Session 1: Facilitating review and data reuse across the research ecosystem

Enhancing the evidence ecosystem for more flexible and efficient data reuse: guideline perspective

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Cochrane

Enhancing the evidence ecosystem for more flexible and efficient data reuse; guideline perspective

For Cochrane Methods Symposium, Session 1

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Declaration of interest: CEO and co-founder MAGIC

Meet John, hospitalized with a new stroke, ready for discharge

65 yrs old, DM2, CVD (on insulin, metformin, clopidogrel and statins), BMI 33

What about SGLT2-I or GLP-RA to reduce cardiorenal outcomes?

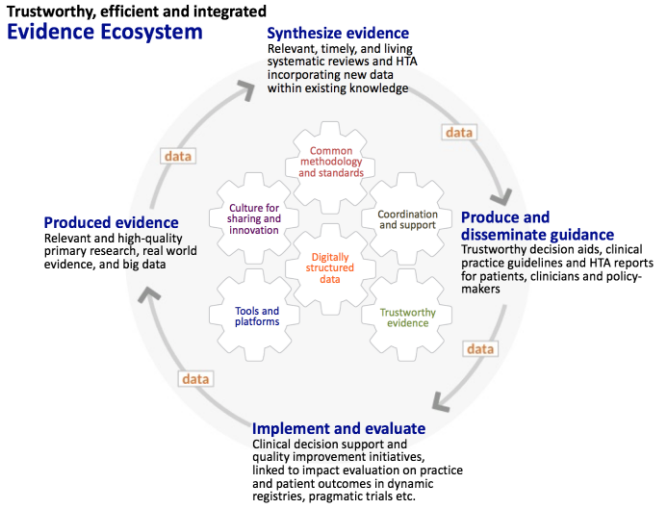
How make sure John gets the right treatment, at the right time in 2023?
How can we enhance the evidence ecosystem
to more efficiently create, re-use and share trustworthy health data?

Agenda

- Clinical practice guideline perspective
  - Progress in EBM standards and methods
  - Why bother with Evidence Ecosystems
  - Experiences from MAGIC
  - Adding multiple comparisons and living evidence to existing challenges with sharing, reusing data

- Wishes from guideline developers and key challenges for systematic reviewers

- A brighter future moving forward together?



Health care professionals (and their patients) need guidelines

to be **trustworthy, timely and accessible**

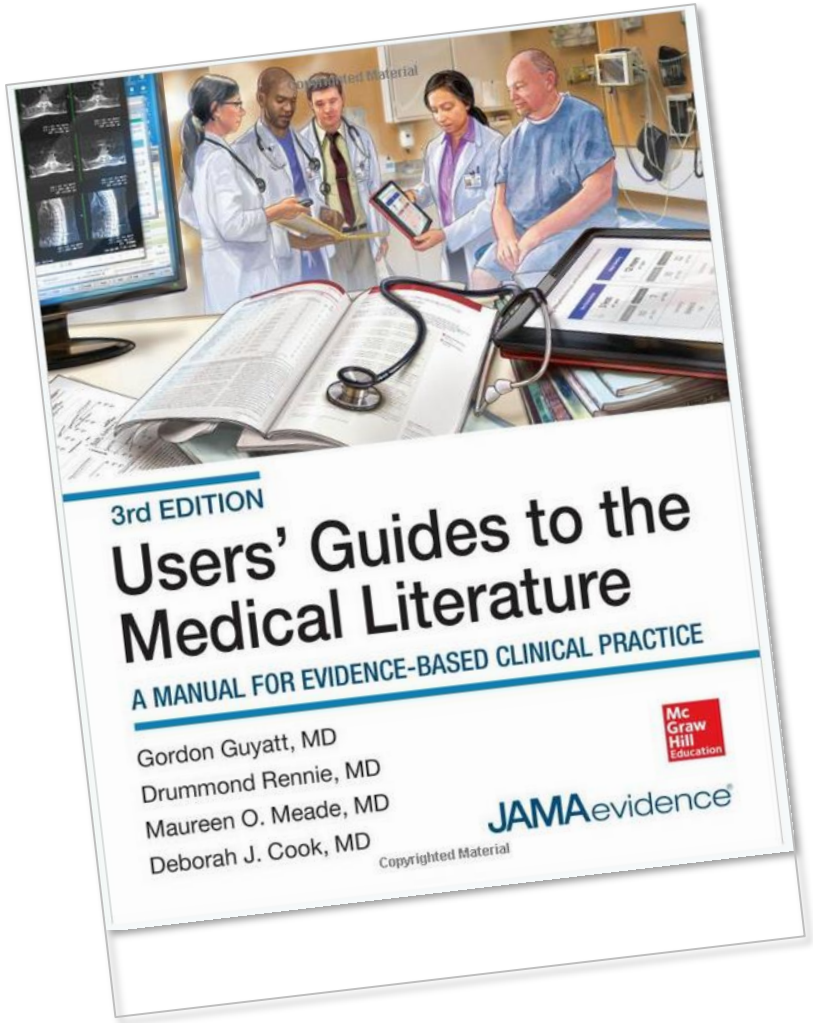
Organisations need to apply best current **standards, methods, platforms and processes**

Great advances in EBM and digitalization can enhance the evidence ecosystem now

CLINICAL PRACTICE GUIDELINES WE CAN TRUST

Guidelines International Network

FHIR



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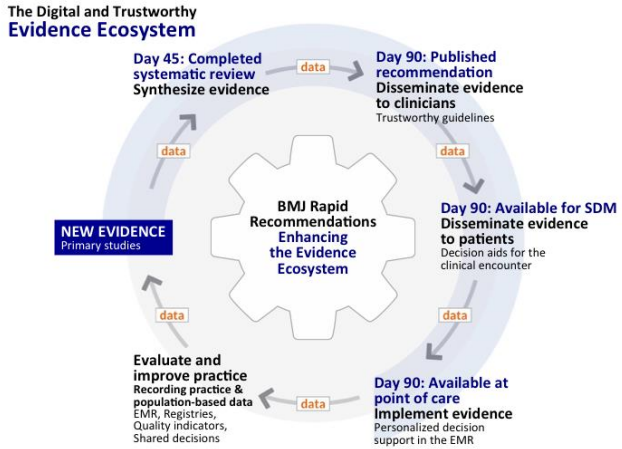
GRADE

MAGIC app



Why bother with Evidence Ecosystems?

How can we let data flow seamlessly from production to impact on care?

Here is one model with key requirements, what about the people?

Vandvik PO, Brandt L. Future of Evidence Ecosystem Series: Evidence ecosystems and learning health systems: why bother? *Journal of Clinical Epidemiology.* 2020. https://doi.org/10.1016/j.jclinepi.2020.02.008

Standards for trustworthy clinical practice guidelines

put high quality systematic reviews and evidence summaries at the core

Table 1. **Summary of the Institute of Medicine's Proposed Standards for a Trustworthy Guideline**

Has an explicit description of development and funding processes that is publicly accessible
Follows a transparent process that minimizes bias, distortion, and conflicts of interest
Is developed by a multidisciplinary panel comprising clinicians; methodological experts; and representatives, including a patient or consumer, of populations expected to be affected by the guideline
Uses rigorous systematic evidence review and considers quality, quantity, and consistency of the aggregate of available evidence
Summarizes evidence (and evidentiary gaps) about potential benefits and harms relevant to each recommendation
Explains the parts that values, opinion, theory, and clinical experience play in deriving recommendations
Provides a rating of the level of confidence in the evidence underpinning each recommendation and a rating of the strength of each recommendation
Undergoes extensive external review that includes an open period for public comment
Has a mechanism for revision when new evidence becomes available

Advanced methods for appraising and presenting evidence

Using common method (e.g.,GRADE) is key, but how can we optimally share and re-use such evidence summaries in user-friendly formats (interactive SoFs)

Glucagon-Like Peptide-1 (GLP-1) receptor agonists vs Standard care

Adults with type 2 diabetes and established CVD (but no CKD)

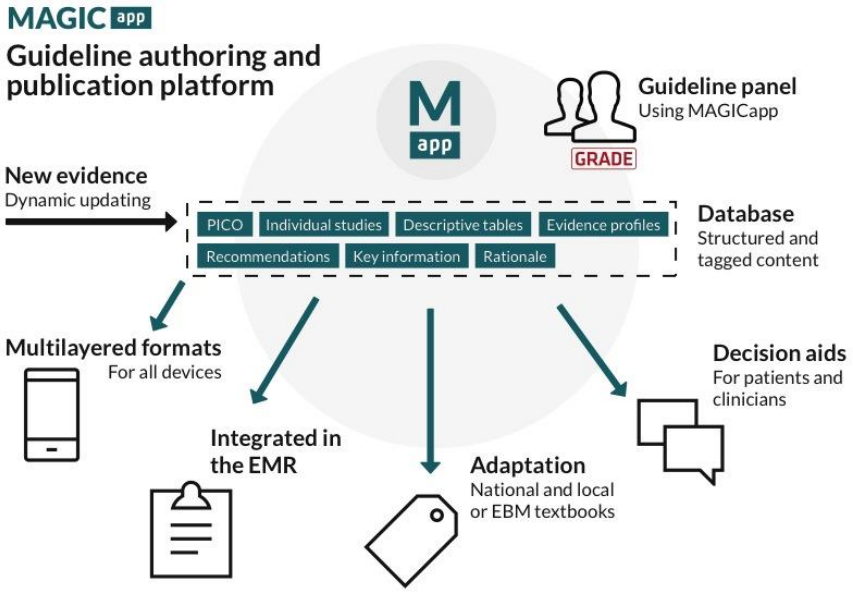
10 Outcomes **11** Practical issues

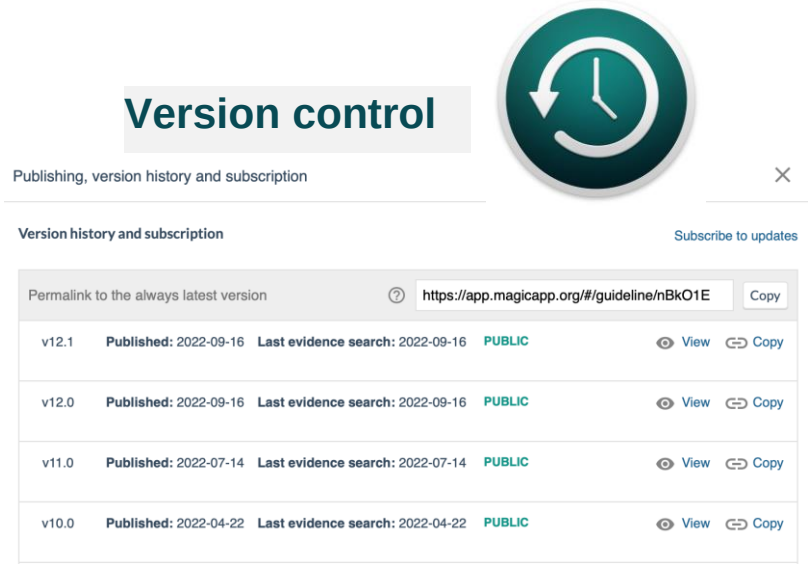
Outcome Timeframe	Study results and measurements	Absolute effect estimates Standard care	 GLP-1 RA	Certainty of the Evidence (Quality of evidence)	Plain language summary
All-cause mortality	Odds ratio 0.88 (CI 95% 0.83 — 0.94) Based on data from 69035 participants in 34 studies	**120** per 1000	**107** per 1000 Difference: **13 fewer per 1000** (CI 95% 18 fewer — 6 fewer)	**Moderate** Due to serious imprecision	GLP-1 receptor agonists probably reduce the risk of death compared with standard care.
Cardiovascular mortality	Odds ratio 0.88 (CI 95% 0.80 — 0.96) Based on data from 63455 participants in 20 studies	**79** per 1000	**70** per 1000 Difference: **9 fewer per 1000** (CI 95% 15 fewer — 3 fewer)	**Moderate** Due to serious imprecision	GLP-1 receptor agonists probably reduce the risk of cardiovascular death compared with standard care.
Nonfatal myocardial infarction	Odds ratio 0.92 (CI 95% 0.85 — 0.99) Based on data from 67956 participants in 32 studies	**108** per 1000	**100** per 1000 Difference: **8 fewer per 1000** (CI 95% 15 fewer — 1 fewer)	**Moderate** Due to serious imprecision	GLP-1 receptor agonists probably reduce the risk of nonfatal myocardial infarction compared with standard care.
Nonfatal stroke	Odds ratio 0.84 (CI 95% 0.76 — 0.93) Based on data from 66900 participants in 29 studies	**108** per 1000	**92** per 1000 Difference: **16 fewer per 1000** (CI 95% 24 fewer — 7 fewer)	**Moderate** Due to serious imprecision	GLP-1 receptor agonists probably reduce the risk of nonfatal stroke compared with standard care.

So, what is the right treatment for John? Hold on, there is more to it….

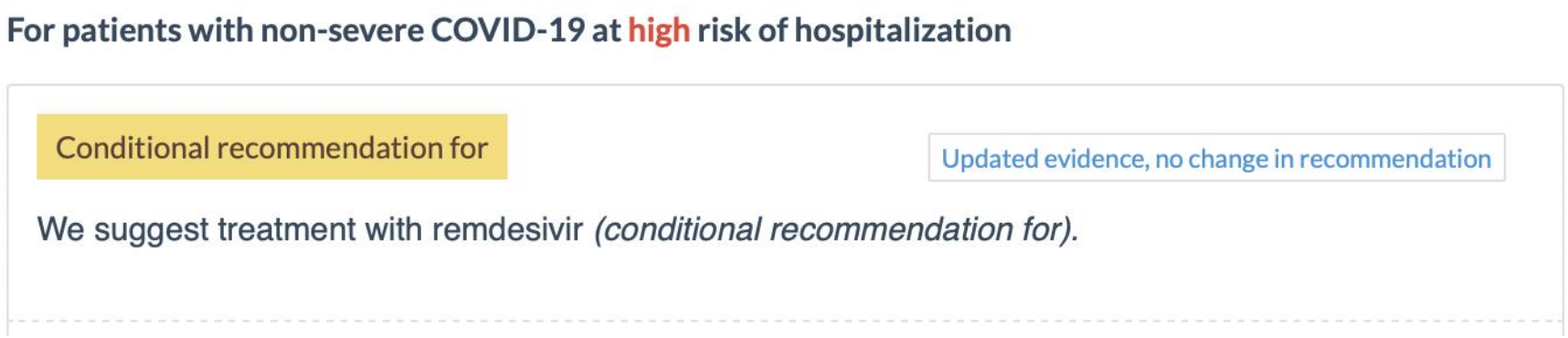
Example of adding technology to advances in EBM

Digitally structured, computable and multilayered guideline content



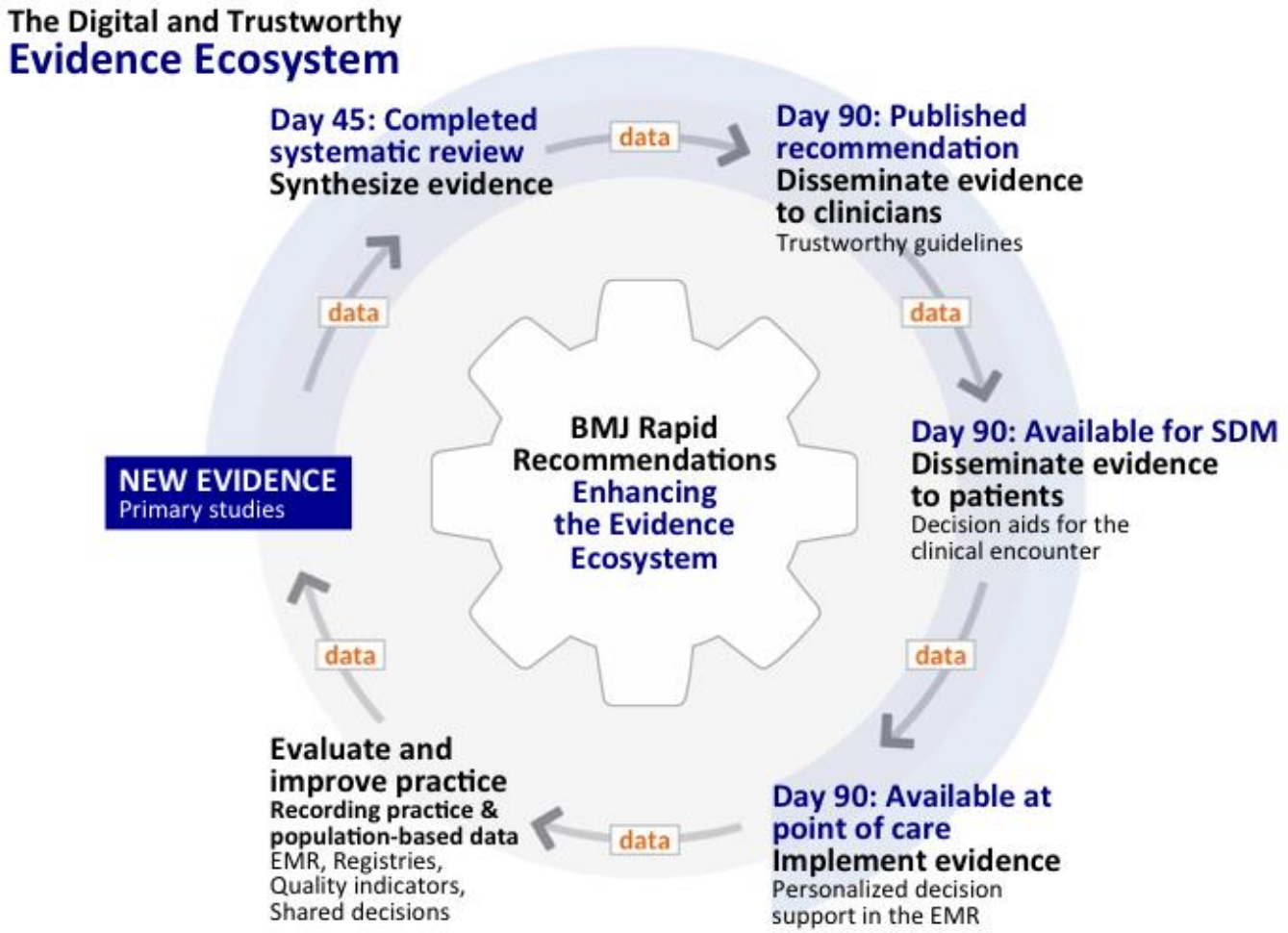


PICOs, evidence summaries (including individual outcomes) and recommendations can be exported/ imported and updated one at a time, with full version control



Enhance processes for efficiency and reduced waste

Our MAGIC lab to innovate the evidence ecosystem, why did we end up doing almost all systematic reviews ourselves, across 22 guidelines?



A guideline answering John, beware multiple options

NMA-update with 10 000 effect estimates, straight from R to MATCH-IT tool

John chose a GLP1-RA through shared decision-making
How share, re-use and dynamically update such complex evidence?
Machine versus human readable (visualizing data)?

COVID-19 breakthrough for living guidelines

Living evidence is here to stay: a call for action while adding challenges

Decision makers need 'living' evidence synthesis

Julian H. Elliott, Rebecca Lawrence, Jan C. Minx, Olufemi T. Oladapo, Philippe Ravaud, Britta Tendal Jeppesen, James Thomas, Tari Turner, Per Olav Vandvik & Jeremy M. Grimshaw

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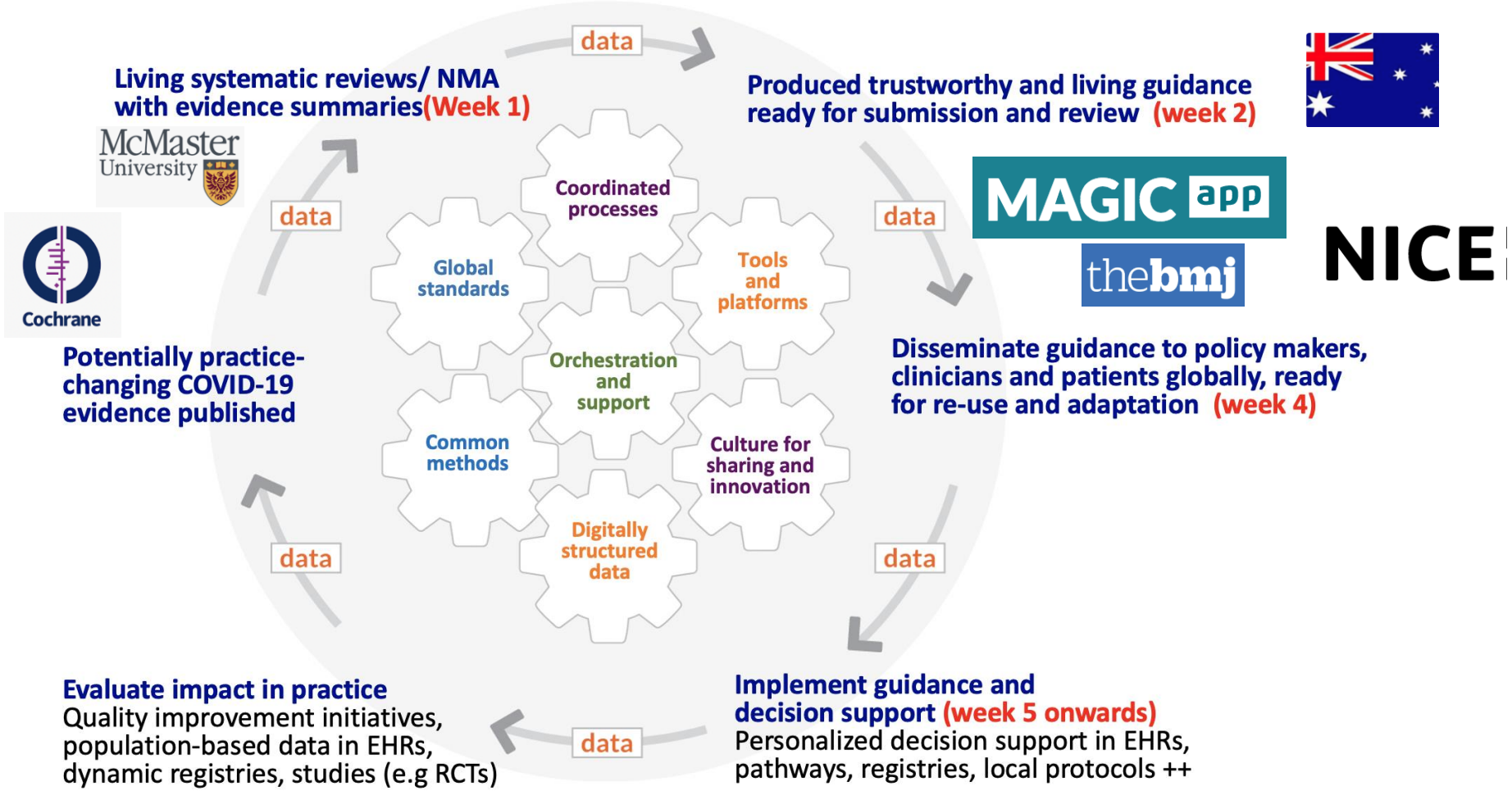
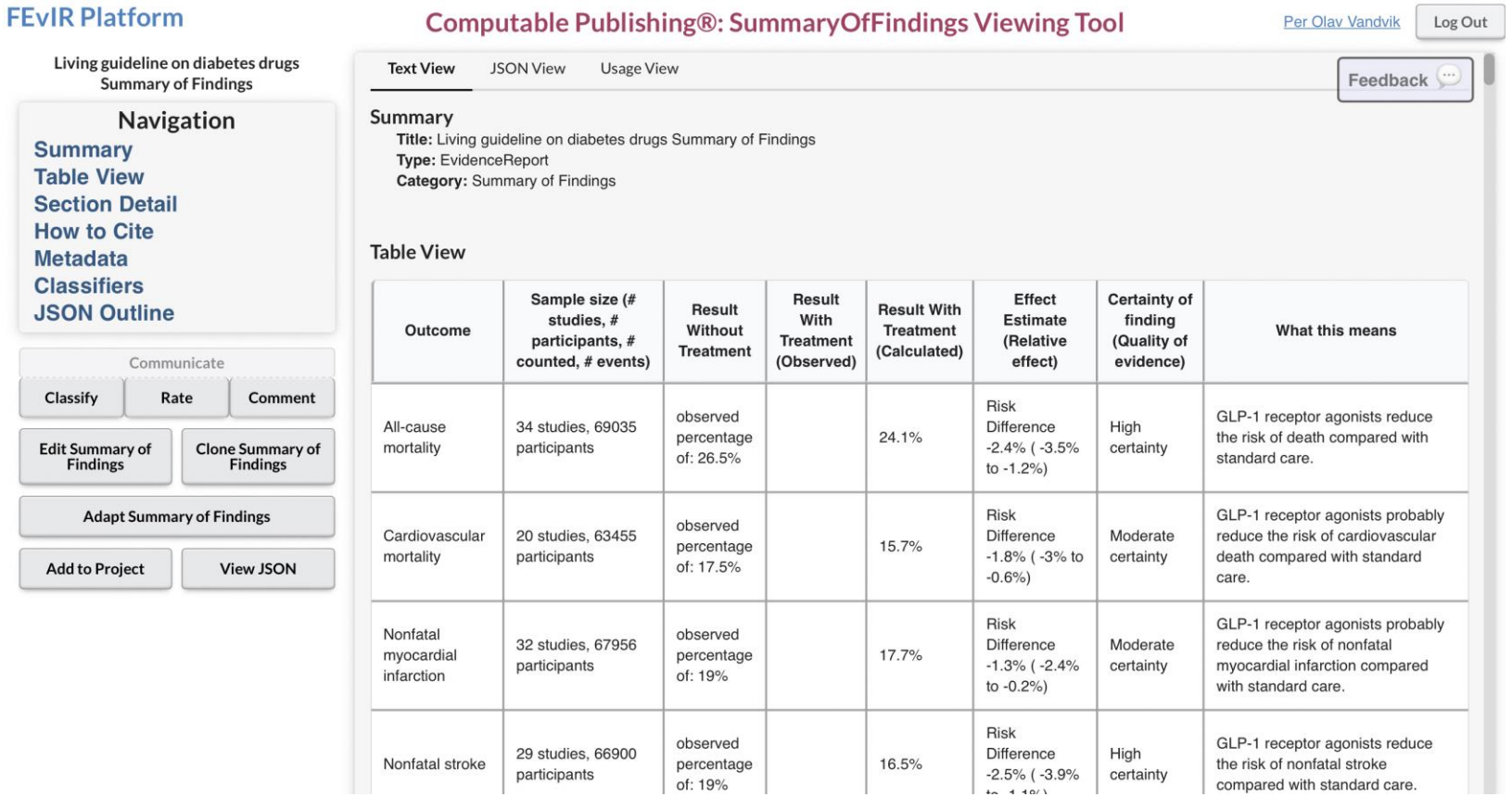
Living guidelines enhancing the evidence ecosystem now

Powered by living systematic reviews and NMA for COVID-19 clinical management



Wishes and key challenges, within the evidence ecosystem

Premise: Guidelines useful end-products to get health data and evidence right



Outcome	Sample size (# studies, # participants, # counted, # events)	Result Without Treatment	Result With Treatment (Observed)	Result With Treatment (Calculated)	Effect Estimate (Relative effect)	Certainty of finding (Quality of evidence)	What this means
All-cause mortality	34 studies, 69035 participants	observed percentage of: 26.5%		24.1%	Risk Difference -2.4% (-3.5% to -1.2%)	High certainty	GLP-1 receptor agonists reduce the risk of death compared with standard care.
Cardiovascular mortality	20 studies, 63455 participants	observed percentage of: 17.5%		15.7%	Risk Difference -1.8% (-3% to -0.6%)	Moderate certainty	GLP-1 receptor agonists probably reduce the risk of cardiovascular death compared with standard care.
Nonfatal myocardial infarction	32 studies, 67956 participants	observed percentage of: 19%		17.7%	Risk Difference -1.3% (-2.4% to -0.2%)	Moderate certainty	GLP-1 receptor agonists probably reduce the risk of nonfatal myocardial infarction compared with standard care.
Nonfatal stroke	29 studies, 66900 participants	observed percentage of: 19%		16.5%	Risk Difference -2.5% (-3.9%	High certainty	GLP-1 receptor agonists reduce the risk of nonfatal stroke compared with standard care.

In summary: Moving forward together for trusted evidence

Need to close the loop and show we can truly share data, evidence and work globally

Word of caution: Warrants explicit agreement on and use of best current

Standards | Methods | Platforms | Processes