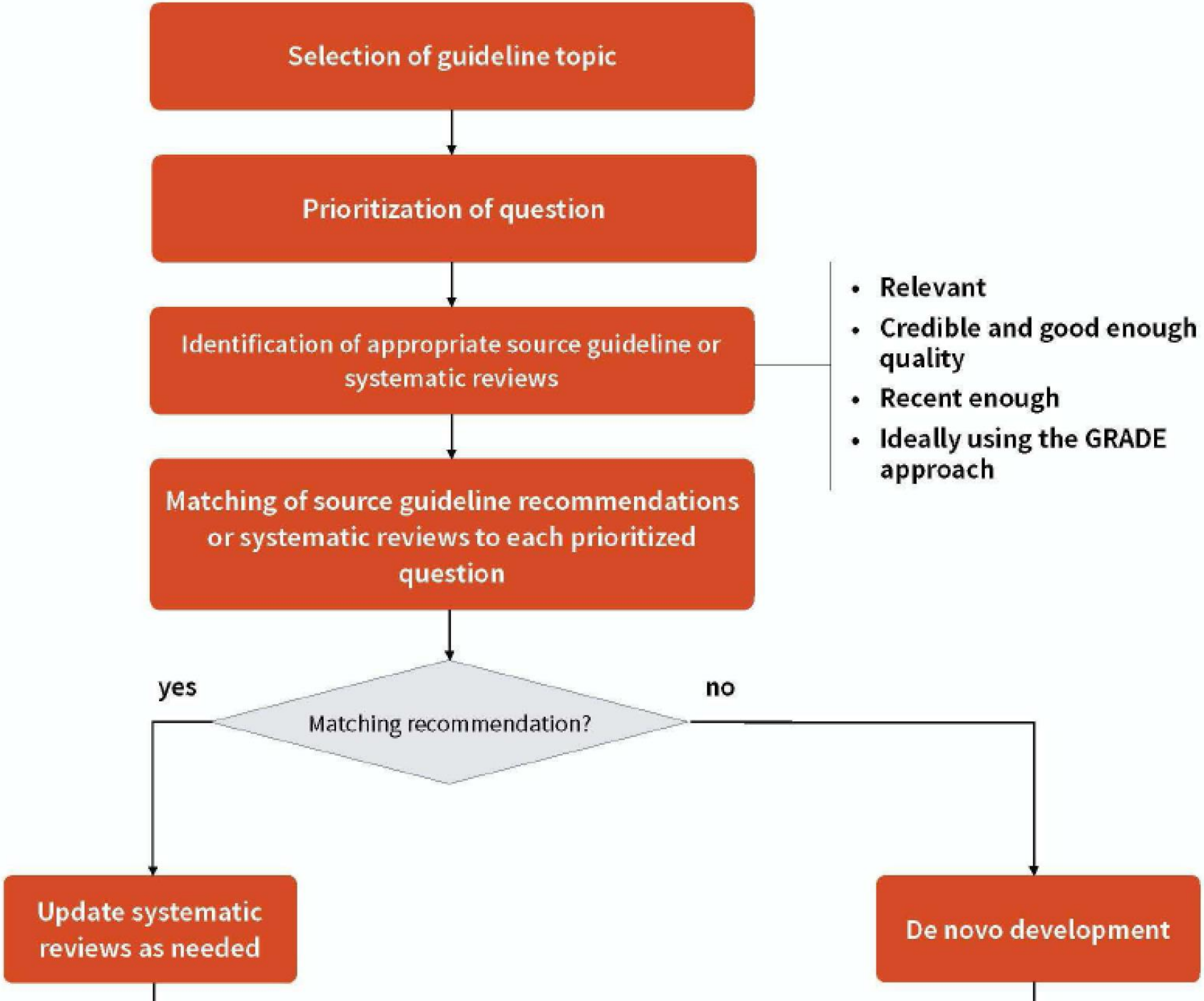
McMaster Guideline Working Group

Saudi Centre for EBHC

Saudi Expert Guideline Panels:

- Prioritization of questions for guidelines
- Suggesting local evidence and input on local data and contextual factors
- Reviewing evidence summaries
- Making judgements and formulating recommendations in final panel meeting
- Dissemination of guidelines


Selection of guideline topic
Prioritization of question
Identification of appropriate source guideline or systematic reviews
Relevant
Credible and good enough quality
Recent enough
Ideally using the GRADE approach
Matching of source guideline recommendations or systematic reviews to each prioritized question
Matching recommendation?
yes
no
Update systematic reviews as needed
De novo development
ETD from source guideline?
no
yes
Develop ETD
Reassess ETD judgements
Develop recommendation
"Adoloped" recommendation similar to source?
yes
no
Adopted recommendation
Adapted recommendation
New recommendation


Selection of guideline topic
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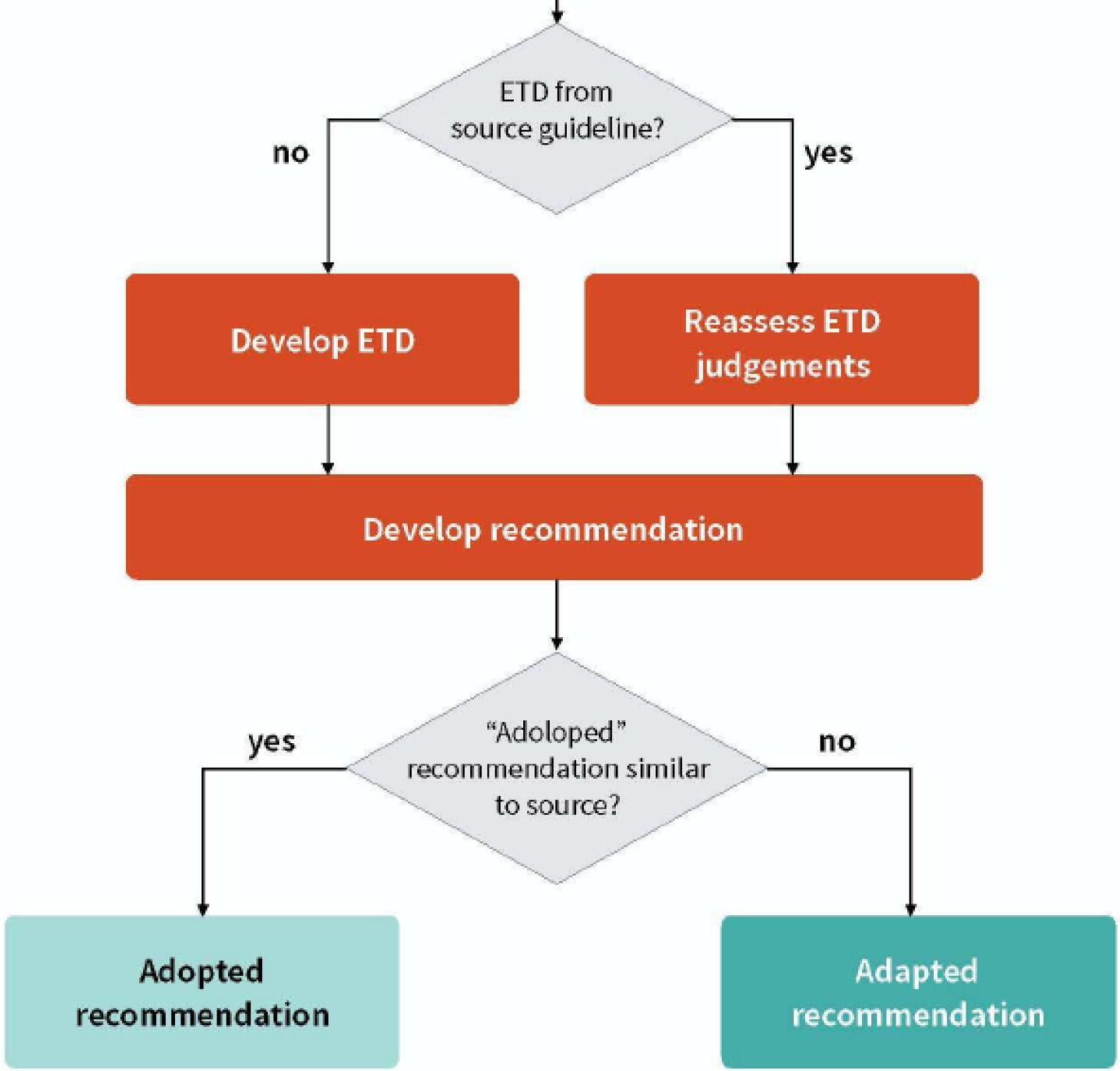
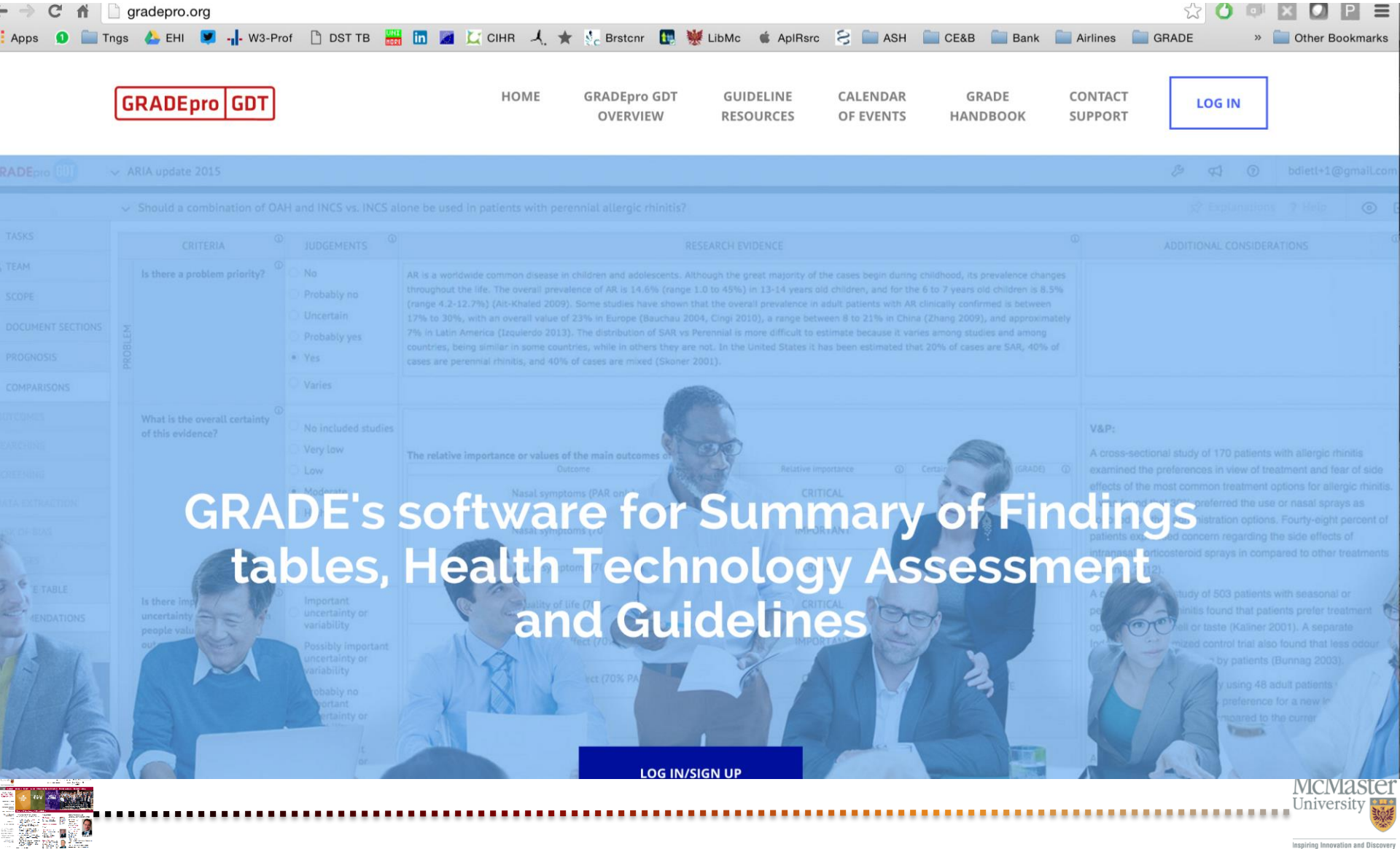
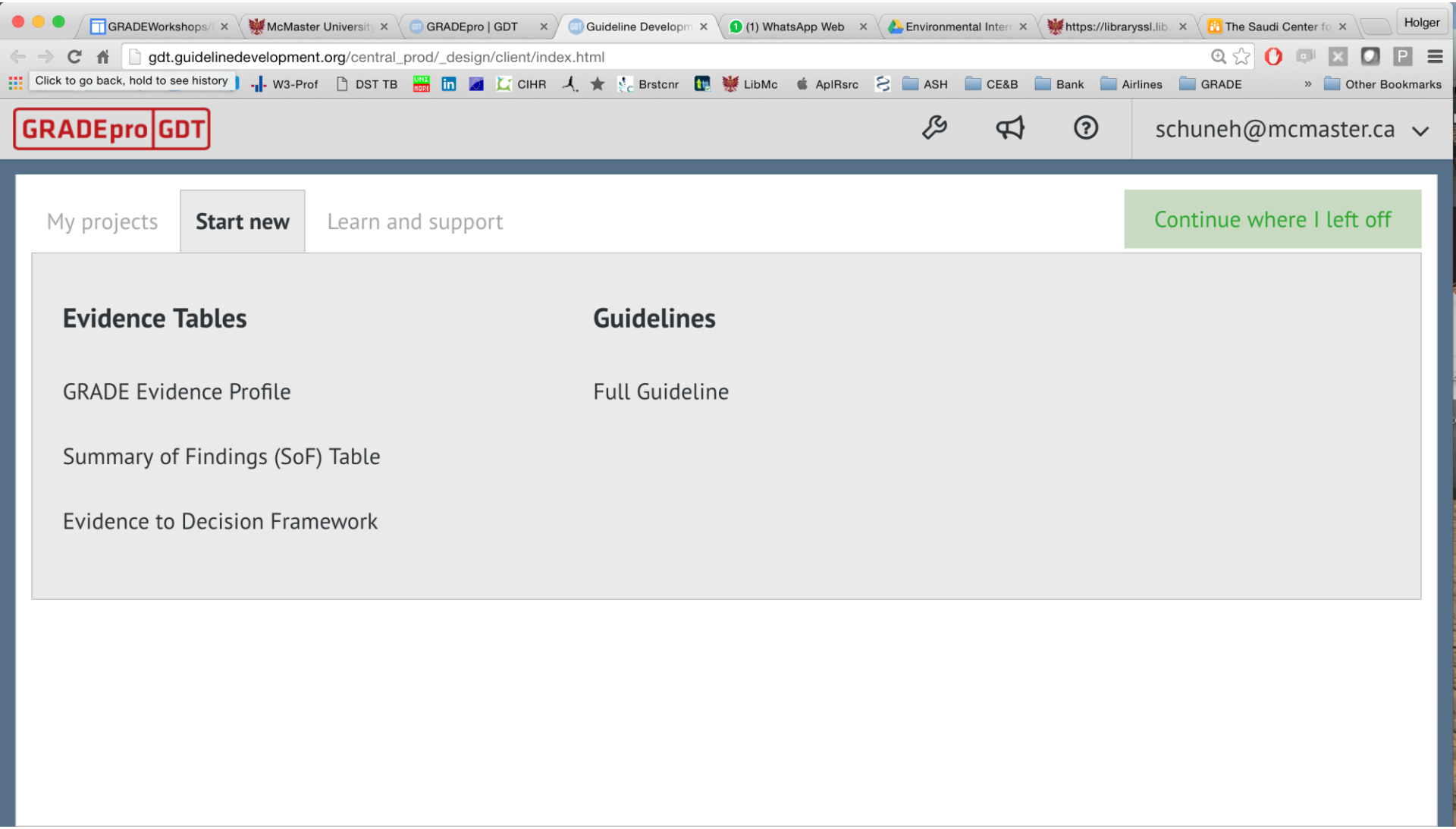
Relevant
Credible and good enough quality
Recent enough
Ideally using the GRADE approach
Matching of source guideline recommendations or systematic reviews to each prioritized question
yes
Matching recommendation?
no
Update systematic reviews as needed
De novo development



www.gradepro.org

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DST TB
CIHR
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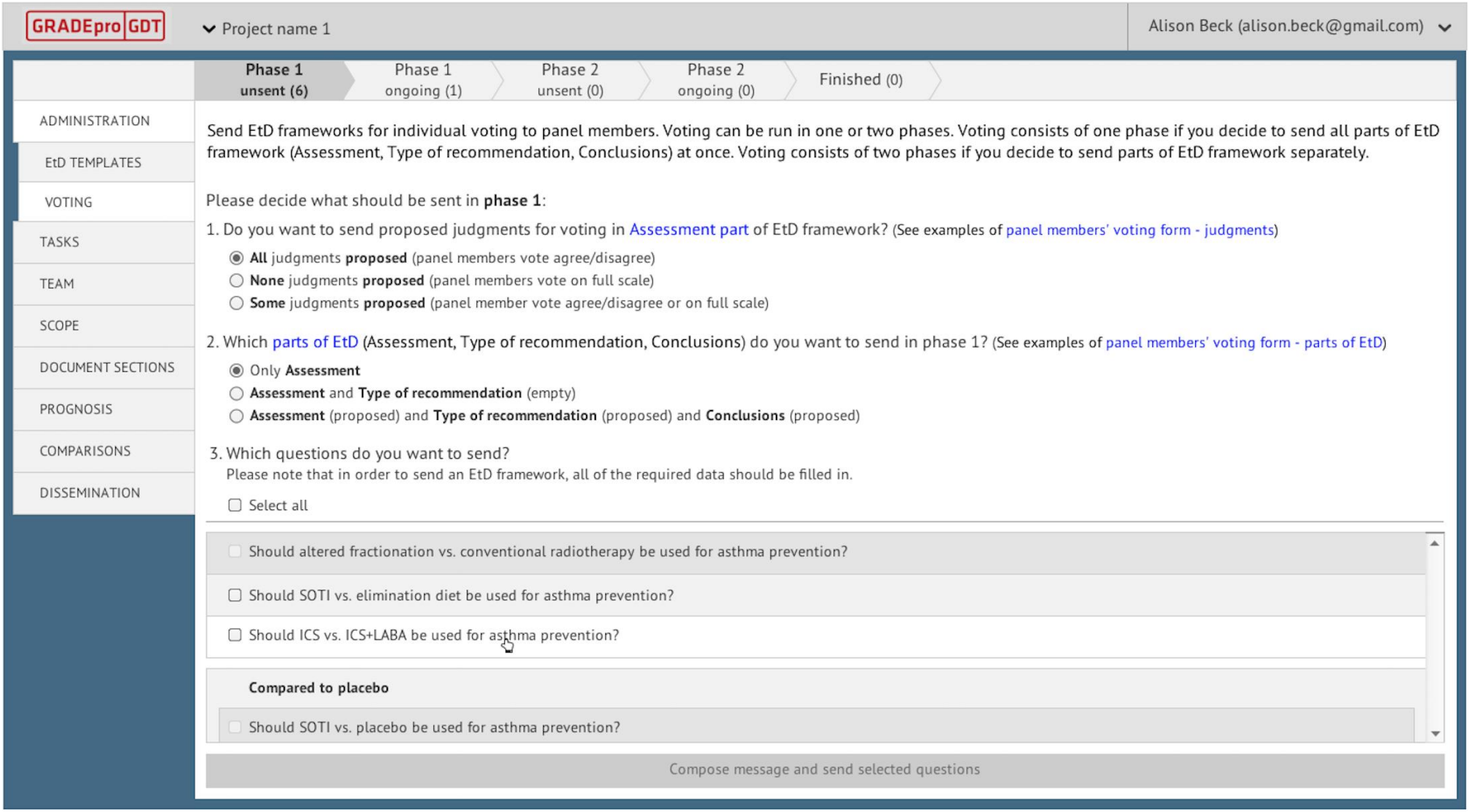
LibMc
ApIRsrc
ASH
CE&B
Bank
Airlines
GRADE
Other Bookmarks
GRADEpro GDT
schuneh@mcmaster.ca
My projects
Start new
Learn and support
Continue where I left off
Evidence Tables
GRADE Evidence Profile
Summary of Findings (SoF) Table
Evidence to Decision Framework
Guidelines
Full Guideline

Online interaction



Question: Should ICS vs. ICS+LABA be used for asthma prevention?

Population: Adults with asthma

Intervention: ICS

Comparison: ICS+LABA

Main outcomes: Any AE (95% CI); Any AE (99% CI); Any AE (90% CI);

Setting: Global

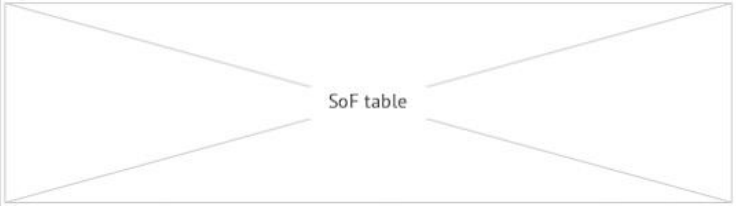
Perspective: Patient

Evidence to Decision framework

Instructions

Review research evidence and make your judgment. Comment on your decision to justify it.

CRITERION	YOUR JUDGMENT	RESEARCH EVIDENCE
PROBLEM: **Is the problem a priority?**	○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know	AR is a worldwide common disease in children and adolescents. Although the great majority of the cases begin during childhood, its prevalence changes throughout the life. The overall prevalence of AR is 14.6% (range 1.0 to 45%) in 13-14 years old children, and for the 6 to 7 years old children is 8.5% (range 4.2-12.7%) (Ait-Khaled 2009). Some studies have shown that the overall prevalence in adult patients with AR clinically confirmed is between 17% to 30%, with an overall value of 23% in Europe (Bauchau 2004, Cingi 2010), a range between 8 to 21% in China (Zhang 2009), and approximately 7% in Latin America (Izquierdo 2013). The distribution of SAR vs Perennial is more difficult to estimate because it varies among studies and among countries, being similar in some countries, while in others they are not. In the United States it has been estimated that 20% of cases are SAR, 40% of cases are perennial rhinitis, and 40% of cases are mixed (Skoner 2001). Comment Provide a reason for your decision or other comments

CRITERION	YOUR JUDGMENT	RESEARCH EVIDENCE
DESIRABLE EFFECTS: **How substantial are the desirable anticipated effects?**	○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	**The relative importance or values of the main outcomes of interest:** 

Comment

Provide a reason for your decision or other comments

cases are SAR, 40% of cases are perennial rhinitis, and 40% of cases are mixed (Skoner 2001).

Comment

Provide a reason for your decision or other comments

CRITERION	YOUR JUDGMENT	RESEARCH EVIDENCE
DESIRABLE EFFECTS: **How substantial are the desirable anticipated effects?**	○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	**The relative importance or values of the main outcomes of interest:** SoF table

Comment

Provide a reason for your decision or other comments

CRITERION	YOUR JUDGMENT	RESEARCH EVIDENCE
UNDESIRABLE EFFECTS: **How substantial are the undesirable anticipated effects?**	○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	**The relative importance or values of the main outcomes of interest:** SoF table

Judgment is required.

Comment

Provide a reason for your decision or other comments

Save | Save and submit

Voting on "Assessment" part when judgments are empty.

Question: Should ICS vs. ICS+LABA be used for asthma prevention?

Population: Adults with asthma

Intervention: ICS

Comparison: ICS+LABA

Main outcomes: Any AE (95% CI); Any AE (99% CI); Any AE (90% CI);

Setting: Global

Perspective: Patient

Evidence to Decision framework

Instructions

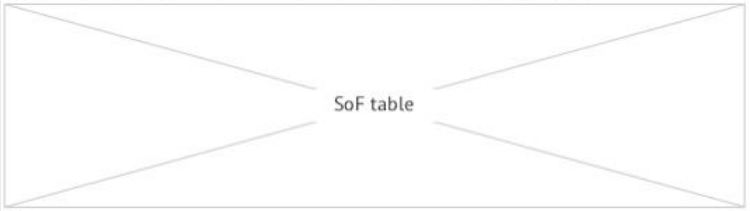
CRITERION	PROPOSED JUDGMENT	RESEARCH EVIDENCE
PROBLEM: **Is the problem a priority?**	No Probably no Probably yes ✓ **Yes** Varies Don't know	AR is a worldwide common disease in children and adolescents. Although the great majority of the cases begin during childhood, its prevalence changes throughout the life. The overall prevalence of AR is 14.6% (range 1.0 to 45%) in 13-14 years old children, and for the 6 to 7 years old children is 8.5% (range 4.2-12.7%) (Ait-Khaled 2009). Some studies have shown that the overall prevalence in adult patients with AR clinically confirmed is between 17% to 30%, with an overall value of 23% in Europe (Bauchau 2004, Cingi 2010), a range between 8 to 21% in China (Zhang 2009), and approximately 7% in Latin America (Izquierdo 2013). The distribution of SAR vs Perennial is more difficult to estimate because it varies among studies and among countries, being similar in some countries, while in others they are not. In the United States it has been estimated that 20% of cases are SAR, 40% of cases are perennial rhinitis, and 40% of cases are mixed (Skoner 2001).

○ Agree ○ Disagree

Comment*

Provide a reason for your decision or other comments

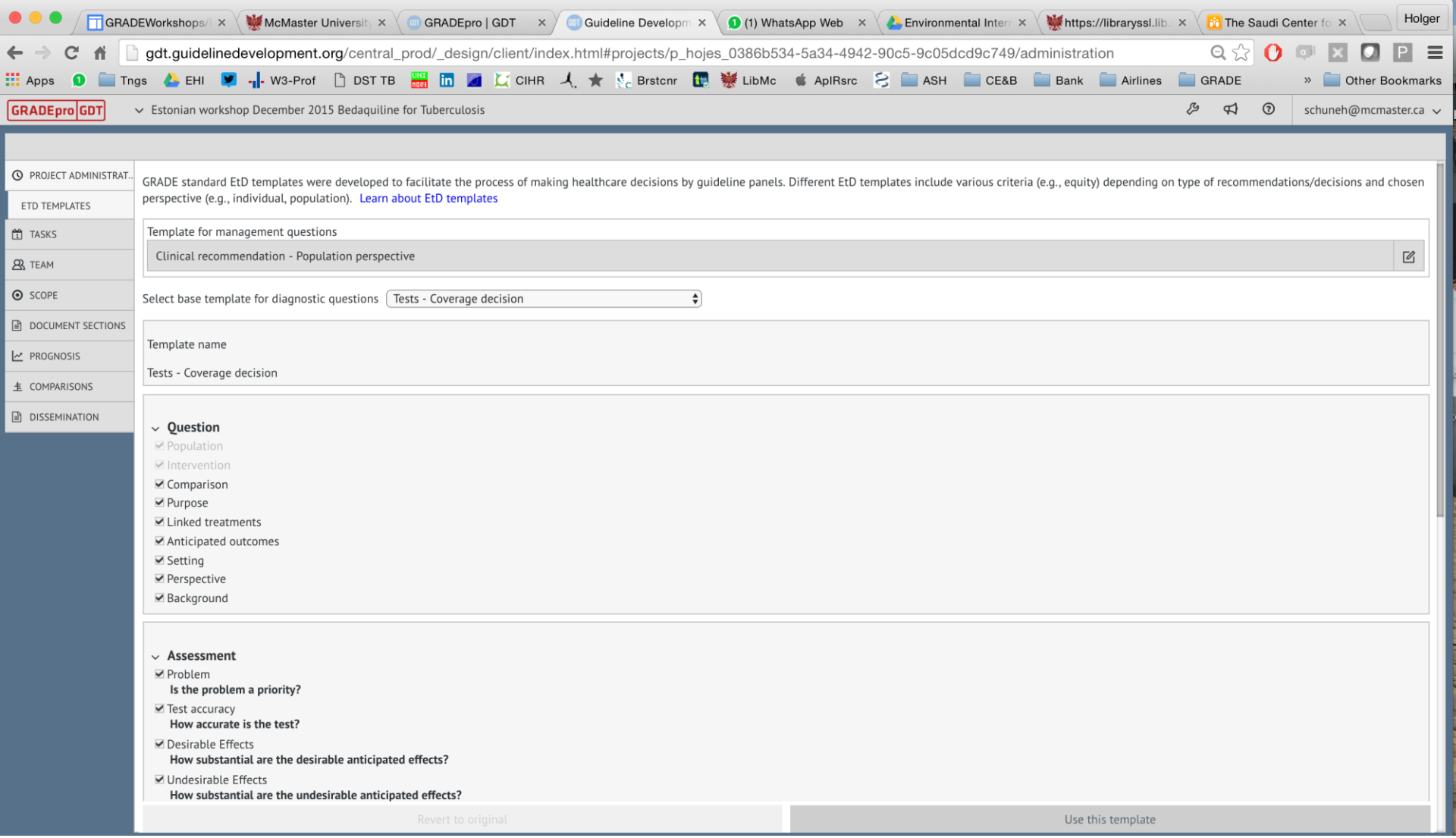
Comment is required. Please give the reason for disagreeing.

CRITERION	PROPOSED JUDGMENT	RESEARCH EVIDENCE
DESIRABLE EFFECTS: **How substantial are the desirable anticipated effects?**	Trivial Small ✓ **Moderate** Large Varies Don't know	**The relative importance or values of the main outcomes of interest:** 

○ Agree ○ Disagree

Comment

Provide a reason for your decision or other comments



Adoption: Hemodialysis

Canadian Society of Nephrology/
Société Canadienne De Néphrologie
CSN/SCN

Box 2 - Recommendation:

For adult patients (>18 years of age) with an eGFR <15 ml/min/1.73m^2, we recommend an 'intent-to-defer' over an 'intent-to-start early' approach for the initiation of chronic dialysis. (*Strong recommendation; moderate quality evidence* ⊕⊕⊕O)

Underlying Values and Preferences

This recommendation places a high value on quality of life, by avoiding the burden associated with earlier initiation of dialysis without clinical indications, while concurrently avoiding complications of uremia. This recommendation also places a high value on resource use, which increases with earlier initiation of dialysis. This recommendation places a low value on surrogate markers including serum albumin, body nitrogen and eGFR levels in the absence of symptoms.

Appendix 1: Evidence-to-Recommendation Table and Evidence Profiles

Evidence to recommendation framework

Among adult patients (age >= 18 years) with advanced (stage V) chronic kidney disease, what are the effects of an intent-to-initiate dialysis early (eGFR 10-14 ml/min) strategy compared with an intent-to-defer dialysis (eGFR 5-7 ml/min) strategy?

Problem: adult patients (>=18 years of age) with an eGFR <15 ml/min/1.73m^2
Option: "intent-to-start-early"
Comparison: "Intent-to-defer"
Setting: Outpatient
Perspective: Health system (*might not be applicable from an individual decision making perspective)

Background: Initiating chronic dialysis has major implications for patients and health care systems around the world and in Saudi Arabia. When patients reach advanced stages of chronic kidney disease (CKD), there is a need to identify a dialysis threshold. Before this proposed threshold starting dialysis will add no benefits but beyond it there may be risks to patients. The limited available dialysis slots Saudi Arabia hospitals and dialysis units emphasize the importance of this guideline to individual patients' care and the healthcare system in general.

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
PROBLEM	Is the problem a priority?	No ☐ / Probably No ☐ / Uncertain ☐ / Probably Yes ☐ / Yes ☒ / Varies ☐	Global prevalence of renal replacement therapy has almost doubled within the past two decades at a rate of > 6% per year. This growth is far beyond what is anticipated secondary to population growth and aging and it adds enormous burden on global health resources. KSA specific evidence (SCOT database)[6] In 2012, there were 14171 dialysis patients out of a population of 28.4 million. Total number of ESRD patients on HD was 12844 in 2012. This number has almost doubled in one decade (was 3357 in 1993 and 7004 in 2003). In 2012, 3187 new cases of HD were registered (was 1733 in 2000).	The prevalence of CKD with its different stages is unknown in KSA. There is large variation in incidence and prevalence among different regions.[20] Increase availability of dialysis services may also have played a role in increasing ESRD population.

BENEFITS & HARMS OF THE OPTIONS

CRITERIA	JUDGEMENTS
What is the overall certainty of this evidence?	No included studies ☐ | Very low ☐ | Low ☐ | Moderate ☒ | High ☐
Is there important uncertainty about how much people value the main outcomes?	Important uncertainty or variability ☐ | Possibly important uncertainty or variability ☐ | Probably no important uncertainty or variability ☐ | No important uncertainty or variability ☒ | No known undesirable outcomes ☐
Are the desirable anticipated effects large?	No ☐ | Probably No ☒ | Uncertain ☐ | Probably Yes ☐ | Yes ☐ | Varies ☐
Are the undesirable anticipated effects small?	No ☐ | Probably No ☐ | Uncertain ☐ | Probably Yes ☒ | Yes ☐ | Varies ☐
Are the desirable effects large relative to undesirable effects?	No ☒ | Probably No ☐ | Uncertain ☐ | Probably Yes ☐ | Yes ☐ | Varies ☐

RESEARCH EVIDENCE

The relative importance or values of the main outcomes of interest:

Outcome	Relative importance	Certainty of the evidence
Mortality	Cretical	Moderate ⊕⊕⊕⊖
Quality of Life	Cretical	
Hospitalization	Important	
Nutritional status	Not important	

Summary of findings: "Intent-to-defer" dialysis compared to "intent-to-start-early" in adult patients with CKD stage 5

Outcome	"intent-to-start-early" (# of patients)	"intent-to-defer" (# of patients)	Difference Per 1000 (95%CI)	Relative effect (95%CI)	Certainty of the evidence (GRADE)
Mortality	152 out of 404	155 out of 424	11 more (from 51 fewer to 81 more)	HR 1.04 (0.83 to 1.3)	Moderate ⊕⊕⊕⊖
Quality of Life (better indicated by lower)	307	355	MD 1 higher (no CI provided)	-	High ⊕⊕⊕⊕
Hospitalization	307	355	MD 8 higher (2 lower to 17 higher)	-	Moderate ⊕⊕⊕⊖

Link to detailed evidence profile (Table 1,3,4,5)

Subgroup considerations:

1. DM vs No DM
2. HD vs PD
3. CVD vs no CVD
4. Hemoglobinuria vs no hemoglobinuria

Link to summary of findings and judgments for subgroups (Table 6)

ADDITIONAL CONSIDERATIONS

We updated the SR done by the Canadian Society of Nephrology. We identified 26 observational studies (29 reports) one randomized controlled trial (RCT)(4 reports)[8,9,10,11]and a published systematic review[12] comparing the effect of early vs late dialysis start on survival. We summarized the evidence informing each of the critical and important outcomes (mortality, quality of life and hospitalization) in GRADE evidence profile (Table1).

The IDEAL trial demonstrated no effect on mortality between patients randomized to the intent-to-start early versus intent-to-defer groups (hazard ratio [HR] 1.04, 95% CI=0.83 to 1.30). The pooled effect estimate from systematic review of observational studies was identical, but with a narrower confidence interval HR =1.04 (95%CI 1.03 to 1.05), and suggested a harmful effect with early initiation of dialysis. Residual confounding was, however, likely severe in this body of evidence. Of note, the patients randomised in the IDEAL trial are generally healthier (have fewer comorbidities) than the advanced CKD patients typically initiating dialysis in Saudi Arabia. (Table 3)

The IDEAL trial reported no significant difference in quality of life between patients randomized to the intent-to-start

Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings ☒	Undesirable consequences *probably outweigh* desirable consequences in most settings ☐	The balance between desirable and undesirable consequences *is closely balanced or uncertain* ☐	Desirable consequences *probably outweigh* undesirable consequences in most settings ☐	Desirable consequences *clearly outweigh* undesirable consequences in most settings ☐

Type of recommendation	We recommend against offering this option ☒	We suggest not offering this option ☐	We suggest offering this option ☐	We recommend offering this option ☐

Recommendation (text)

The KSA guideline panel recommends against "intent- to- start-early" rather than "intent-to-defer" strategy for initiating dialysis in adult patient (ag 18 years or more) with stage 5 CKD (an eGFR <15 ml/min/1.73m^2)

Justification

- This recommendation applies to adult patients who are 18 years old or older and does not apply to adolescence between 13 and 18 years old. The Saudi Expert Panel agreed that patients aged 13-18 years are likely to behave clinically different than adults for many reasons including small body size and going through maturity period. This group of patients (13-18 years old) is considered adult by the KSA MoH regulations and they are typically admitted to adult inpatient services. This creates a challenge in managing dialysis patients in this age group due to variation in comfort level among adult nephrologists who are expected to deal with this group especially when admitted.
- This recommendation applies to patients planning to use either chronic hemodialysis or chronic peritoneal dialysis. We do not consider pre-emptive transplantation, initiation of dialysis after failed transplant, urgent initiation of dialysis for acute kidney failure, conservative management without dialysis, or paediatric populations.
- Patients comorbidities and age, modality education and selection, rate of decline in eGFR, local waiting time for access (vascular access creation and maturation or peritoneal dialysis catheter insertion), access to interventional radiology and diagnostic imaging and availability of staff, physical space, equipment, or other resources requires for provision of a chosen modality are all factors that may influence the decision about timing of initiation of dialysis.
- Adherence to this recommendation requires availability of timely follow-up with a nephrologist to closely monitor clinical indications for dialysis initiation. These clinical indications for the initiation of dialysis include: symptoms of uremia, refractory fluid overload, hyperkalemia or acidemia, or other conditions or symptoms that are likely to be ameliorated by dialysis. In the absence of these factors, eGFR should not serve as a sole criterion for the initiation of dialysis unless it is ≤ 6 ml/min/1.72m^2.
- The 'intent-to-defer' strategy pertains specifically to timing of dialysis initiation, and does not mean that patients should be referred to nephrologists at a later stage (lower level of kidney function).

Subgroup considerations

We found no evidence to support a subgroup effect for patients:
1. initiating peritoneal or hemodialysis, 2. patients with or without diabetes, or 3. patients with high vs. low levels of comorbidity and outcome for intent-to-defer versus intent-to-start early strategies

Message

- Complete practice change of authorities in the field
- Also true for other recommendations

Adaptation

Breast cancer screening

CMAJ GUIDELINES

Recommendations on screening for breast cancer in average-risk women aged 40–74 years

The Canadian Task Force on Preventive Health Care

See related commentary by Gøtzsche on page 1957 and at www.cmaj.ca/lookup/doi/10.1503/cmaj.111721

Women aged 40–49 years

For women 40–49 years of age, we recommend not routinely screening for breast cancer with mammography. (Weak recommendation; moderate-quality evidence.)

Recommendations

Recommendation 1:

The Saudi Expert Panel suggests screening with mammography in women aged 40–49 years every 1 to 2 years. (Conditional recommendation; low-quality evidence)

Appendix 1: Evidence-to-Recommendation Tables and Evidence Profiles

BENEFITS & HARMS OF THE OPTIONS

CRITERIA	JUDGEMENTS
What is the overall certainty of this evidence?	☐ No included studies ☐ Very low ☒ Low ☐ Moderate ☐ High
Is there important uncertainty about how much people value the main outcomes?	☐ Important uncertainty or variability ☒ Possibly important uncertainty or variability ☐ Probably no important uncertainty or variability ☐ No important uncertainty or variability ☐ No known undesirable outcomes
Are the desirable anticipated effects large?	☐ No ☐ Probably No ☒ Uncertain ☐ Probably Yes ☐ Yes ☐ Varies
Are the undesirable anticipated effects small?	☐ No ☒ Probably No ☐ Uncertain ☐ Probably Yes ☐ Yes ☐ Varies
Are the desirable effects large relative to undesirable effects?	☐ No ☐ Probably No ☒ Closely balanced ☐ Probably Yes ☐ Yes ☐ Varies

RESEARCH EVIDENCE

The relative importance or values of the main outcomes of interest:

Outcome	Relative importance	Certainty of the evidence
Breast cancer mortality	Critical	Low
All cause mortality	Critical	High
False positive results	Important	Low
Overdiagnosis	Important	Low
Unnecessary biopsies or surgery	Important	Low
Radiation exposure	Important	Low
Anxiety, distress, or other psychological responses	Important	Low

Summary of findings: Screening for breast cancer with mammography (digital) vs no screening (40-49 years)

Outcome (follow-up: 11 yr)	Without screening	With mammography	Difference (per 1,000,000) (95%CI)	Relative effect (RR) (95%CI)	Certainty of the evidence (GRADE)
Breast cancer mortality	625 per 195,919	448 per 152,300	474 fewer (115 fewer to 792 fewer)	**RR 0.85** (0.75 to 0.96)	LOW
All cause mortality	2,388 per 132,172	1,373 per 79,098	484 fewer (1,615 fewer to 726 more)	**RR 0.97** (0.91 to 1.04)	HIGH
False positive results	-	32,700 per 100,000	-	-	LOW

ADDITIONAL CONSIDERATIONS

The opinion of guideline panel members was divided – 2 thought the outcome false positives were critical, two thought it was important. After further imput from a patient that attended the panel meeting, the outcome false positve results was rated down from critical to important.

To save one life from breast cancer over about 11 years in this age group, about:

- 2,100 women would need to be screened every 2 to 3 years
- 75 women would have an unnecessary breast biopsy
- 690 women will have a false positive mammogram leading to unnecessary anxiety and follow-up testing

§ Overdiagnose: Any invasive or noninvasive breast cancer

Remarks:

Based on local cancer registry data, the incidence of breast cancer in the KSA seems to be higher than in the other countries in which studies were conducted. This fact may indicate that higher benefit on breast cancer mortality justifies a recommendation in favor of implementing breast cancer screening using mammography in this age group. Since the guideline panel determined that there is a close balance between desirable and undesirable consequences, they also suggest implementing shared-decision making strategies as a way to incorporate actively patients' perspective into the decision.

Reason

- Different baseline risk in Saudi Arabia

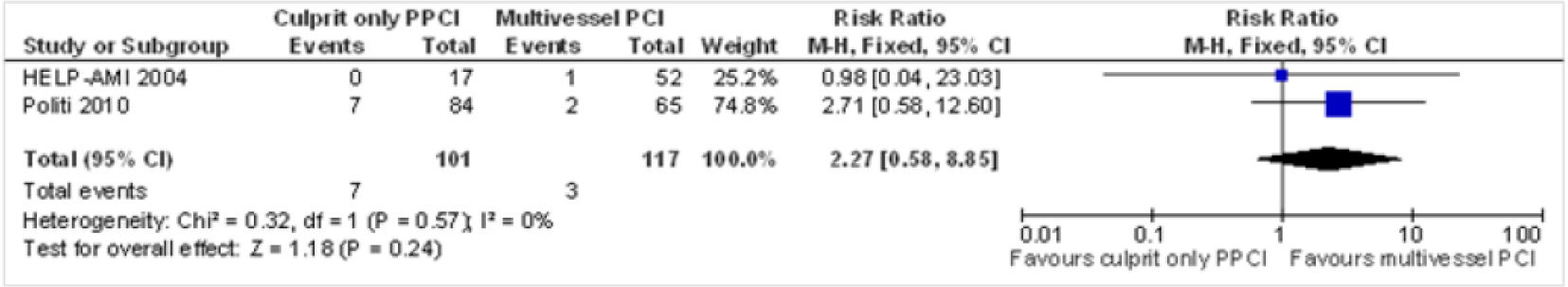
De novo recommendation: Multi vessel vs single vessel intervention for myocardial infarction

National Clinical Guideline Centre

I.5 Culprit versus complete revascularisation

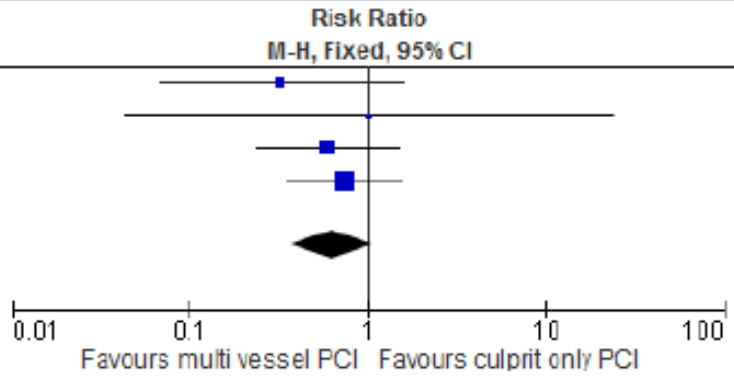
I.5.1 Culprit-only PPCI versus immediate multivessel PCI

Figure 180: RCTs: all-cause mortality (≤ 30 days)



Study or Subgroup	Multi vessel PCI Events	Total	Culprit only PCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
CvLPRIT 2015	2	150	6	146	17.7%	0.32 [0.07, 1.58]
Di Mario 2004	1	52	0	17	2.2%	1.02 [0.04, 23.91]
Politi 2010	6	65	13	84	33.1%	0.60 [0.24, 1.48]
Wald 2013	12	234	16	231	47.0%	0.74 [0.36, 1.53]
Total (95% CI)		**501**		**478**	**100.0%**	**0.63 [0.37, 1.05]**
Total events	21		35			

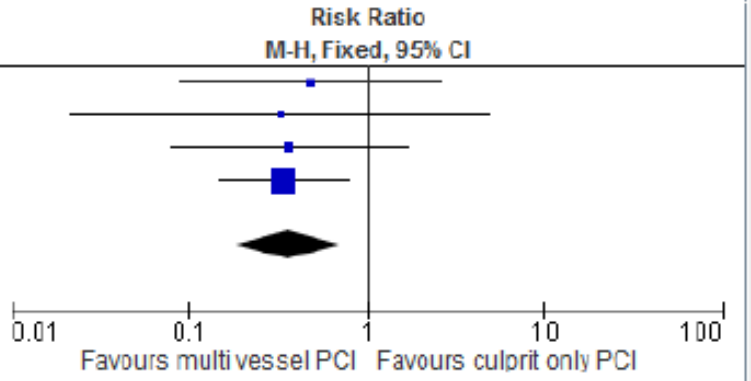
Heterogeneity: Chi² = 0.97, df = 3 (P = 0.81); I² = 0%
Test for overall effect: Z = 1.76 (P = 0.08)



Mortality-long term

Study or Subgroup	Multi vessel PCI Events	Total	Culprit only PCI Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
CvLPRIT 2015	2	150	4	146	12.7%	0.49 [0.09, 2.62]
Di Mario 2004	1	52	1	17	4.7%	0.33 [0.02, 4.95]
Politi 2010	2	65	7	84	19.2%	0.37 [0.08, 1.72]
Wald 2013	7	234	20	231	63.3%	0.35 [0.15, 0.80]
Total (95% CI)		**501**		**478**	**100.0%**	**0.37 [0.19, 0.71]**
Total events	12		32			

Heterogeneity: Chi² = 0.13, df = 3 (P = 0.99); I² = 0%
Test for overall effect: Z = 2.99 (P = 0.003)



Reinfarction

Two small trials vs four trials ~200 vs 1000 patients

Evidence Profile: Multi-vessel PPCI compared to culprit only PPCI in patients with STEMI and multi-vessel coronary artery disease undergoing PPCI

Author(s): Veena Manja & Wojtek Wiercioch
Date: 2014-12-15

Quality assessment							№ of patients		Effect		Quality	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	multi-vessel PPCI	culprit only PPCI	Relative (95% CI)	Absolute (95% CI)		
Mortality - long term												
4	randomised trials	serious [1]	not serious	not serious	serious [2]	none	21/501 (4.2%)	35/478 (7.3%)	**RR 0.63** (0.37 to 1.05)	27 fewer per 1000 (from 4 more to 46 fewer)	⊕⊕◯◯ LOW	CRITICAL
Reinfarction												
4	randomised trials	serious [1]	not serious	not serious	not serious	none	12/501 (2.4%)	32/478 (6.7%)	**RR 0.37** (0.19 to 0.71)	42 fewer per 1000 (from 19 fewer to 54 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Revascularization												
4	randomised trials	serious [1]	not serious	not serious	not serious	none	38/501 (7.6%)	92/478 (19.2%)	**RR 0.37** (0.26 to 0.53)	121 fewer per 1000 (from 90 fewer to 142 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL

Message

- Saudi Arabian panel more certain in decision/recommendation
- Reason:
  - NEW EVIDENCE IDENTIFIED during our effort

Summary for adolopment

Advantages

- Builds in part on existing evidence syntheses
- Transparent consideration of factors beyond QoE (EtDs) with focus on local/regional setting
- Builds capacity
- By recommendation rather than by guideline

Challenges

- SRs required as starting point
- Challenging if existing SR restricted inclusion to RCTs or highly selected outcomes
- Reviews of “other information”
- Panels need to commit to follow rigorous methodological approach and stick to timelines

How to get started

- Would begin with extracting all PICO questions and list them for identifying priorities
  - From existing guideline (go to website of TB guidelines)

Slides for Holger

- Will show example from a recent thromboembolism guideline we developed on surveymonkey on how to prioritize
  - Use those that are most important or all
  - Agree in meeting with panel members
- Extract information to iEtD or use iEtDs
- Demonstrate agreement on individual criteria
  - Online or in person
- Demonstrate policy maker modification

Discussion