MAGICapp for evidence synthesizers in an emerging Trustworthy and Digital Evidence Ecosystem

Cochrane Webinar  August 23 2017
Per Olav Vandvik, associate professor MD, Ph.D
Disclosures: Head of MAGIC, a non-profit research and innovation program
Cochrane and MAGIC announce partnership

Cochrane and MAGIC are delighted to announce the launch of an official partnership, aimed at supporting and further strengthening the use of health evidence within the context of a digital and trustworthy evidence ecosystem for health care.

MAGIC (formally known as the MAking GRADE the Irresistible Choice (MAGIC) organization) is a non-profit research and innovation programme set up to make evidence summaries and recommendations that work for clinicians at the point of care and to facilitate shared decision-making with patients. Established in 2010, the MAGIC project has, among a number of other initiatives, developed the MAGICapp, a web-based platform for preparing guidelines using structured data systems and validated methods.
2016: Time for a post-guidelines era in health care?

Major limitations EBM and guidelines

- Developers
  - Not trustworthy, ignore other knowledge
  - Resource-demanding, extreme duplication

- Clinicians and patients
  - Available, useful, understandable?
  - Allow shared, personalized decisions?
  - Up to date?
  - Integrated in the electronic health record?

Time to respond to calls from the opponents?
Major challenges with EBM, systematic reviews and guidelines but also advances in standards, methods and tools..
Can technology help? Platforms and tools ready for use
(e.g., www.magicapp.org)
A peek into MAGICapp, for end-users and authors

1. Scope of the Guideline and How To Use the Guideline

2. Background and methods

3. Initiation and Dosing of Opioids in Patients with Chronic Noncancer Pain

**Recommendation 1:** When considering therapy for patients with chronic non-cancer pain

*Strong recommendation*

We recommend optimization of non-opioid pharmacotherapy and non-pharmacological therapy, rather than a trial of opioids...

**Recommendation 2:** For patients with chronic noncancer pain, without current or past substance use disorder and without other active psychiatric disorders, who have persistent problematic pain despite optimized nonopioid therapy

*Weak recommendation*
Challenges beyond guidelines, for patients and society
Do not despair, we are not lost;-)
Visionary “techy, fun and nice to work with” people in our community linking data in platforms through G-I-N/ Cochrane/ GRADE Tech
Our vision:
A Digital and Trustworthy Evidence Ecosystem
Some hurdles to overcome: Organizations fit for purpose?
How can we rapidly get potentially practice-changing evidence into practice? Collaborative network approach, partnering with innovative medical journal?
The BMJ-RapidRecs project: methods and process

• Guideline panel, network of the right people
  ✓ Trustworthy guideline standards, GRADE
  ✓ Focus on conflict of interest, patient involvement....

• Linked high quality systematic reviews
  ✓ effects, prognosis, values and preferences
  ✓ Separate teams, closely interacting with guideline panel

Rapid Recommendations process step by step (with target times)

Step 1: Monitor and identify potentially practice changing evidence

Step 2: Executive + chair triggers process and RapidRecs panel (day 7)

Step 3: Systematic reviews created by separate teams (day 45)

Step 4: RapidRecs created in MAGICapp and as synopsis paper (day 60)

Step 5: RapidRecs + reviews submitted for peer review (day 60)

Step 6: RapidRecs and reviews disseminated globally (day 90)
**BMJ Rapid Recommendations**, check it out...*

---

Transcatheter or surgical aortic valve replacement for patients with severe, symptomatic, aortic stenosis at low to intermediate surgical risk: a clinical practice guideline

*BMJ* 2016; 354 doi: http://dx.doi.org/10.1136/bmj.i5085 (Published 28 September 2016)

Cite this as: *BMJ* 2016;354:i5085

---

**Choice of intervention for those with severe aortic stenosis**

- **Transfemoral TAVI**
  - Inserting a new valve into the aortic valve's place without open heart surgery. Delivery is through the femoral artery.

- **SAVR**
  - Open-heart surgery, to remove the narrowed aortic valve. Replacement with tissue valve.

---

**Recommendations**

<table>
<thead>
<tr>
<th>Population</th>
<th>Favours TAVI</th>
<th>Favours SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 85+</td>
<td>Strong</td>
<td>Why?</td>
</tr>
<tr>
<td>Age 75–84</td>
<td>Weak</td>
<td>Why?</td>
</tr>
<tr>
<td>Age 65–74</td>
<td>Weak</td>
<td>Why?</td>
</tr>
<tr>
<td>Age under 65</td>
<td>Strong</td>
<td>Why?</td>
</tr>
</tbody>
</table>

---

* All papers open access and for you to scrutinize, adapt and use for your purposes
Digital and Trustworthy Evidence Ecosystem
From RapidRecs pilot to closing the loop in Finland and Belgium

NNT=10

23 trials
n=4000

Offer probiotics

Baseline: 3 of 100 offered probiotics
WikiRecs for probiotics in MAGICapp:
https://www.magicapp.org/app#/guideline/1170

2 Probiotics for children receiving antibiotics for an infection

Children 1 month to 2 years old receiving antibiotics for an infection.

Strong recommendation
Benefits clearly outweigh the drawbacks/harms.

We recommend adjunctive probiotics rather than no probiotics.

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 1 month to 2 years old</td>
<td>Adjunctive probiotic therapy</td>
<td>No probiotic therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAD &lt;2 years</td>
<td>Relative risk 0.46 (CI 95% 0.35 - 0.61) Based on data from 3898 patients in 22 studies Follow up: 1-12 weeks.</td>
<td>180 per 1000 83 per 1000</td>
<td>Moderate Due to serious inconsistency.</td>
<td>Probiotics appear to decrease the incidence of AAD.</td>
</tr>
</tbody>
</table>
None of the 16 trials (n = 2459) that reported on adverse events documented any serious adverse events attributable to probiotics.

Table

<table>
<thead>
<tr>
<th>Project Settings</th>
<th>Term Recognition</th>
</tr>
</thead>
<tbody>
<tr>
<td>None of the 16 trials (n = 2459) that reported on adverse events documented any serious adverse events attributable to probiotics.</td>
<td>Aucuns des 16 essais (n = 2459) qui ont mentionné des événements indésirables n’ont démontré d’événements indésirables graves attribuables aux probiotiques.</td>
</tr>
<tr>
<td>16 Most participants were under 6 years of age.</td>
<td>La plupart des participants avaient un âge inférieur à 6 ans.</td>
</tr>
<tr>
<td>17 The studies compared probiotics to placebo, active alternative prophylaxis, or no treatment and measured the incidence of diarrhea secondary to antibiotic use.</td>
<td>Les études ont comparé les probiotiques au placebo, la prophylaxie alternative active, ou aucun traitement et a mesuré l’incidence de la diarée liée à l’usage d’antibiotiques.</td>
</tr>
<tr>
<td>18 Trials included treatment with either Baciocell spp., Bifidobacterium spp., Clostridium butyricum, Lactobacillus spp., Leuconostoc cremoris, Saccharomyces spp., or Streptococcus spp., alone or in combination.</td>
<td>Les essais comprenaient un traitement aux espèces Bacille, aux espèces bifidobactéries, au Clostridium butyricum, aux espèces Lactobacillus, aux espèces Leuconostoc, aux espèces Saccharomyces ou Streptococcus, seules ou combinées.</td>
</tr>
<tr>
<td>19 Eleven studies used a single strain probiotic, four combined two strains, and eight studies combined three or more strains.</td>
<td>Parmi les études, onze d’entre elles ont utilisé une souche de probiotique, quatre ont combiné deux souches et huit études ont combiné trois souches ou plus.</td>
</tr>
<tr>
<td>20 The probiotic species with most data were Lactobacillus rhamnosus or Saccharomyces boulardii, at a dose of 5 to 40 billion colony forming units/day.</td>
<td>Les espèces de probiotiques aux données les plus importantes étaient le Lactobacillus rhamnosus ou le Saccharomyces boulardii, à la dose de 5 à 40 milliards d’unités formante une colonie/jour.</td>
</tr>
<tr>
<td>21 The incidence of AAD in the probiotic group was 8% (16/200) compared to 19% (364/1900) in the control group (RR 0.46, 95% CI 0.36 to 0.61; I² = 65%, 3988 participants), NNT 10 (95% CI 3 to 12).</td>
<td>L’incidence de la DAA dans le groupe de probiotiques était de 8% (16/200) comparé à 19% (364/1900) dans le groupe témoin (RR 0.46, IC 95% CI 0.36 à 0.61; I² = 65%, 3988 participants), NNT 10 (IC 95% CI 3 à 12).</td>
</tr>
<tr>
<td>22 Single-strain probiotics appeared as effective as multiple-strain preparations.</td>
<td>Les probiotiques à souche unique semblaient aussi efficaces que les préparations à souche multiples.</td>
</tr>
<tr>
<td>23 None of the 16 trials (n = 2459) that reported on adverse events documented any serious adverse events attributable to probiotics.</td>
<td>Aucuns des 16 essais (n = 2459) qui ont mentionné des événements indésirables n’ont démontré d’événements indésirables graves attribuables aux probiotiques.</td>
</tr>
</tbody>
</table>

8/30/2017
To practice: Meet “Stella Artois” 17 months old, with pneumonia prescribed with antibiotics in Belgian primary care
Doctor prescribes antibiotics in the EHR....
Drilling back to the Evidence if needed
EBM guidelines – MAGICapp - all the way to the meta-analysis?

### Probiotics for children receiving antibiotics

**v1.2 published on 9/2/16**

#### Research evidence

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 1 month to 2 years old</td>
<td>Adjunctive probiotic therapy</td>
<td>No probiotic therapy</td>
</tr>
</tbody>
</table>

#### Evidence profile

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AAD &lt;2 years</strong></td>
<td>Relative risk 0.46 (CI 95% 0.35 - 0.61) Based on data from 3898 patients in 22 studies. Follow up: 1-12 weeks.</td>
<td>180 per 1000</td>
<td>Moderate</td>
<td>Probiotics appear to decrease the incidence of AAD.</td>
</tr>
<tr>
<td><strong>Severe AAD &lt;2 years</strong></td>
<td>0.46 (CI 0.25 - 0.61) Based on data from 3898 patients in 22 studies. Follow up: 1-12 weeks.</td>
<td>18 per 1000</td>
<td>Low</td>
<td>Probiotics may decrease the incidence of severe AAD by a small amount.</td>
</tr>
<tr>
<td><strong>GI side effects</strong></td>
<td>Relative risk 1 (CI 95% 0.71 - 1.29) Based on data from 2465 patients in 16 studies. Follow up: 1-4 weeks.</td>
<td>35 per 1000</td>
<td>Moderate</td>
<td>Probiotics do not appear to increase the risk of gastrointestinal side effects.</td>
</tr>
</tbody>
</table>
Acting on – and implementing - the evidence, together
And same goes for Finland

Automatic reminder triggered in a Finnish medical record:
The patient got a prescription of antibiotics (Amoxin). Probiotics (Lactobacillus or Saccharomyces boulardii) are recommended for the prevention of antibiotic diarrhea. In immunosuppressed patients their...
In summary

- Better methods, tools and systems available across an emerging evidence ecosystem in health care

- **People:** culture for sharing work, evidence and common understanding of research methods, including different sources of knowledge

- **Technology:**
  - Rapidly evolving platforms with digitally structured data. G-I-N, Cochrane and others joining forces
  - MAGICapp a useful tool for evidence synthesizers (?)

- BMJ-RapidRecs as a model: Will organizations get the work done or do we need a disruptive innovation, in health care like elsewhere?
Ilkka Kunnamo 2016:

Jules Verne imagined that you could travel around the world in 80 days.

The Evidence Ecosystem summarized, circulated and implemented the evidence in 85 days.

One day evidence can be circulated as quickly as you travel today.

Want to join the journey?
Remaining challenges and unmet needs in the Ecosystem-