Challenges and Solutions for HTA:

An agenda for the 21st century.

Don Husereau

(1) Adjunct Professor, School of Epidemiology and Public Health, University of Ottawa
(2) Senior Associate, Institute of Health Economics
(3) President & CEO, 9363980 Canada Inc.

Disclosures

- I have worked for public and private sector organizations that might be interested in what I have to say.

Public / not-for-profit

Ontario Ministry 2019- • Ontario CED member 2015-2019 • PMPRB Advisor / Working Group member • CADTH (pCODR EGP 2015-present, pERC committee member 2015-2017, Strategic advisor (early scientific advice / real-world evidence), CDR)• PAAB consultant (code changes) • Health Canada Strategic Policy Branch • Federal Innovation Council • Genome Canada • CD Howe Institute • ISPOR • IHE • HTAi • CPhA • CHEO Research Institute

Private / for-profit

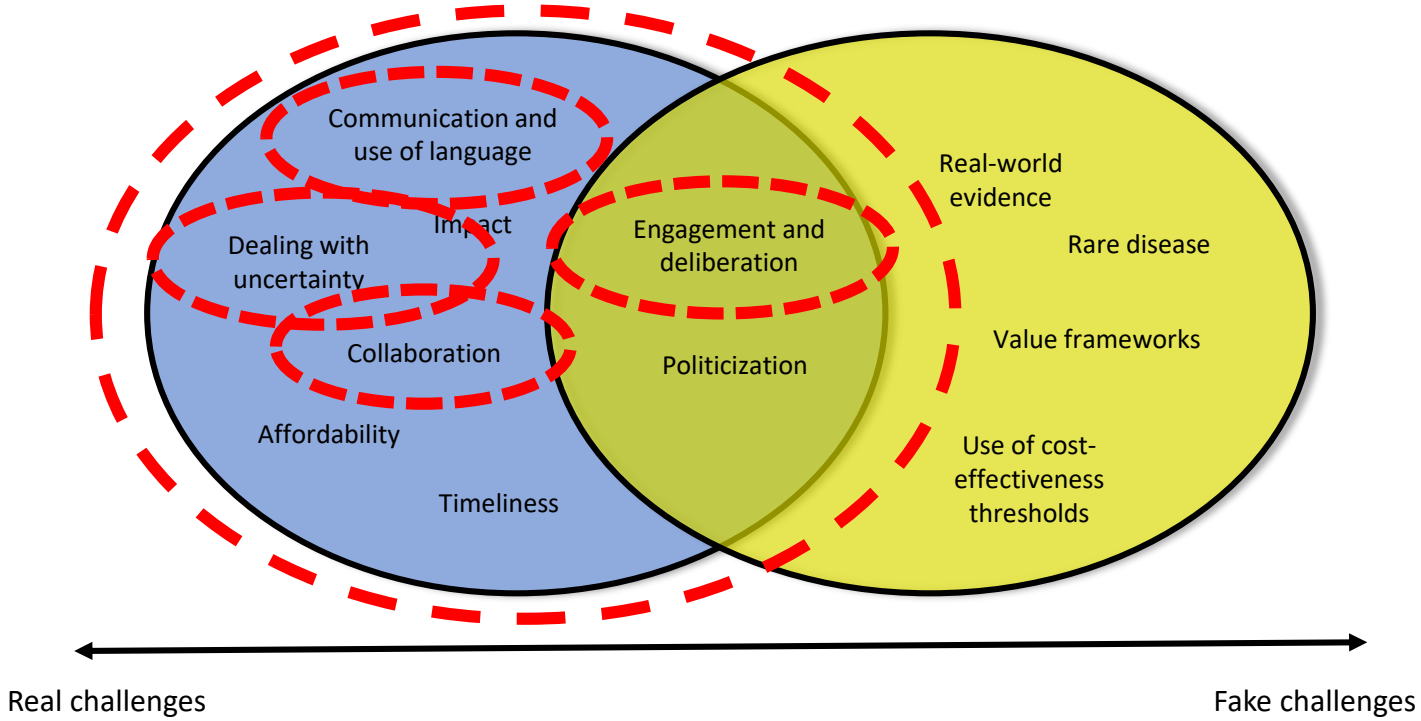
AbbVie • Amgen • AstraZeneca • Bei-Gene Boehringer Ingelheim (Canada) Ltd. • Bristol Meyers Squibb • Celgene • CSL Behring • Ferring Global and Canadian consultancies (Cornerstone, Evidera, IQVIA, Maple, PDCI/McKesson, Pivina etc.) • Danish Life Sciences Council • Eli Lilly • Elvium • Esai • GSK • Hoffman-La Roche • Janssen • Leo Pharma • Lundbeck • Merck • Novo Nordisk • Otsuka • Pfizer • Purdue • Taiho • Takeda • ThermoFisher • Legal firms (as expert witness)

About me

- I worked with CADTH, 2001-2011
  - I served as a Director / Senior Adviser
  - I have also served on expert committees
    - From 2015-2017, I served on the pCODR Expert Review Committee (pERC) as a health economist
    - From 2016-2019, I served on the Ontario Ministry of Health and Long-term Care Committee to Evaluate Drugs (CED)

- I have been an Editorial Advisor for Value In Health Journal (2013-19); BMC Medicine (2014-), and PharmacoEconomics (2021-)
- Since 2011, I have been involved with health and innovation policy research, with a focus of providing advice on health technology or systems of HTA.
- I am a professional magician, and greatly interested in framing effects, cognitive biases and the (mis) interpretation of information

Challenges?

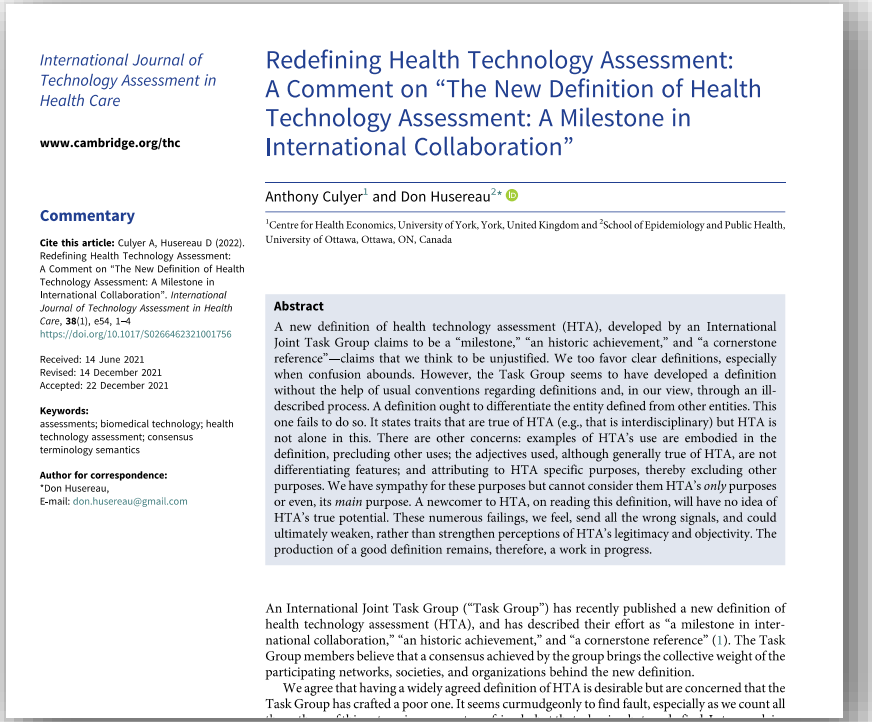

Communication and use of language
Impact
Dealing with uncertainty
Collaboration
Affordability
Timeliness
Engagement and deliberation
Politicization
Real-world evidence
Rare disease
Value frameworks
Use of cost-effectiveness thresholds
Real challenges
Fake challenges

1. Communication (a)

HTA Definition:

"A multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system. "(1)

- Not really a definition
- Created by an ill-defined process without careful attention to language
- Sends all the wrong messages



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Commentary

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Author for correspondence:
*Don Husereau,
E-mail: don.husereau@gmail.com

Redefining Health Technology Assessment: A Comment on "The New Definition of Health Technology Assessment: A Milestone in International Collaboration"

Anthony Culyer[1] and Don Husereau[2]*

[1]Centre for Health Economics, University of York, York, United Kingdom and [2]School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada

Abstract

A new definition of health technology assessment (HTA), developed by an International Joint Task Group claims to be a "milestone," "an historic achievement," and "a cornerstone reference"—claims that we think to be unjustified. We too favor clear definitions, especially when confusion abounds. However, the Task Group seems to have developed a definition without the help of usual conventions regarding definitions and, in our view, through an ill-described process. A definition ought to differentiate the entity defined from other entities. This one fails to do so. It states traits that are true of HTA (e.g., that is interdisciplinary) but HTA is not alone in this. There are other concerns: examples of HTA's use are embodied in the definition, precluding other uses; the adjectives used, although generally true of HTA, are not differentiating features; and attributing to HTA specific purposes, thereby excluding other purposes. We have sympathy for these purposes but cannot consider them HTA's *only* purposes or even, its *main* purpose. A newcomer to HTA, on reading this definition, will have no idea of HTA's true potential. These numerous failings, we feel, send all the wrong signals, and could ultimately weaken, rather than strengthen perceptions of HTA's legitimacy and objectivity. The production of a good definition remains, therefore, a work in progress.

An International Joint Task Group ("Task Group") has recently published a new definition of health technology assessment (HTA), and has described their effort as "a milestone in international collaboration," "an historic achievement," and "a cornerstone reference" (1). The Task Group members believe that a consensus achieved by the group brings the collective weight of the participating networks, societies, and organizations behind the new definition.

We agree that having a widely agreed definition of HTA is desirable but are concerned that the Task Group has crafted a poor one. It seems curmudgeonly to find fault, especially as we count all

(1) O'Rourke B, Oortwijn W, Schuller T, IJT Group (2020) The new definition of health technology assessment: a milestone in international collaboration. Int J Technol Assess Health Care 36, 187–90.

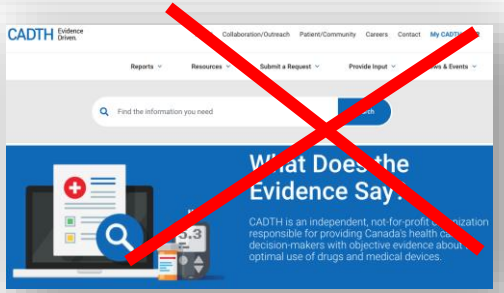
1. Communication (b)

Many other examples

- Key "principles" for HTA not actual principles (they are social values) (1)
- Interchangeable, evolving, and overlapping terms: "Patients / public / consumers"(2)
- Real world data vs. real world evidence / observational evidence / 'evidence'
- "Value"; "Costs"; "Evaluation"; "Appraisal"; "Rare" diseases

Public members of the expert committee present the patient input at the outset of the committee's deliberations (section 8.3), and a summary of the patient input discussion is included in the committee's recommendation.

- CADTH Procedures for the CADTH Common Drug Review and Interim Plasma Protein Product Review
March 2020

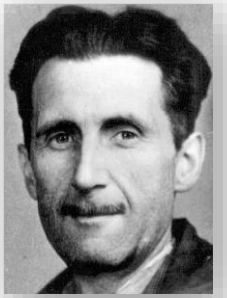


(1) Bond K, Stiffell R, Ollendorf DA. Principles for deliberative processes in health technology assessment. Int J Technol Assess Health Care. 2020 Aug;36(4):445–52.
(2) Hailey D, Nordwall M. Survey on the involvement of consumers in health technology assessment programs. Int J Technol Assess Health Care. 2006;22(4):497–9.

1. Communication – solutions?

But if thought corrupts language, language can also corrupt thought. A bad usage can spread by tradition and imitation, even among people who should and do know better.

- George Orwell



- Recognize the challenge – ask for and demand consensus definitions
- Eliminate jargon, convenience and influence words
- Use communication and language specialists
- Contribute to international and editorial standards

2. Engagement and deliberation

It's not just about the outcome…

- Much emphasis on interpretation of facts:
  - Systematic reviews
  - Conflicts of interest
  - Subject matter expertise
  - Guidance for interpretation

…it's about the *process…*

- Too little emphasis on how outcomes are achieved!
  - *What information was shared?*
  - *By who?*
  - *Who do deliberants represent? Themselves?*
  - *Are their conflicting views?*
  - *Are their professional or reputational conflicts?*
  - *How were they selected?*
  - *How are viewpoints exchanged?*
  - *What supports were provided?*
  - *What social values were represented?*

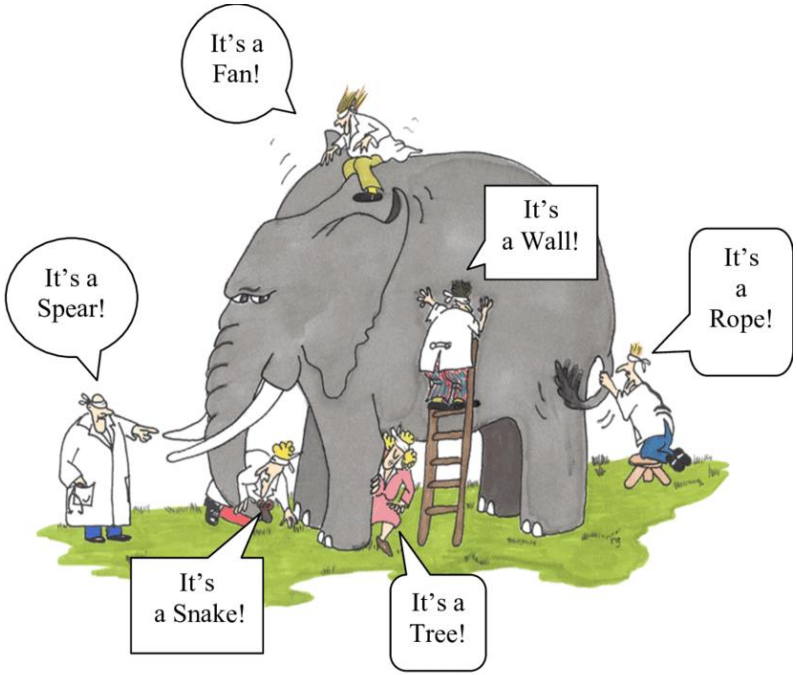
2. Engagement and deliberation, cont.

Why deliberate?

- Different perspectives about:

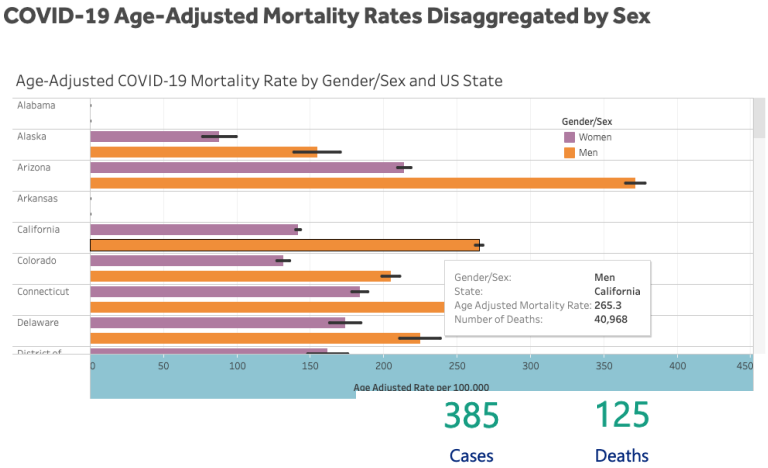
(1) Facts

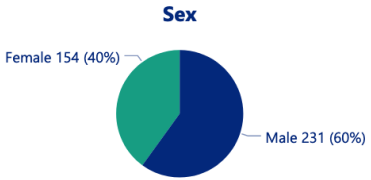
(2) Values



Policy proposal: MANCLINICS

- Men dying and hospitalized at up to twice (195%) the rate of women
- Represent highest unmet need
  - Obese men / older men at even higher risk
- MANCLINICS that ensure men older than 50 receive services *first represent savings to the healthcare system*





https://www.genderscilab.org/gender-and-sex-in-covid19

https://www.ottawapublichealth.ca/en/reports-research-and-statistics/daily-covid19-dashboard.aspx

Social values?

MANCLINICS

- Requires additional nurses, doctors and support staff
- Will reduce rates of premature mortality:
  - could produce **3 additional QALYs** for every 1000 men sent to the front of the line
- Will reduce hospitalization
  - Could reduce hospitalization rates by 25%
- Requires **$20 million** annual investment
- **Will get men aging men back to work!**

($$$)

NEWBORN SCREENING PROGRAM

- Also requires additional health human resources
- Will reduce rates of premature mortality
  - Also produce **3 additional QALYs** for every 1000 babies screened
- Will reduce hospitalization
  - Also reduces hospitalization rates by 25%
- Requires **$20 million** annual investment
- **Will create more mouths to feed**

($$$)

2. Engagement and deliberation - solutions

Guidance on deliberative processes for HTA

- Oortwijn W, Husereau D, Abelson J, Barasa E, Bayani DD, Canuto Santos V, et al. Designing and Implementing Deliberative Processes for Health Technology Assessment: A Good Practices Report of a Joint HTAi/ISPOR Task Force.
    - Value in Health. Vol 25, Issue 6, p. 869-886, June 1, 2022. https://doi.org/10.1016/j.jval.2022.03.018
    - Int J Technol Assess Health Care. 2022 Jun 3;38(1):e37. doi 10.1017/S0266462322000198
- The target audience for this guidance is the executive and legislative actors responsible for establishing and managing HTA processes, particularly HTA bodies
- Secondary audiences are stakeholders and researchers

3. Uncertainty

Ill-defined, room for improvement

- Failure to distinguish between different types of uncertainty:
  - Aleatory Probability: The probability of chance.
  - Epistemic Probability: The probability of belief.
- Typically, objective Bayesian approaches are used
  - Represents a single probability distribution
  - Often focused on the value of stochastic uncertainty, from epidemiologic data
  - Bolstered by VOI, and probabilistic approaches to economic evaluation

Consider the following problem. I have, on the desk in front of me, a closed bag containing coloured marbles. I intend to shake the bag, to reach into it and to draw out one marble.

What is the probability that I will draw a red marble?

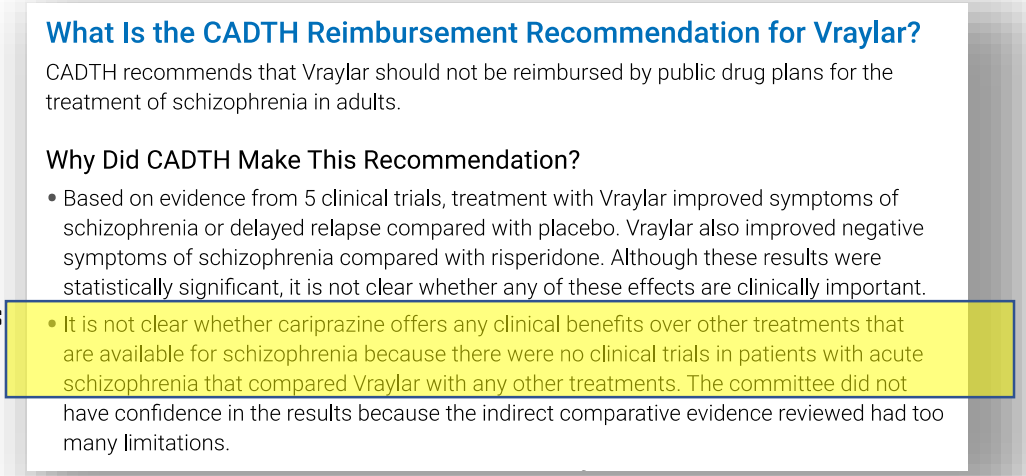
From Walley (1)

(1) Walley P. Inferences from Multinomial Data: Learning about a Bag of Marbles. Journal of the Royal Statistical Society Series B (Methodological). 1996;58(1):3–57.

3. Uncertainty

- Increasing issue in HTA
  - e.g., basket trials, single-arm trials
  - Global trials with different patient, structural, health service delivery characteristics
  - Indirect treatment comparisons

- Payers / HTA may take an all or nothing approach
  - CADTH negative listing recommendations often characterized as having "too much uncertainty"



What Is the CADTH Reimbursement Recommendation for Vraylar?

CADTH recommends that Vraylar should not be reimbursed by public drug plans for the treatment of schizophrenia in adults.

Why Did CADTH Make This Recommendation?

- Based on evidence from 5 clinical trials, treatment with Vraylar improved symptoms of schizophrenia or delayed relapse compared with placebo. Vraylar also improved negative symptoms of schizophrenia compared with risperidone. Although these results were statistically significant, it is not clear whether any of these effects are clinically important.
- It is not clear whether cariprazine offers any clinical benefits over other treatments that are available for schizophrenia because there were no clinical trials in patients with acute schizophrenia that compared Vraylar with any other treatments. The committee did not have confidence in the results because the indirect comparative evidence reviewed had too many limitations.

3. Uncertainty – solutions?

- Structural uncertainty should consider different modelling approaches (1)
  - Weather prediction uses multiple models – yet predicting what is valuable in healthcare often relies on *one model*
- Subjective Bayesian approaches through structured expert elicitation (2)
- Potential for bias through quantitative bias analyses (3)
  - When is ITC truly *infeasible?*
  - Not good enough to say trials are too imbalanced (I^2 value does not tell us)
- Sadly, latest GPF document provides little guidance!
  - "Possible next steps to more openly and inclusively manage how uncertainty is considered in HTA and communicated to the wider public, as highlighted in this paper, require further vigorous debate and discussion, and additional topics and related recommendations may be identified." (4)

(1) Afzali HHA, Karnon J. Exploring structural uncertainty in model-based economic evaluations. Pharmacoeconomics. 2015 May;33(5):435–43.
(2) Peel A, Jenks M, Choudhury M, Lovett R, Rejon-Parrilla JC, Sims A, et al. Use of Expert Judgement Across NICE Guidance-Making Programmes: A Review of Current Processes and Suitability of Existing Tools to Support the Use of Expert Elicitation. Appl Health Econ Health Policy. 2018 Dec;16(6):819–36.
(3) Lash TL, Fox MP, MacLehose RF, Maldonado G, McCandless LC, Greenland S. Good practices for quantitative bias analysis. Int J Epidemiol. 2014 Dec 1;43(6):1969–85.
(4) Trowman R, Powers A, Ollendorf DA. Considering and communicating uncertainty in health technology assessment. International Journal of Technology Assessment in Health Care. 2021 ed;37(1):e74.

4. Collaboration

- Good news: collaboration is happening!
  - EMA / EUnetHTA joint work plan
    - Desire to collaborate with regulators
  - CADTH / regulator collaboration
  - CADTH / Australia / NICE / Healthcare Improvement Scotland / Health Technology Wales / All Wales Therapeutics and Toxicology Centre.

- Bad news: further conditions to optimize collaboration needed
  - Shared standards required
  - Global cooperation across organizations and jurisdictions needed – no time for politics!
  - Collaboration with innovators required – too much work at cross-purposes
  - Collaboration with HSR , data science, others helpful

Summary

- There are a lot of challenges with HTA currently
  - Some are real and unrecognized
  - Some are false and too-often recognized

- Some key challenges for the future of HTA:
  (1) Clarity of communication and language
  (2) Improving engagement and perceived legitimacy of HTA
  (3) More nuanced analysis of uncertainty
  (4) Collaboration and consistency in approach internationally

Thanks. Q?

Those who have knowledge, don't predict. Those who predict, don't have knowledge.

--Lao Tzu, 6th Century BC

@DonHusereau

Don Husereau

+16132994379

don.husereau@gmail.com