G-I-N Nordic Ecosystem for trustworthy guideline creation, dissemination and updating
Declaration of interests
Meet Jon, 63 years old bus driver

- Hospitalized with stroke
- Proximal anterior circulation occlusion
- Received thrombolysis within 3 hrs
- Should we do thrombectomy?
- 4 trials published showing positive results in NEJM 2015
- How find trustworthy answers?
One of four studies in NEJM 2015

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Thrombectomy (N = 103)</th>
<th>Control (N = 103)</th>
<th>Effect Variable</th>
<th>Unadjusted Value (95% CI)</th>
<th>Adjusted Value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome: score on modified Rankin scale at 90 days</td>
<td>NA</td>
<td>NA</td>
<td>Common odds ratio</td>
<td>1.7 (1.04 to 2.7)</td>
<td>1.7 (1.05 to 2.8)</td>
</tr>
<tr>
<td>Secondary outcome</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Score of 0 to 2 on modified Rankin scale at 90 days — no. (%)†</td>
<td>45 (43.7)</td>
<td>29 (28.2)</td>
<td>Odds ratio</td>
<td>2.0 (1.1 to 3.5)</td>
<td>2.1 (1.1 to 4.0)</td>
</tr>
<tr>
<td>Dramatic neurologic improvement at 24 h — no./total no. (%)‡</td>
<td>59/100 (59.0)</td>
<td>20/100 (20.0)</td>
<td>Odds ratio</td>
<td>5.5 (2.9 to 10.3)</td>
<td>5.8 (3.0 to 11.1)</td>
</tr>
<tr>
<td>Median NIHSS score at 90 days (IQR)</td>
<td>2.0 (0.0 to 8.0)</td>
<td>6.0 (2.0 to 11.0)</td>
<td>Beta</td>
<td>−2.7 (−4.4 to −0.9)</td>
<td>−2.4 (−4.1 to −0.8)</td>
</tr>
<tr>
<td>Barthel Index score of 95 to 100 at 90 days — no./total no. (%)§</td>
<td>47/82 (57.3)</td>
<td>23/87 (26.4)</td>
<td>Odds ratio</td>
<td>3.7 (2.0 to 7.1)</td>
<td>4.2 (2.1 to 8.4)</td>
</tr>
<tr>
<td>Median EQ-5D score at 90 days (IQR) ¶</td>
<td>0.65 (0.21 to 0.79)</td>
<td>0.32 (0.13 to 0.70)</td>
<td>Beta</td>
<td>0.13 (0.03 to 0.23)</td>
<td>0.11 (0.02 to 0.21)</td>
</tr>
<tr>
<td>Infarct volume at 24 hr</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients evaluated on CT:diffusion-weighted MRI — no.</td>
<td>91:10</td>
<td>98:5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR) — ml</td>
<td>16.3 (8.3 to 58.5)</td>
<td>38.6 (11.9 to 86.8)</td>
<td>P value</td>
<td>P = 0.02</td>
<td></td>
</tr>
</tbody>
</table>
Finding trustworthy answers to clinical questions

Thrombectomy for stroke?

FOCUSED QUESTIONS

Search for recommendations in evidence-based guidelines

AUDIT

IMPLEMENT

Can you trust and use those recommendations?

Apply the recommendations on individual patients

Incorporate clinical expertise and patient preferences
How good are we at answering our questions?

Clinical Questions Raised by Clinicians at the Point of Care
A Systematic Review

Guilherme Del Fiol, MD, PhD; T. Elizabeth Workman, PhD, MLIS; Paul N. Gorman, MD

RESULTS In 11 studies, 7012 questions were elicited through short interviews with clinicians after each patient visit. The mean frequency of questions raised was 0.57 (95% CI, 0.38-0.77) per patient seen, and clinicians pursued 51% (36%-66%) of questions and found answers to 78% (67%-88%) of those they pursued. Overall, 34% of questions concerned drug treatment, and 24% concerned potential causes of a symptom, physical finding, or diagnostic test finding. Clinicians’ lack of time and doubt that a useful answer exists were the main barriers to information seeking.

CONCLUSIONS AND RELEVANCE Clinicians frequently raise questions about patient care in their practice. Although they are effective at finding answers to questions they pursue, roughly half of the questions are never pursued. This picture has been fairly stable over time despite the broad availability of online evidence resources that can answer these questions. Technology-based solutions should enable clinicians to track their questions and provide just-in-time access to high-quality evidence in the context of patient care decision making. Opportunities for improvement include the recent adoption of electronic health record systems and maintenance of certification requirements.
Evidence-based medicine: Great advances
Finding best current recommendations and evidence within 2 minutes

- **UpToDate**
  - Reporfusion therapy for acute ischemic stroke
  - Neuroimaging of acute ischemic stroke
  - More Results...

- **Best Practice**
  - Overview of stroke
  - Ischaemic stroke
  - More Results...

- **Systematic reviews**

- **PLUS Syntheses**
  - Stroke in the TOTAL trial: a randomized trial of routine thrombectomy vs. percutaneous coronary intervention alone in ST elevation myocardial infarction. *(Systematic Review)*

- **Oppsummerte Enkeltstudier**

- **ACP Journal Club (selected via PLUS)**
  - Adding neurovascular thrombectomy to IV t-PA reduced disability in acute ischemic stroke
  - In STEMI, manual thrombectomy before PCI did not reduce CV-related outcomes but increased stroke
  - More Results...

- **PLUS Studies**
  - Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *(Original Study)*
  - Thrombectomy within 8 hours after symptom onset in ischemic stroke. *(Original Study)*
UpToDate provides an answer

Basics topic (see "Patient information: Stroke (The Basics)"

Beyond the Basics topics (see "Patient information: Stroke symptoms and diagnosis (Beyond the Basics)" and "Patient information: Ischemic stroke treatment (Beyond the Basics)"

SUMMARY AND RECOMMENDATIONS

Randomized controlled trials have shown that intravenous alteplase (recombinant tissue-type plasminogen activator or tPA) improves functional outcome from ischemic stroke and that the benefits outweigh the risks for patients who receive treatment within 4.5 hours of symptom onset (or within 4.5 hours of when the patient was last seen normal in cases when onset time is unknown). The benefit of intravenous thrombolysis decreases continuously over time from symptom onset. Therefore, treatment must be given as soon as possible, rather than near the end of the time window. (See 'Intravenous thrombolysis' above and 'Treatment within 3 hours' above and 'Treatment from 3 to 4.5 hours' above and 'Pooled data' above.)

The most important factor in successful thrombolytic treatment of acute ischemic stroke is early treatment. Nonetheless, selection of appropriate candidates for thrombolysis (table 1) demands a neurologic evaluation and a neuroimaging study. For eligible patients with acute ischemic stroke, we recommend intravenous alteplase therapy, provided that treatment is initiated within 3 hours of clearly defined symptom onset (Grade 1A). For patients who cannot be treated in less than 3 hours, we suggest intravenous alteplase therapy, provided that treatment is initiated within 3 to 4.5 hours of clearly defined symptom onset (Grade 2A). Recommendations for the use of intravenous alteplase are discussed separately. (See "Intravenous fibrinolytic (thrombolytic) therapy in acute ischemic stroke: Therapeutic use".)

Recanalization is generally associated with improved outcome and reduced mortality in acute ischemic stroke. A number of factors may affect the response to thrombolytic therapy, including location of the occlusion in the arterial tree, availability of collateral blood supply, and clot-specific features such as size, composition, and source. (See 'Recanalization' above and 'Factors affecting recanalization' above.)

For patients with ischemic stroke caused by a large artery occlusion in the proximal anterior circulation, we recommend early treatment with intra-arterial mechanical thrombectomy using a second-generation stent retriever device, whether or not the patient received treatment with intravenous tPA, if the following conditions are fulfilled (Grade 1A) (see 'Mechanical thrombectomy' above and 'Selecting patients for mechanical thrombectomy' above):

- Neuroimaging (eg, CT without contrast) is consistent with a small infarct core (ie, minimal or no signs of early ischemic change) and excludes hemorrhage
- Angiography (eg, CT angiography) demonstrates a proximal large artery occlusion in the anterior circulation
- Thrombectomy is performed at a stroke center with expertise in the use of stent retrievers
- Intra-arterial thrombectomy is initiated within 6 hours of stroke symptom onset
What does our national guideline (from 2010) say?

3.5.1 Reperfusjonsbehandling

**Underkapitler**
- Intravenøs trombolytisk beh
- Intra-arteriell behandling

**Anbefalinger: akutt reperfusjonsbehandling**

<table>
<thead>
<tr>
<th>Anbefalinger</th>
<th>Grad</th>
<th>Nivå</th>
</tr>
</thead>
<tbody>
<tr>
<td>i.v. trombolyse med r-tPA (alteplase) er en effektiv behandling som bør tilbys utvalgte pasienter * med akutt hjerneinfarkt innen 3 t etter sykdomsstart* og bør startes tidligst mulig.</td>
<td>A</td>
<td>1a</td>
</tr>
<tr>
<td>i.a. trombolyse eller i.a. embolektomi kan vurderes hos utvalgte pasienter med kontraindikasjoner mot i.v trombolyse eller store proksimale okklusjoner, men klare</td>
<td>D</td>
<td>4</td>
</tr>
</tbody>
</table>
We need to create trustworthy guidelines according to new definitions and standards

New definition

“Clinical Practice Guidelines are statements that include recommendations intended to optimize patient care. They are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options“
Systematic review

Guideline development

Formulate recommendations:
- For or against (direction)
- Strong or weak/conditional (strength)

By considering:
- Quality of evidence
- Balance benefits/harms
- Values and preferences

Revise if necessary by considering:
- Resource use (cost)

Create evidence profile with GRADEpro
Rate quality of evidence for each outcome

Summary of findings & estimate of effect for each outcome

Grade overall quality of evidence across outcomes

Illustration from Holger Schunemann and Yngve Falck Ytter
How are the Nordic countries coping?

- Lots in common, but work in silos
- Guidelines made independently
- Extremely resource-demanding
- Huge duplication, waste!!
- No established collaboration, uniform data models and formats for creating and disseminating
- Major Nordic guideline producers now cooperating through G-I-N Nordic Regional working group
We aim to solve global problems

- Although considered crucial for safe and high quality health care most current clinical practice guidelines suffer from
  - lacking trustworthiness
  - a cumbersome development process,
  - suboptimal presentation formats
  - inefficient dissemination
  - being outdated
  - sub-optimal facilitation of shared decision making
G-I-N Nordic: Overall goal

- In this project GIN Nordic aims to **develop, test and evaluate a Nordic ecosystem for developing, disseminating and updating evidence based Nordic guidelines**.
- The project shall be **considered a pilot within GIN International**, as a **framework for international collaboration and adaptation** that may be recommended and further shared through GIN International.
Guideline authoring and publication platform (MAGICapp)

- **PICO**
- Individual studies
- Descriptive tables
- Evidence profiles
- Recommendations
- Key information
- Rationale

**New evidence**

**Dynamic updating**

**Multilayered formats**

**for all devices**

**Integrated in the EMR**

**Adaptation**

- National/ local or EBM Textbooks

**Database**

structured and tagged content

**Decision aids**

for patients and clinicians

**MAGIC with DECIDE**

**Guideline making GRADE the irresistible choice**

**MAGIC**

Guideline authoring and publication platform (MAGICapp)
A trustworthy recommendation for thrombectomy? Not anymore!
A trustworthy and digital evidence ecosystem
Work package 1 - Cooperation & adaptation

- Guidelines for stroke, dementia and ADHD

- Overall goal is to
  ✓ establish forums for cooperation, sharing and adaptation of guidelines
  ✓ avoid redundant work and significantly increase guideline development efficiency and quality
Work package 2 - guideline development by professional societies

1. Fluid resuscitation in critically ill general ICU patients with acute circulatory failure

**HES**

- **Sterk anbefaling**

  We recommend that crystalloids are used for resuscitation in general ICU patients rather than HES

**Albumin**

- **Svak anbefaling**

  We suggest that crystalloids are used for resuscitation in general ICU patients rather than albumin

**Gelatin**

- **Svak anbefaling**

  We suggest that crystalloids are used for resuscitation in general ICU patients rather than gelatin

2. Fluid resuscitation in critically ill septic patients with acute circulatory failure
Work Package 3: Test bed for software developers
Take home messages

- Great advances in standards and systems for EBM, guidelines and decision support tools
- Technology will play a key role in creating, disseminating and updating trustworthy evidence in a digital world
- EBM not enough: Evidence Ecosystem a solution?
- G-I-N Nordic is ongoing innovation project, results to come