



Evidence-Based Guideline on Hemophilia Care: **A Model for Rare Disease Guidelines**

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Conflict of Interest Disclosure

- ▶ I will not discuss off label use or investigational use of drugs/devices/procedures in my presentation.
- ▶ I have no relevant financial relationships to disclose

Learning Objectives

- ▶ Describe the challenges of guideline creation in rare diseases
- ▶ Learn how novel guideline creation methods were used in an evidence-based guideline on hemophilia care
- ▶ Discuss the NHF-McMaster Guidelines recommendations around models of care

Guideline Creation in Rare Diseases

"Guidelines are recommendations intended to assist providers and recipients of health care and other stakeholders to make informed decisions. Recommendations may relate to clinical interventions, public health activities, or government policies."

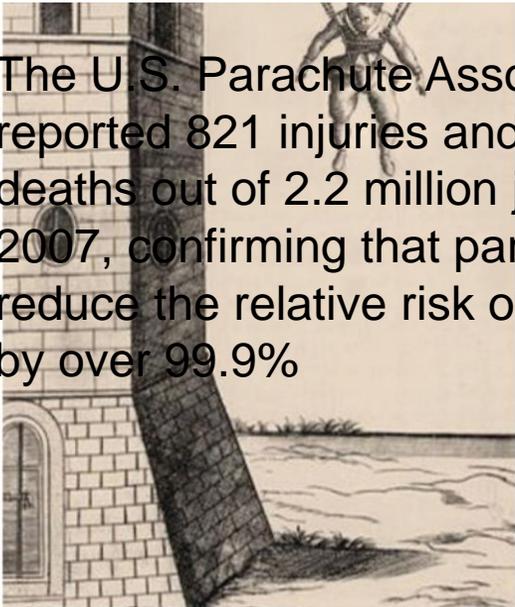
- WHO 2007

Sometimes Decision Making is Easy

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

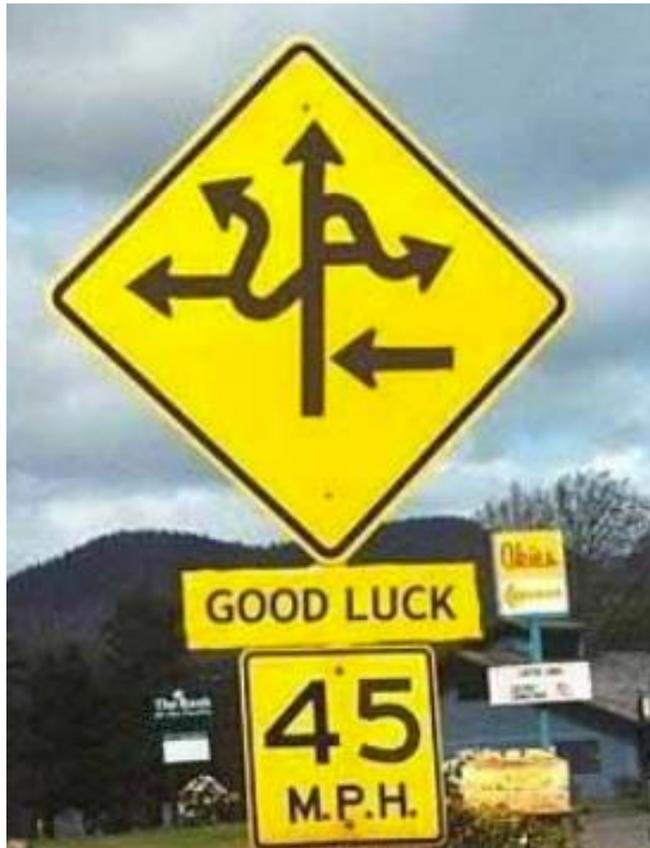
Gordon C S Smith, Jill P Pell

The U.S. Parachute Association reported 821 injuries and 18 deaths out of 2.2 million jumps in 2007, confirming that parachutes reduce the relative risk of death by over 99.9%



Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials

Sometimes Decision Making is Hard



How Do We Make Good Decisions?

- ▶ Understand the evidence behind our choices
- ▶ Understand the impact of our choices (good and bad!)
- ▶ Personalize our decision to the patient and their family



Guideline development for rare diseases is challenging for many reasons

Guideline development

- Lack of data on key, patient-important outcomes
- Poor quality data
- Heterogeneous data

The NHF- McMaster Guidelines on Models of Care in Hemophilia

APPLYING NOVEL
STRATEGIES TO
GUIDELINE CREATION
IN RARE DISEASES

A Unique Sponsoring Organization

- ▶ National Hemophilia Foundation (NHF)
 - ▶ Find better treatments and cures for all bleeding disorders and prevent complications through education, advocacy and research support
- ▶ Recognition of the changing healthcare environment
- ▶ Urgent need to strengthen evidence-base for hemophilia care



Priority setting by the National Hemophilia Foundation (NHF)

It's r

compression
physiotherapy
treatment
ice
rfVIIa
FEIBA

ver,

1. Integrated (comprehensive) care settings
▶ Is integrated care the optimal model of care for hemophilia?
2. Specialists in a non-specialized setting
▶ What is the range of care providers and services that are most important to PWH?
3. Non-specialists in a non-specialized setting

test

Goals of the NHF-McMaster Guideline

1. To identify best practices in haemophilia care delivery and discuss the range of care providers and services that are most important for persons with haemophilia (PWH) across the United States
2. To support patient-centred clinical decision-making and optimize haemophilia care for each patient

Project grounded in transparent,
internationally accepted processes



Agency for Healthcare Research and Quality
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*The National
Academies of*

SCIENCES
ENGINEERING
MEDICINE



Generating questions that are important to patients

- Q2: For individuals with hemophilia, should a hematologist, a specialized hemophilia nurse, a physical therapist, a social worker, and round-the-clock access to a specialized coagulation laboratory be part of the integrated care team, versus an integrated care team with a lesser complement?
- Q1: Should integrated care versus non-integrated care be used for people with hemophilia (PWPH)?

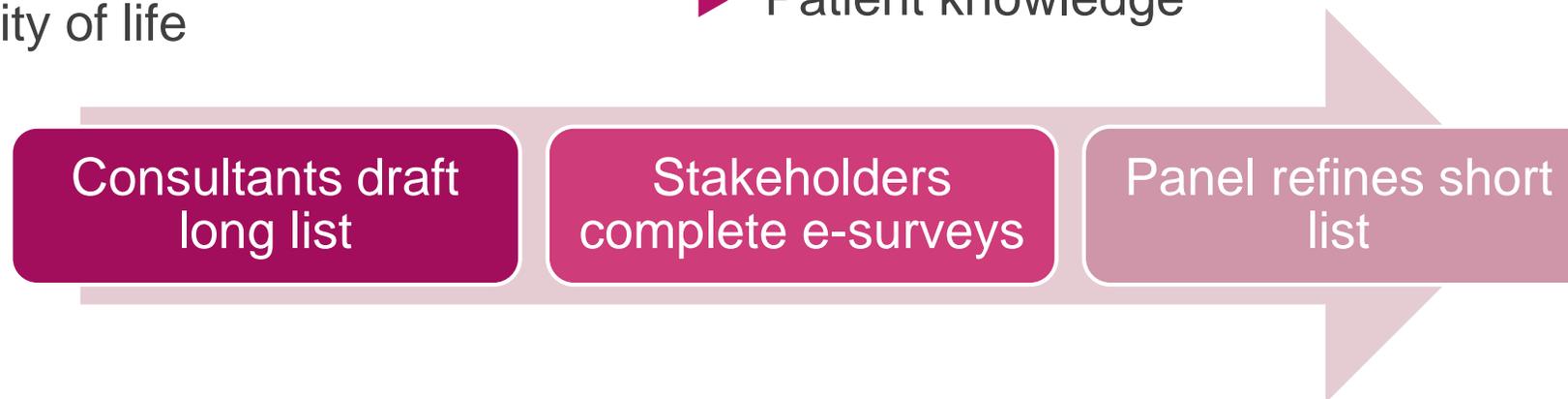
Consultants draft questions

Stakeholders complete e-surveys

Panel refines questions

Selecting outcomes that are important to patients

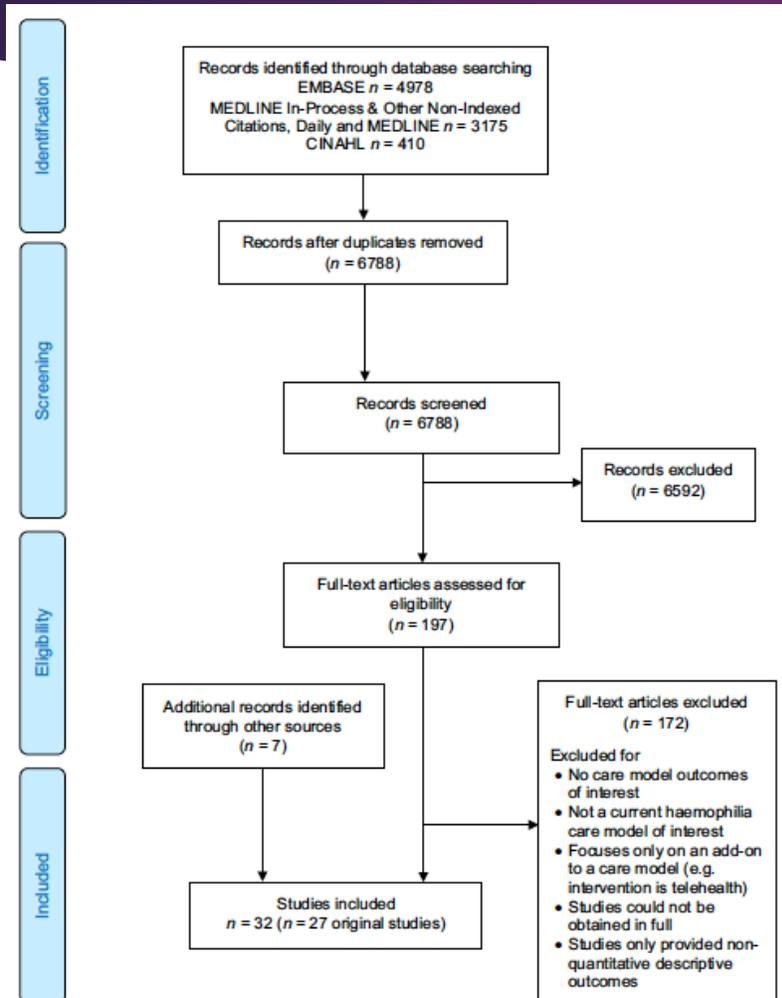
- ▶ Mortality / survival
- ▶ Missed days from work/school
- ▶ Number of ER visits
- ▶ Length of in-patient stay
- ▶ Quality of life
- ▶ Functional outcomes - joint damage/joint disease
- ▶ Educational attainment
- ▶ Patient adherence
- ▶ Patient knowledge



Building the Foundation: Identifying published evidence

- ▶ Systematic reviews of published literature were performed by McMaster Consultants
- ▶ Answer our two questions:
 - ▶ **Give answers with DIRECTION:** Identify information on outcomes, as well as information on patients' values and preferences, equity, acceptability, feasibility, and resource use
 - ▶ **Give answers with STRENGTH:** Identify non-comparative observational studies, comparative observational studies, randomized trials, and systematic reviews

High Quality Evidence was Scarce



Little published evidence to guide us!

Filling in the Gaps: Parallel Searches of Other Diseases

- ▶ Parallel systematic searches of other chronic diseases
 - ▶ Congestive heart failure
 - ▶ Chronic obstructive pulmonary disease,
 - ▶ Asthma
 - ▶ Diabetes
- ▶ Panel decided how indirect the evidence was, then extrapolated it to inform recommendations for hemophilia

Characteristics of the review	Your comments	Judgment – Is the evidence sufficiently direct?			
Population: children (mean age 26) and adults (mean age 36 to 47) with asthma		<input type="checkbox"/> Yes	<input type="checkbox"/> Probably yes	<input type="checkbox"/> Probably no	<input type="checkbox"/> No
Intervention: Studies published from 1999-2004. Care provided in an asthma clinic by primarily nurses and general practitioners		<input type="checkbox"/> Yes	<input type="checkbox"/> Probably yes	<input type="checkbox"/> Probably no	<input type="checkbox"/> No
Outcome: Missed days of school or work		<input type="checkbox"/> Yes	<input type="checkbox"/> Probably yes	<input type="checkbox"/> Probably no	<input type="checkbox"/> No
Outcome: Number of emergency room visits		<input type="checkbox"/> Yes	<input type="checkbox"/> Probably yes	<input type="checkbox"/> Probably no	<input type="checkbox"/> No
Outcome: Quality of life using scales specific to respiratory and asthma conditions		<input type="checkbox"/> Yes	<input type="checkbox"/> Probably yes	<input type="checkbox"/> Probably no	<input type="checkbox"/> No
Final judgment about indirectness across domains:	<input type="checkbox"/> No indirectness	<input type="checkbox"/> Serious indirectness	<input type="checkbox"/> Very serious indirectness		

Filling in the Gaps: Qualitative interview-based study

- ▶ Additional information to inform good recommendations:
 - ▶ What outcomes are valued?
 - ▶ What is the impact on health inequities?
 - ▶ What options are acceptable and feasible?
- ▶ 29 interviews with stakeholders in 18 states, 26 centers



Filling in the Gaps: Structured “Expert” Observations

What is your centre like?

What are the roles of
HCPs in your centre?

**“Expert”
Observations**

What is the perceived
impact of HCPs on key
outcomes?

Comments (including
unpublished data)

Final Recommendations from the Guideline Panel

For persons with hemophilia

The integrated care model should be used over non-integrated care models

- Clear health benefits + complete absence of health harms of this model in common diseases... So we can probably EXTRAPOLATE to hemophilia
- This model appears equitable, feasible, and acceptable
- Resource use appears “worth it” when you consider benefits
- Thought to benefit all subgroups

Final Recommendations from the Guideline Panel

For persons with hemophilia with inhibitors and those at high risk for inhibitor development

The integrated care model should be used over non-integrated care models

- Absolute benefit of integrated care is likely larger in this group of persons with hemophilia, since (at baseline) they have a higher absolute risk of harms

Final Recommendations from the Guideline Panel

For persons with hemophilia

Team should include:
hematologist,
specialized
hemophilia nurse,
physical therapist,
social worker, and
round-the-clock
access to
specialized
coagulation
laboratory

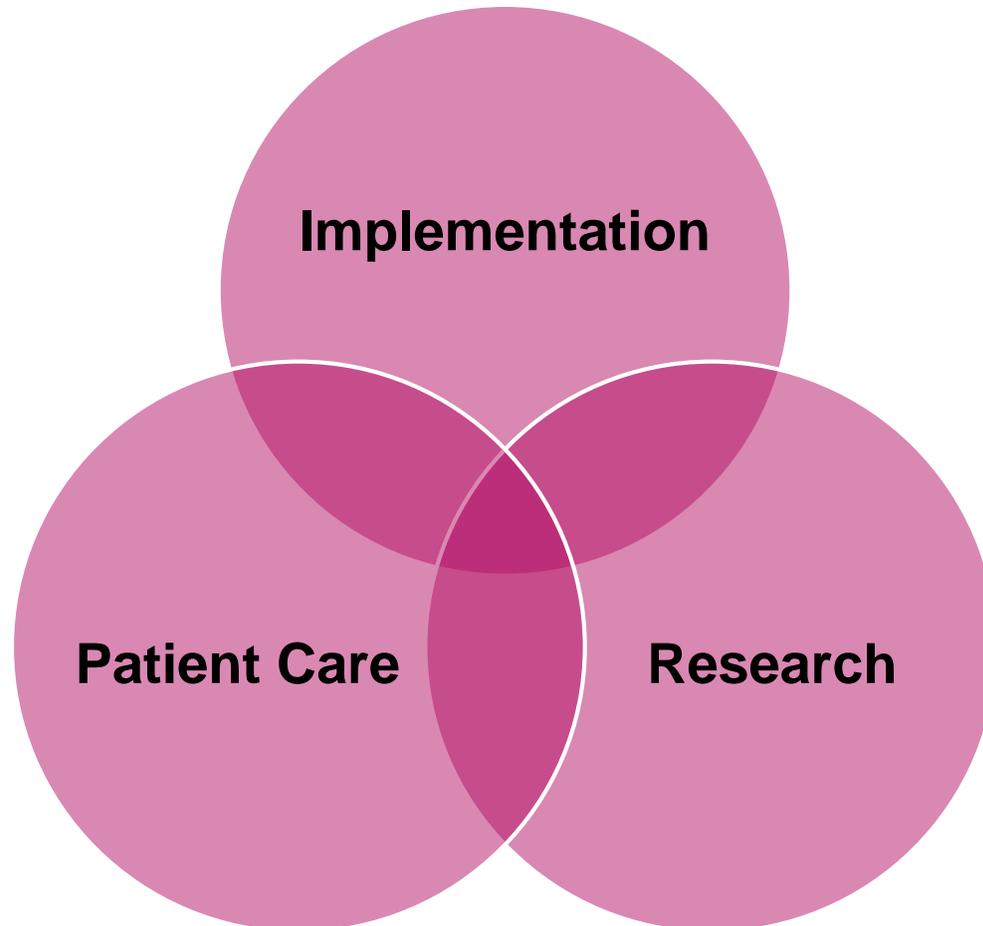
- Survey studies, stakeholder interviews, and “expert” evidence suggest each part of integrated care model has value
- Difficult to tease out contribution of each component



Next steps

HOW DO WE USE THIS
GUIDELINE TO
IMPROVE QUALITY OF
CARE IN HEMOPHILIA...
AND OTHER RARE
DISORDERS?

Guidelines impact three major domains



Going Beyond the Guidelines: How do we IMPLEMENT this guideline?

- ▶ Identify and address barriers to accessing care
 - ▶ Age, geographic location, race/ethnicity, insurance status, capacity of centres, stable funding streams for centres
- ▶ Standardize components of integrated care team
- ▶ Train, recruit and retain specialized health care team members
- ▶ Develop and track performance measures to ensure PWH get the resources and care they need

Going Beyond the Guidelines: How can this guideline improve CARE?

- ▶ **Provides guidance for payers and insurers, hospitals and healthcare systems, and policymakers at all levels**
- ▶ Guideline is a framework to evaluate successes and shortcomings of models of care delivery
 - ▶ Confirms impact of integrated care on outcomes that matter to patients
 - ▶ Confirms that integrated care centres continue to provide high quality care for hemophilia
 - ▶ Suggests that integrated care centres can play a role in:
 - ▶ Tracking safety and efficacy of therapies
 - ▶ Developing cost-effective treatment paradigms

Going Beyond the Guidelines: How can this guideline improve CARE?

- ▶ **Provides guidance for individual healthcare providers and researchers**
- ▶ Suggests evidence-based performance benchmarks to evaluate the system and individual care centres
 - ▶ Is this a step towards self-audit?
 - ▶ Is this a step towards external accreditation?
- ▶ Calls for new studies to determine the coordinated set of diagnostic, therapeutic, and auxiliary / supplemental services that most important for persons with hemophilia

Going Beyond the Guidelines: How can this guideline improve CARE?

- ▶ **Provides guidance for patients and families**
- ▶ Establishes a “standard of care”
- ▶ Empowers patients to communicate with their providers to...
 - ▶ Advocate for a core complement of services
 - ▶ Advocate for care in an integrated setting
- ▶ Acknowledges that every patient has unique needs

Going Beyond the Guideline: How can we push RESEARCH forward?

- ▶ Gaps in data around rare bleeding disorders exist!
 - ▶ Populations to study
 - ▶ Interventions to study
 - ▶ Outcomes to study
- ▶ Hemophilia Treatment Centres must build data collection and analysis capacity, to conduct high quality, well-organized studies

Guideline Endorsements

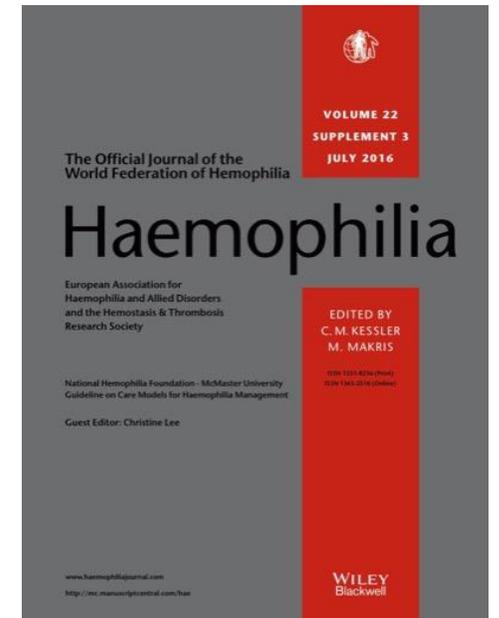
- ▶ Endorsed by World Federation of Hemophilia, American Society of Hematology, International Society for Thrombosis and Haemostasis
- ▶ Included in National Guidelines Clearinghouse
 - ▶ Guideline summary: NHF-McMaster guideline on care models for haemophilia management. In National Guideline Clearinghouse (NGC) [Web site]. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2016 Jul 01. [cited 2017 Feb 06]. Available: <https://www.guideline.gov>



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Helping hematologists conquer blood diseases worldwide

Guideline Dissemination

- ▶ Detailed guideline, introduction to care models in hemophilia, methods paper, two systematic reviews, and qualitative study published in Haemophilia in July 2016.
- ▶ Archived in National Guideline Clearinghouse: <https://www.guideline.gov>
- ▶ Additional information: www.hemophilia.org



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WFH

WORLD FEDERATION OF HEMOPHILIA

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Big Picture Summary

- ▶ Rare diseases pose a unique challenge to guideline methodologists
- ▶ We need to use rigorous, transparent, and creative strategies to create guidelines that improve patient care
 - ▶ Extrapolating from more common diseases
 - ▶ Interviewing key stakeholder groups
 - ▶ Accessing “expert evidence” in a systematic way
- ▶ Integrated care model appears to provide high quality, multifaceted care for PWH, and has a favourable profile in terms of costs, acceptability, feasibility, and implementability

Thank you to the
patients, families,
health care providers,
and policy makers
who work to optimize
bleeding disorder
care every day!

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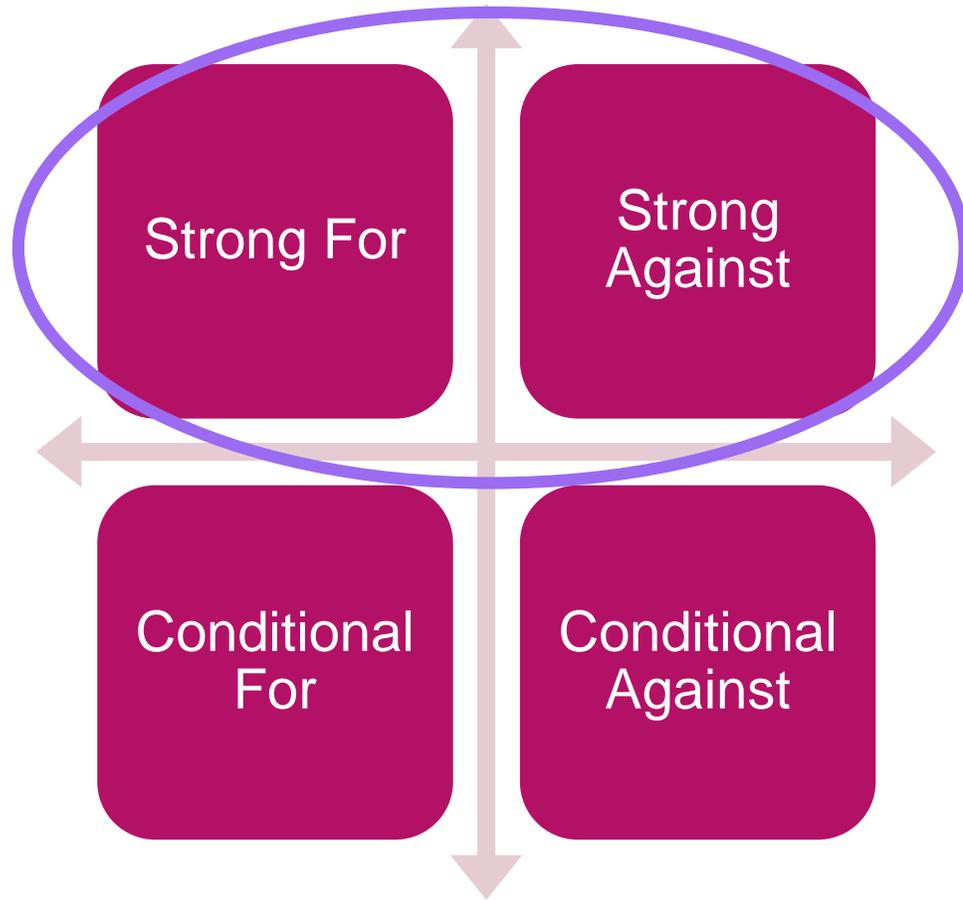
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EXTRA SLIDES

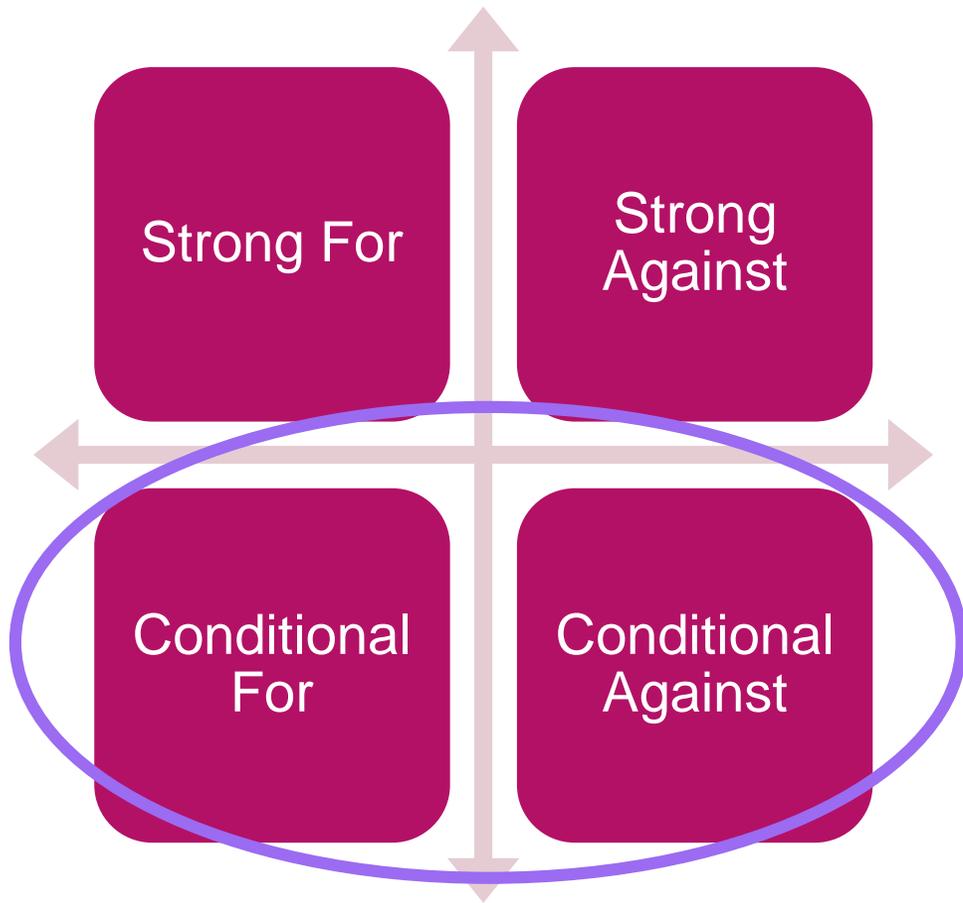
Strength of recommendation



▶ STRONG RECOMMENDATION

- ▶ Policy makers: The recommendation can be adapted as a policy in most situations
- ▶ Clinicians: Most patients should receive the recommended course of action
- ▶ Patients: Most people in this situation would want the recommended course of action. Only a small proportion would not

Strength of recommendation



▶ **CONDITIONAL RECOMMENDATION**

- ▶ Policy makers: Need for substantial debate and involvement of stakeholders
- ▶ Clinicians: Be more prepared to help patients make a decision consistent with their own values. Use decision aids and shared decision making.
- ▶ Patients: Most people in this situation would want the recommended course of action. Many would not.