



**Multicriteria decision analysis (MCDA) for drug coverage decision by a public health plan: case study of tramadol for chronic non-cancer pain (CNCP) in Canada**

**17 May 2010, Atlanta**

**Michele Tony BSc,<sup>1</sup> Mireille M Goetghebeur PhD,<sup>1</sup> Monika Wagner PhD,<sup>1</sup>  
Hanane Khoury PhD,<sup>1</sup> Donna Rindress PhD,<sup>1</sup> Paul Oh MD<sup>2</sup>**

<sup>1</sup>BioMedCom, Montreal, Quebec, Canada

<sup>2</sup>Toronto Rehabilitation Institute, Toronto, Ontario, Canada

\*MSc Candidate, University of Montreal

# Acknowledgments

## Committee members

- ❖ Drug Advisory Committee, Workplace Safety Insurance Board (WSIB) of Ontario, Toronto, Canada

## Web developers

- ❖ Patricia Campbell BSc & Peter Melnyk PhD, BioMedCom, Montreal, Canada

## Funding

- ❖ Internal sources of support provided by BioMedCom and WSIB



## Structuring the natural thinking process

# Background: MCDA & EVIDEM

## ❖ Multicriteria decision analysis (MCDA)

- ❖ Reflection on criteria at play in healthcare decisionmaking
- ❖ Reflection on perspectives, values and priorities
- ❖ Simultaneous consideration & quantification of a wide range of criteria of decision (beyond cost-effectiveness model)

## ❖ EVIDEM Collaboration

- **Framework\***: Comprehensive set of standard criteria of decision with tools and processes to consider them (HTA, MCDA, ethics & values)
- **Collaborative Registry**: open web based interactive relational database with synthesized evidence for decisionmaking contexts globally

# Standard criteria of decision

## Quantitative considerations (intrinsic value - MCDA matrix)

### Disease impact

- Disease severity
- Size of population affected by disease

### Context of intervention

- Clinical guidelines
- Comparative intervention limitations

### Intervention outcomes

- Improvement of efficacy/effectiveness
- Improvement of safety and tolerability
- Improvement of patient reported outcomes

### Type of benefit

- Public health interest (e.g., prevention, risk reduction)
- Type of medical service (e.g., symptom relief, cure)

### Economics

- Budget impact on health plan (cost of intervention)
- Impact on other spending (e.g., hospitalization, disability)
- Cost-effectiveness of intervention

### Quality/uncertainty of evidence

- Adherence to requirements of decisionmaking body
- Completeness and consistency of reporting evidence
- Relevance and validity of evidence

## Qualitative considerations (extrinsic value - tool)

### Ethical framework

- Goals of healthcare - **utility**
- Opportunity costs - **efficiency**
- Population priority & access - **fairness**

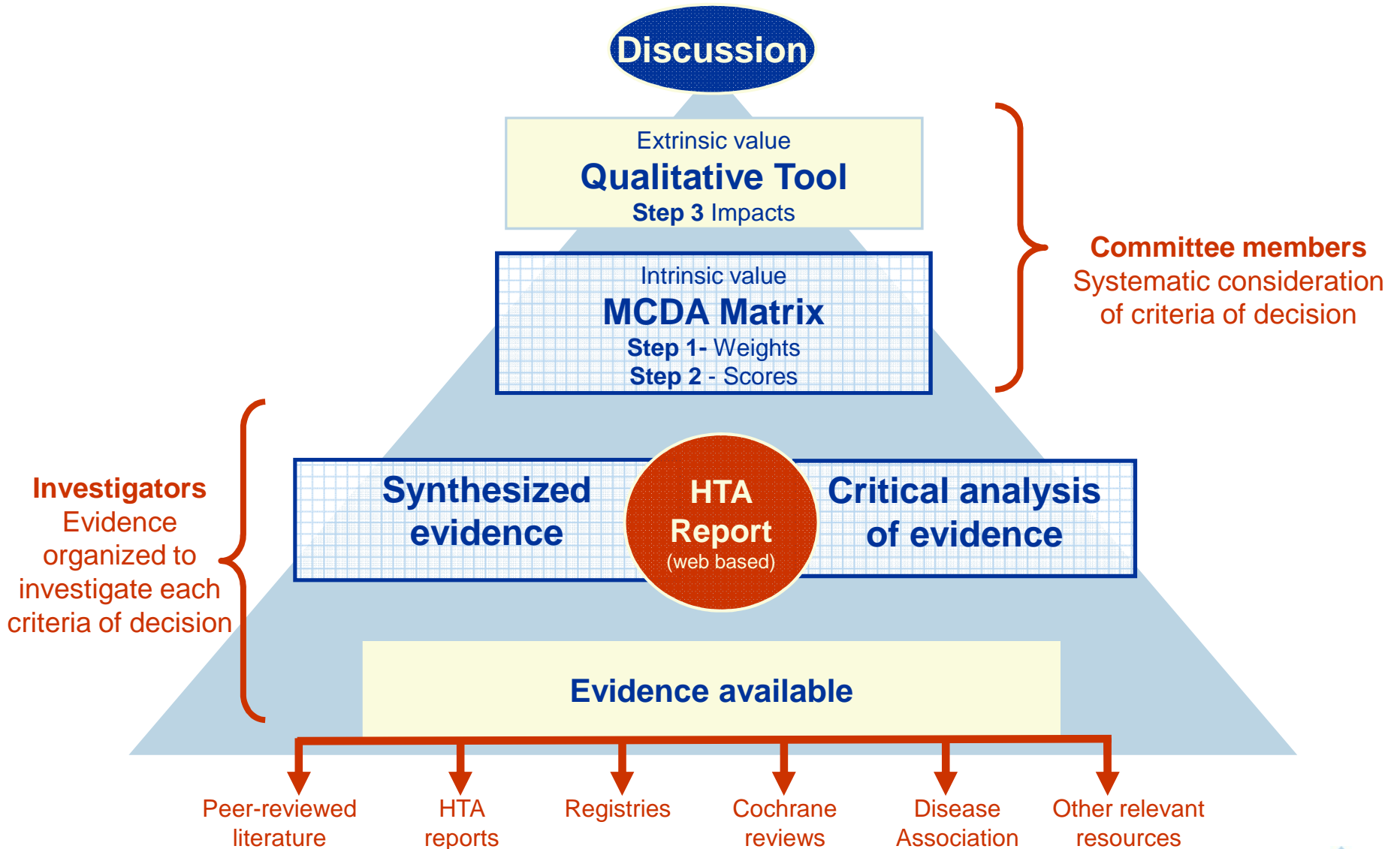
### Other system-related criteria

- System capacity and appropriate use of intervention (e.g., infrastructure)
- Stakeholder pressures (e.g., media)
- Political/historical context (e.g. precedence, national priority)

# Objectives

- ❖ To field-test a decision support framework (EVIDEM) and explore its utility to a drug advisory committee using tramadol for chronic non-cancer pain (CNCP) as a case study.

# Methods



# Data collection & analyses

- ❖ **Weights, scores and impacts:** elicited during workshop sessions with committee members
- ❖ **Feedback on framework :** elicited via survey & discussion during workshop sessions
- ❖ **MCD A estimate:** linear model [sum of value contribution ( $V_x$ ) of combined normalized weights ( $W_x$ ) and scores ( $S_x$ ) for applicable criteria ( $n$ ) of the matrix]

$$V = \sum_{x=1}^n V_x = \sum_{x=1}^n \left( \frac{W_x}{\sum_{x=1}^n W_x} \times S_x \right)$$

# Results - Web based interactive HTA reports

- ❖ Open source software (Tikiwiki)
- ❖ Access to evidence
  - ❖ Structured by criterion of decision
  - ❖ Synthesized evidence
  - ❖ Full text sources of data
- ❖ Data entry & collection
  - ❖ Weights, scores, impacts, feedback
  - ❖ Data collection (MySQL database)

## Record menu

### PREAMBLE

The prototype below includes data on tramadol for patients with chronic non-cancer pain in Canada. To access highly synthesized data with hyperlinks to details and sources, visit [EVIDEM lite](#).

The objective of the EVIDEM framework is to support systematic consideration of criteria of decision when evaluating a healthcare intervention. The framework includes a standard set of criteria of decision with a process to report evidence tailored to investigate each criterion of decision. These components are categorized as:

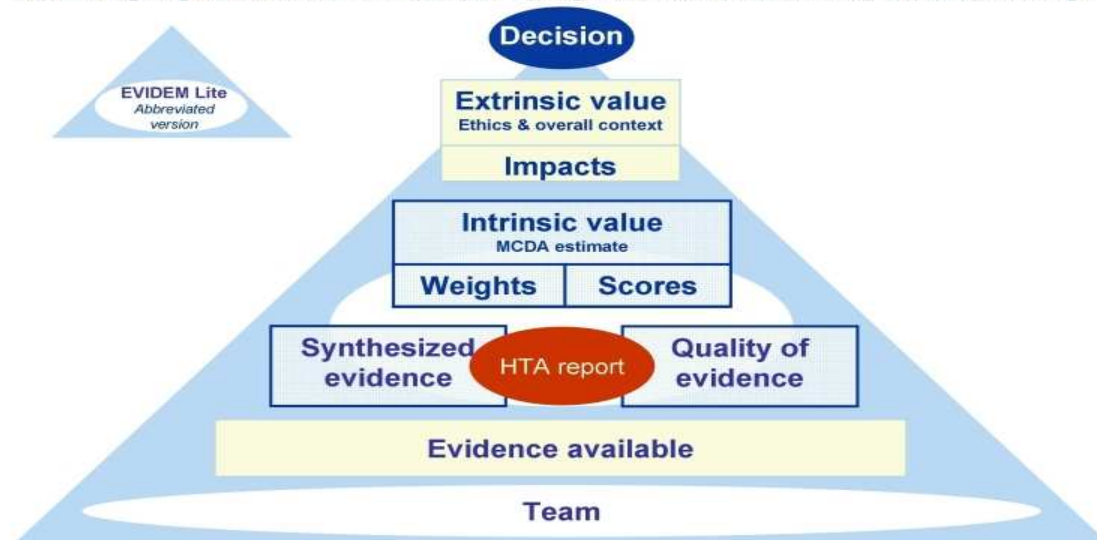
- quantifiable from a universal standpoint - defining the intrinsic value of an intervention, estimated using the MCDA Matrix (steps 1 & 2)
- not quantifiable from a universal standpoint and related to healthcare system, ethics and priorities - defining the extrinsic value of an intervention explored using the Extrinsic Criteria Tool (step 3)

### Tramadol for chronic non-cancer pain in Canada

See methodology to develop this EVIDEM record

### EVALUATOR INSTRUCTIONS

Step 1: Weighting MCDA Matrix criteria ; Step 2: Scoring intervention (MCDA Matrix); Step 3: Considering impact of extrinsic criteria tool; Step 4: See my data



EVIDEM team, Evidence Available, Synthesized Evidence, Quality Matrix, Weighting MCDA Matrix criteria, Scoring intervention - MCDA Matrix , Impact of Extrinsic components, EVIDEM Lite

## QUANTIFIABLE CRITERIA (INTRINSIC VALUE)

MCDA estimate is obtained by combining normalized weights assigned independent of intervention and scores based on synthesized data available (MCDA Matrix)

	Intrinsic criteria	Highly synthesized information	Minimum score for intervention (0)	Maximum score for intervention (3)
	<b>Disease impact</b>			
D1	Disease severity	Chronic non-cancer pain includes nociceptive (tissue damage) and neuropathic (nerve pathology) pain; 37% of low back pain of neuropathic origin. Disabling condition interfering with activities of daily living (28% patients), work (lost income in 49% patients) and education. Associated with depression and/or anxiety (40% patients). <i>(Assign score/ See data details)</i>	Not severe	Very severe
D2	Size of population	<b>Prevalence/Incidence:</b> Canadian pain study 2004 (N=1055 in general population): 25% with chronic pain (88% moderate or severe); mean duration 9.8 years. <i>(Assign score/ See data details)</i>	Very rare disease	Common disease
	<b>Context of intervention</b>			
C1	Clinical guidelines	<b>Canadian Pain Society guidelines:</b> <b>Chronic non-cancer pain (2002):</b> no mention of tramadol - mild to moderate: 1st line non-opioid, 2nd line opioid (moderate to severe pain: switch to opioid earlier) <b>Chronic neuropathic pain(2007):</b> 3rd line tramadol/conventional opioid <b>Other countries recommending tramadol for:</b> <b>*Osteoarthritis:</b> 2nd line, USA <b>*Chronic low back pain:</b> 2nd line, USA and Europe <b>*Fibromyalgia:</b> 2nd line, USA <i>(Assign score/ See data details)</i>	No recommendation	Strong recommendation
C2	Comparative interventions limitations	<b>NSAIDs and COX-2 inhibitors:</b> ceiling effect in pain reduction; organ damage after long term use (cardiac and renal; and gastric for NSAIDs) <b>Opioids:</b> not efficacious in pain of neuropathic origin; gastrointestinal (constipation, nausea, vomiting), respiratory (respiratory depression) and neurologic (dizziness, somnolence) side effects; risk of tolerance/dependence/abuse <b>Specific to neuropathic pain:</b> <b>*Anticonvulsants</b> (e.g.,gabapentin, pregabalin): sedation, dizziness, ataxia, somnolence, confusion <b>*Tricyclic antidepressants</b> (e.g., amitriptyline): sedation, dry mouth, constipation, orthostatic hypotension, weight gain <b>*SNRIs</b> (e.g.,duloxetine, venlafaxine): nausea, dyspepsia, sweating, somnolence and insomnia <b>*SSRIs</b> (e.g. fluoxetine): agitation, anxiety, sleep disturbance, tremor, sexual dysfunction and headache <i>(Assign score/ See data details)</i>	No or very minor limitations	Major limitations
	<b>Intervention outcomes</b>			
I1	Improvement of efficacy/ effectiveness	<i>Trial results obtained with WOMAC and other scales were recalculated to be expressed on a normalized scale from 0 (minimum improvement) to 100 (maximum improvement). If not mentioned, no significant difference</i> <b>5 Head to head randomized controlled trials</b> (osteoarthritis, low back pain & other; 4 to 12 weeks; N =108 to 1001; 1 in Canada, 4 in USA): <b>*Pain intensity reduction from baseline:</b> tramadol: 15-24; diclofenac: 16; celecoxib: 26 (P=0.05 vs placebo); placebo: 19 (significant difference for all vs baseline) <b>*Pain intensity reduction after 6 hrs:</b> tramadol: 21; codeine: 18  <b>Placebo randomized controlled trials (Cochrane reviews):</b> <b>*Pain intensity reduction versus placebo:</b> <b>*8.5</b> (osteoarthritis, 3 trials, N= 92 to 307) , <b>*10.8</b> (chronic low back pain, 3 trials, N= 254 to 336) <b>*Patients achieving 50% pain relief:</b> 63% tramadol vs 37% placebo (neuropathic pain, 3 trials, N=67 to 127) <i>(Assign score/ See data details)</i>	Lower than comparators	Major improvement
I2	Improvement of safety &	<b>Summary of common AEs</b> (> 5% of patients in RCTs and frequency > twice of placebo in tramadol product	Lower than	Major improvement

# I1 Improvement of efficacy/effectiveness

## SCORING INSTRUCTIONS

- Score the efficacy/effectiveness of the intervention in relation to comparative interventions presented (consider clinical significance of outcomes measures)
- Score from a relative point of view (relative to comparative interventions)
- Comments may be provided to communicate data needs

Scoring example (for information only):

0: Lower efficacy/ effectiveness than comparators

1: Same efficacy as comparator

2: Some improvement in efficacy/ effectiveness

3: Major improvement in efficacy/effectiveness, larger eligible population

Score	Comments
<input type="radio"/> 0 Lower efficacy/effectiveness than comparators presented	
<input type="radio"/> 1	
<input type="radio"/> 2	
<input type="radio"/> 3 Major improvement in efficacy/effectiveness	

<input type="checkbox"/> Low Score due to data limitation - specify Scoring by memberall
--

Submit, return to scoring menu

## SYNTHESIZED EVIDENCE

**5 Head to head randomized clinical trials (osteoarthritis, low back pain)**  
**Inclusion criteria for trials:** Age: ≥ 18 years; adults patients with chronic pain  
**Exclusion criteria for trials:** patients not relevant to the insured population, postoperative pain, and acute flares of chronic conditions

Results in trials recalculated to be expressed on a normalized scale from 0-100  
**Pain intensity reduction from baseline:** tramadol: 15-24; diclofenac: 15-24  
**Pain intensity reduction after 6 hrs:** tramadol: 21; codeine: 18

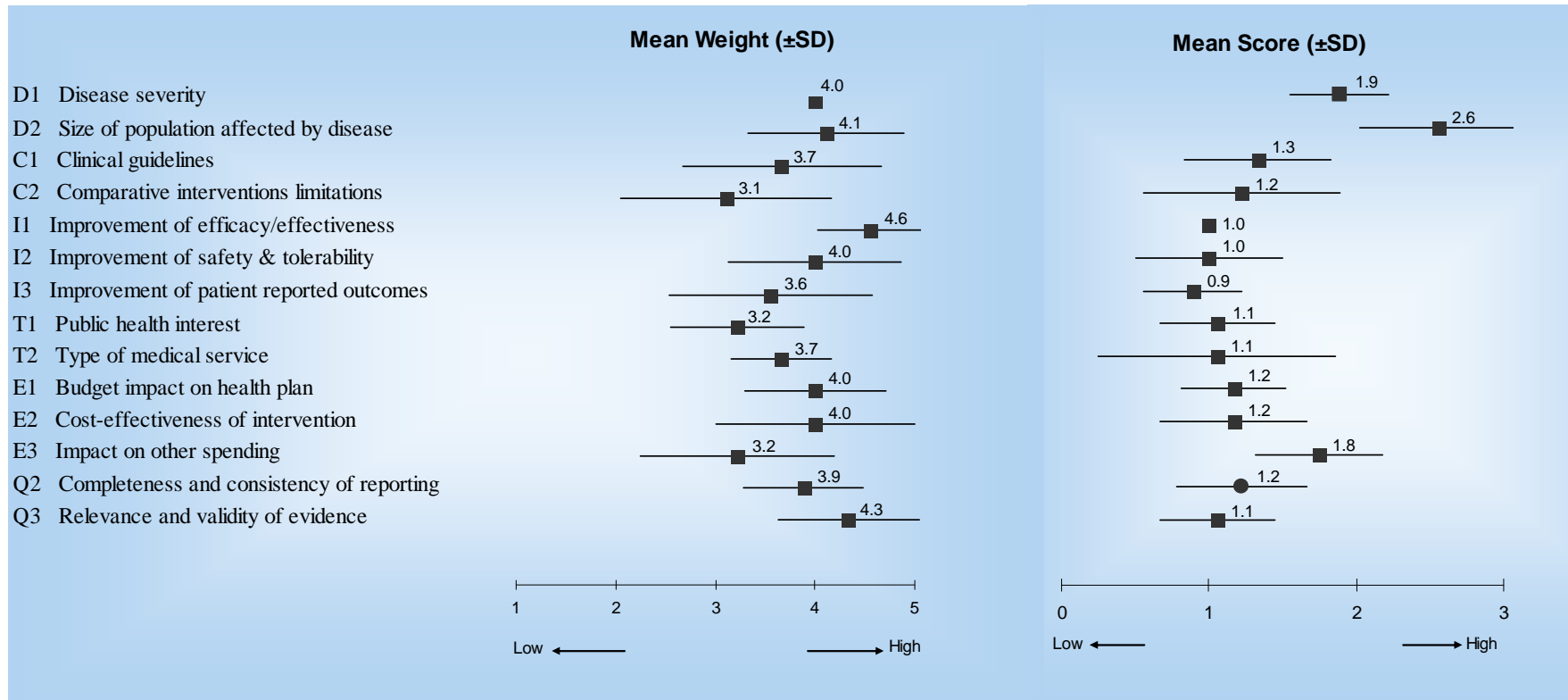
Trial	Population (N)	Duration
<b>Beaulieu et al 2008</b>	<b>Osteoarthritis</b>	<b>6 weeks</b>
Tramadol 200-400 mg CR*	62	
Diclofenac 75-140 mg SR*	66	
<b>Pavelka et al 1998</b>	<b>Osteoarthritis</b>	<b>4 weeks†</b>
Tramadol 200-400 mg CR*	62	
Diclofenac 75-140 mg SR*	66	
<b>Mullican et al 2001</b>	<b>Low back pain &amp; Osteoarthritis</b>	<b>4 weeks (data at day 22)</b>
Tramadol/APAP 37.5-375 mg/325-3250 mg	309	

The screenshot shows a web browser window displaying a PubMed search result. The browser's address bar shows the URL: <http://www.ncbi.nlm.nih.gov/pubmed/18443672?dopt=Citation>. The page title is "Once-daily, controlled-release tramadol and sustained-release diclofenac relieve chronic pain due to osteoarthritis: a randomized controlled trial". The search bar contains "PubMed" and the search button is visible. The article title is prominently displayed, followed by the authors: "Beaulieu AD, Peloso PM, Haraoui B, Bensen W, Thomson G, Wade J, Quigley P, Eisenhoffer J, Harsanyi Z, Darke AC." and the journal information: "Pain Res Manag. 2008 Jul-Aug;13(4):342." The abstract text is visible, starting with "OBJECTIVE: The present study was a randomized, parallel, double-blind comparison between controlled-release (CR) tramadol and sustained-release (SR) diclofenac in patients with chronic pain due to osteoarthritis of the hips and/or knees." The page also includes a "Related citations" section with several links to other articles, and a "Recent activity" section at the bottom right.

# Appraisal of tramadol - raw data

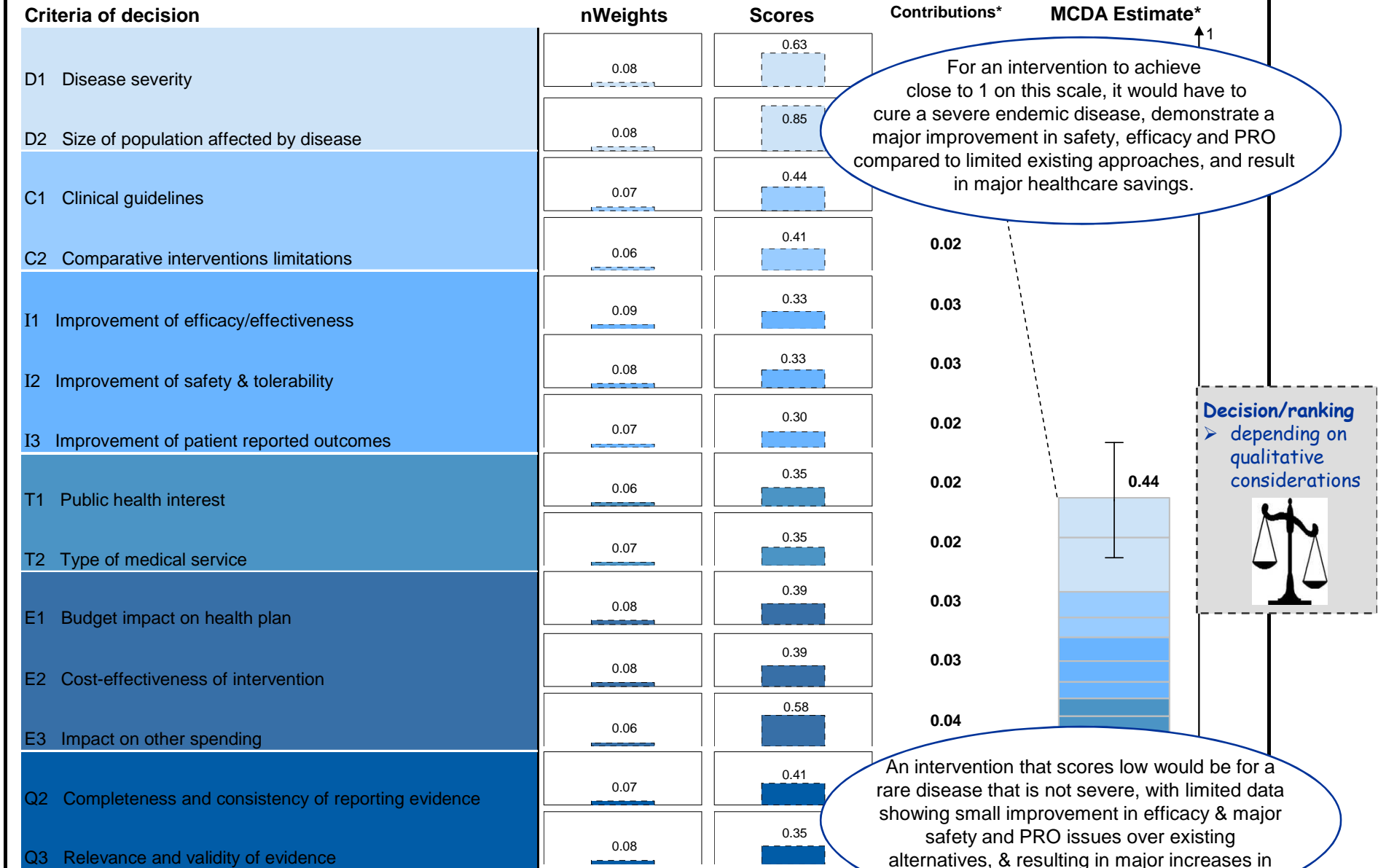
→ Step 1 - MCDA weights values of committee

→ Step 2 - MCDA scores tramadol for chronic non-cancer pain



→ Step 3 - Qualitative impact of extrinsic criteria

# Appraisal of tramadol for chronic non-cancer pain in Canada



For an intervention to achieve close to 1 on this scale, it would have to cure a severe endemic disease, demonstrate a major improvement in safety, efficacy and PRO compared to limited existing approaches, and result in major healthcare savings.

An intervention that scores low would be for a rare disease that is not severe, with limited data showing small improvement in efficacy & major safety and PRO issues over existing alternatives, & resulting in major increases in healthcare spending

\*Normalized (n) weights x Scores, linear additive model

# Outcomes of applying framework

- ❖ Transparent record of evidence for each criteria of decision
  
- ❖ Quantitative considerations
  - ❖ Preferences (weights) of the committee
  - ❖ Performance of intervention (scores)
  - ❖ MCDA estimate
    - ❖ Specific to committee
    - ❖ Comprehensive measure
  
- ❖ Qualitative considerations: positive, neutral or negative impact on value of intervention

➔ Decision: ranking & striking a balance



# Feedback from committee members

## ❖ Criteria of the framework

- ❖ Most criteria should be systematically considered

## ❖ Advantages

- ❖ Systematic consideration of all aspects of decision
- ❖ Consistency of decision process
- ❖ Transparency & clarity

## ❖ Challenges

- ❖ Language & understanding of some criteria of decision
- ❖ Perceived difficulties in distilling information/evidence to populate framework
- ❖ Lack of reference point for MCDA estimates (ranking)

# Future developments

❖ **Collaborative studies:** field testing\*, validation

❖ **Web collaborative registry:** open access to evidence and ranking

⇒ **Applications:**

⇒ decisionmaking and priority setting

⇒ knowledge translation,

⇒ communication

⇒ research planning

➔ **Optimize resources, decisions and health**

⇒ Framework tools available from the  
EVIDEM Collaboration

[www.evidem.org](http://www.evidem.org)

Thank you

# Standard criteria of decision

Quantitative considerations  
(intrinsic criteria\* - MCDA matrix)

Qualitative considerations  
(extrinsic criteria - tool)

## Disease impact

- Disease severity

## Context of intervention

- Clinical guidelines

## Intervention outcomes

## Type of benefit

- Public health interest (e.g., prevention)
- Type of medical service (e.g., surgery)

## Economics

## Quality/uncertainty of evidence

- Adherence to requirements of clinical research
- Completeness and consistency of reporting evidence
- Relevance and validity of evidence

## Ethical framework

- Goals of healthcare - utility
- Opportunity costs - efficiency

## Other system related factors for criteria

- System capacity and appropriate use of intervention
- Stakeholder pressures
- Political/historical context