Why do we need guidelines?

(and the implications for guideline producing bodies and also for quality assessment programs)

W. Van Biesen, chair of European Renal Best Practice
Renal Division, Ghent University Hospital
Where are we coming from?
Eloquence based medicine
Emotion based medicine

Stu's Views
The Problem With Juries

His tie is too blue. I'm voting for the other guy.
Eminence based medicine

Don't worry! I've done this hundreds of times!

Experience can just mean making the same mistake with increasing confidence.

www.european-real-best-practice.org
TO MAINTAIN A HEALTHY BODY, YOU MUST DRINK AT LEAST 8-10 GLASSES OF WATER PER DAY.

GLUG GLUG
GLUG GLUG
GLUG GLUG GLUG
GLUG GLUG GLUG
GLUG GLUG
GLUG GLUG
GLUG GLUG
GLUG GLUG
GLUG GLUG

One size fits all
Evidence Based Medicine (old school)

This is a whale
Evidence Based Medicine
Where are we coming from?

And where we should go to......
Evidence Based Medicine

Decision making on (medical) actions, intentionally based on a transparent and systematic analysis of available evidence, and this applied to a real-life clinical context
Evidence Based Medicine

Decision making on (medical) actions, intentionally based on a transparent and systematic analysis of available evidence, and this applied to a real-life clinical context

With the goal to decrease the discrepancy between medical actions And Medical knowledge
Evidence Based Medicine is a way of thinking about your everyday caring for patients
Evidence Based Medicine

1. Individual level
   a) Individual patient individual physician
   b) Individual physician and his patients with a specific problem (systematic review)
Evidence Based Medicine

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   a) Individual patient individual physician
   b) Individual physician and his patients with a specific problem
      (systematic review)

2. Organisational (Hospital) level
   a) Group of physicians and their patients with a specific problem
      (Protocolized medicine, standing orders)
   b) Different groups of physicians and a patient
      • with one problem on the borderline of different specialties
      • With different comorbidities
Evidence Based Medicine

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3. Society level
   • Sustainability
   • Fairness/Equity (guidance/guidelines)
ERBP Mission

improve the outcome of patients with kidney disease in a sustainable way, through enhancing the accessibility of knowledge on patient care, in a format that stimulates its use in clinical practice.
Do we need guidelines?

Do we need guidelines?

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Do we need guidelines?
Why we need guidelines

1° Objective scientific reasons
(because science is not always scientific)

2° Asking the right question
(WYSIATI effects and anchoring effects)

3° Subjective reasons
(because we take emotional decisions)

4° Socio-economic
(because we want to make people healthy, not ill)
(because a Euro can only be spent once, even in Cyprus or Greece)
Why we need guidelines
Objective scientific reasons (because science is not always scientific)

1. too much information, but also too much information lacking
Why we need guidelines

Objective scientific reasons (because science is not always scientific)

1. too much information

Pubmed: Mesh term “acute kidney injury”: yield 30885 papers

Of these: only 211 are randomised controlled trials

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Impact of non-published evidence: the reboxetine case

Eyding et al, BMJ, 2010

Fig 6 | Forest plot showing meta-analyses of published, unpublished, and all trials. Publication bias (right column) is presented as the ratio of odds ratios of published results versus overall results. The extent of publication bias is expressed as
Why we need guidelines

Objective scientific reasons (because science is not always scientific)

1. too much information, but also too much information lacking
2. Available information presented in a biased way
Why we need guidelines

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The incidence of hyponatremia is estimated to be as high as 30% in the hospitalized setting\(^4\) and 21% in ambulatory patients.\(^5\) Importantly, the incidence of hyponatremia increases with age and has been reported in up to 53% of elderly patients in chronic care settings.\(^2,6-8\) Hyponatremia is associated with complications of comorbid conditions,\(^9\) significantly greater length of hospital stay,\(^10\) and higher readmission rates.\(^11\) Further, hyponatremia is a strong predictor of both inpatient and postdischarge mortality. Inhospital mortality rates of 16% have been reported in patients >65 years of age with hyponatremia compared with 8% in those with normal sodium concentrations on admission.\(^12\)
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11. Adrogué HJ. Consequences of inadequate management of...
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Study of Heart and Renal Protection

Interpretation: Reduction of LDL cholesterol with simvastatin 20mg plus ezetimibe 10mg daily safely reduced the incidence of major atherosclerotic events in a wide range of patients with advanced kidney disease

Relative risk reduction: 17%

Baigent et al, Lancet 2011
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Number needed to treat: 50

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**Absolute risk reduction:** from 619/4620 to 526/4650 so from 13.4% to 11.3% or **2.1%**

**Number needed to treat:** 50

**So:** you need to treat 50 patients during 5 years to avoid one event

**No difference in mortality:** 68 of 93 events were “revascularisation”

“there was no good evidence that the treatment effect was different in any of the subgroups”

**HOWEVER:** Palmer et al, Ann Int Medicine, 2012: SHARP data to assess interaction of subgroups on treatment effect were not available; conclusion of their meta-analysis: Moderate- to high-quality evidence indicated that statins had little or no effect on all-cause mortality (RR, 0.96 [CI, 0.88 to 1.04]), cardiovascular mortality (RR, 0.94 [CI, 0.82 to 1.07]), or cardiovascular events (RR, 0.95 [CI,0.87 to 1.03]) in persons receiving dialysis.

Baigent et al, Lancet 2011
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1. too much information, but also too much information lacking
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3. Available information prejudiced based on “surrogate outcomes” (CKD-MBD, anaemia)
Impact of calcimimetics on outcome

### A Primary Composite End Point

- **No. at Risk**
  - Placebo: 1935, 1804, 1693, 1579, 1476, 1384, 1312, 1224, 1160, 1109, 1053, 996, 940, 650, 404, 114
  - Cinacalcet: 1948, 1842, 1739, 1638, 1556, 1472, 1334, 1303, 1230, 1177, 1115, 1051, 989, 679, 399, 113

- **Hazard ratio**, 0.93 (95% CI, 0.85–1.02)
- **P** = 0.11 by log-rank test

### B Death

- **No. at Risk**
  - Placebo: 1935, 1882, 1828, 1754, 1694, 1622, 1559, 1486, 1426, 1388, 1334, 1283, 1232, 886, 537, 162
  - Cinacalcet: 1948, 1903, 1845, 1779, 1736, 1680, 1621, 1565, 1507, 1462, 1412, 1354, 1292, 899, 546, 167

- **Hazard ratio**, 0.94 (95% CI, 0.85–1.04)
- **P** = 0.25 by log-rank test
Why we need guidelines

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1. too much information, but also too much information lacking
2. Available information Biased
3. Available information prejudiced based on “surrogate outcomes” (CKD-MBD, anaemia)
4. Available information Incomplete or not answering the right question
5. Problem of generalisibility
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4. Available information Incomplete
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Table 3  Percentage of individuals who potentially meet eligibility criteria for included asthma randomised controlled trials

<table>
<thead>
<tr>
<th>RCT reference</th>
<th>Current asthma (%)</th>
<th>Current asthma on treatment (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>14</td>
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<td>10</td>
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<td>9</td>
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<td>16</td>
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<td>0</td>
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<td>18</td>
<td>4</td>
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<td>19</td>
<td>2</td>
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<td>22</td>
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<td>11</td>
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<td>24</td>
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<td>25</td>
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<td>2</td>
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<td>26</td>
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<td>27</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>28</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>29</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>

RCT, randomised controlled trial.
Asking the right (clinical) question rigorously

1. Question : PICOM

- Patient
- Population

- Intervention

- Comparator

- Outcomes

- Methodology: question type, best feasible study design
Asking the right (clinical) question

1. Question : PICOM

P: Patient
   - Population

I: Intervention

C: Comparator

O: Outcomes

M: Methodology: question type, best feasible study design


2. Systematic Search

• Goal: to retrieve the relevant studies
  - Without bias ↔ those you know/believe
  - Efficient: balance between
    • Sensitivity: avoids missing relevant studies
    • Specificity: avoids too many irrelevant studies: noise
    • Time-efficient

• World-wide accepted methodology:
  - Electronic database-search: Cochrane Library, Medline using PICOM
Why we need guidelines

3° Subjective reasons (because we take emotional decisions)
Why we need guidelines

3° Subjective reasons
(because objective information does not exist)
(because we take emotional decisions)
Question 1

• A 85 year old women with long standing diabetes and amputations, dialysis dependence, bilateral diabetic retinopathy, is hospitalised because of diarrhea.

• A last Chest X ray before dismission shows an enlarged hilus, suspicious for a malignancy. What do you do?
  – A: you plan a CT thorax and a bronchoscopy to establish the diagnosis more certain.
  – B: you plan a CT thorax, a PET scan, a bone scintigraphy and a bronchoscopy for a complete staging.
  – C: you just dismiss the patient as planned
  – D: You ask the opinion of the patient and discuss the option of withdrawal of dialysis if things go worse
  – E: You ask the opinion of the family, but do not speak with the patient
Question 1

- Your 85 year old grandmother with long standing diabetes and amputations, dialysis dependence, bilateral diabetic retinopathy, is hospitalised because of diarrhea.

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  - E: You ask the opinion of the family, but do not speak with the patient
Thinking errors
Anchoring (Halo effect)
Attribution
Availability
METFORMIN
in advanced CKD:

METFORMIN in advanced CKD:

LACTIC ACIDOSIS
**A coctail of risk aversion and WYSIATI effects**

<table>
<thead>
<tr>
<th></th>
<th>Metformin-associated lactic acidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of lactic acidosis or severe hypoglycaemia in type 2 DM (number per 100,000 patient years)</td>
<td>6.3 [4]</td>
</tr>
<tr>
<td>Mortality (percentage; most pessimistic available figure)</td>
<td>50% [22]</td>
</tr>
<tr>
<td>Predicted absolute no. of deaths (number per 100,000 pt years)</td>
<td>3</td>
</tr>
</tbody>
</table>

ARGUMENTS AGAINST-

IT'S IN MY BACKYARD!
ARGUMENTS AGAINST-

NUCLEAR

OIL

COAL

IT'S IN MY BACKYARD!
A cocktail of risk aversion and WYSIATI effects

Table 1  Predicted absolute number of deaths caused by the life-threatening complications of metformin and sulphonylureas

<table>
<thead>
<tr>
<th></th>
<th>Metformin-associated lactic acidosis</th>
<th>Sulphonylurea-induced hypoglycaemia</th>
<th>Insulin-induced hypoglycaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>or severe hypoglycaemia in type 2 DM (number per 100,000 patient years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality (percentage; most pessimistic available figure)</td>
<td>50% [22]</td>
<td>4.3% [21]</td>
<td>4.3% [21]</td>
</tr>
<tr>
<td>Predicted absolute no. of deaths (number per 100,000 pt years)</td>
<td>3</td>
<td>43</td>
<td>77.4</td>
</tr>
</tbody>
</table>

Impact of “evidence based medicine”

Q1: change to “newer” treatment if shown to be superior
Q2: change to “older” treatment if shown to be equally effective but less expensive than “newer”
Why we need guidelines

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1° Physicians
2° Patients
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- Buridan’s donkey
- Immediate vs anticipated emotions
- Hyperbolic distortion
- Harm vs benefit
Evidence Based Medicine

This is a whale
7. Recommendations/GRADE

**Strength of Recommendation**

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>“Strong”</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>“Weak”</td>
<td></td>
</tr>
</tbody>
</table>

**Quality of evidence**

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>Very low</td>
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Strong

- most patients would want the treatment, most clinicians would want to provide it: “We recommend...”
- most patients would not want the treatment, most clinicians would not want to provide it: ”We do not recommend...”

Weak

- Some patients would want the treatment, some clinicians would want to provide it, but others might not, dependent on their values and preferences: “We suggest...”
7. Recommendations/GRADE

**Strength of Recommendation**

- **1** “Strong”

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- **A** High
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- **D** Very low

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Differing Levels of Clinical Evidence: Exploring Communication Challenges in Shared Decision Making
Quentin W. Smith, Richard L. Street, Jr., Robert J. Volk and Michael Fordis
Med Care Res Rev 2013 70: 3S originally published online 6 December 2012
DOI: 10.1177/1077558712468491

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(because a Euro can only be spent once)
Proposed Psychiatrists' Disorders:
1. MANIC AGGRESSIVE DIAGNOSIS (M.A.D.)

Knowing they did not need definitive research, an accurate test or effective treatment made developing new conditions for DSM-6 so much easier.
Fig. 2 Five-year cost utility and gained 5-year quality-adjusted life years (QALYs) for acute renal replacement therapy stratified according to age. Bars mark cost utility and solid line gained QALYs in different age groups. Dotted line marks the limit for cost-effective treatment (50,000 €/QALY)
ERBP Mission

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What to do when there is no evidence?

This is an easy job.
What to do when there is no evidence?

How do we get everybody on board?

What are patient important outcomes?

How do we improve available evidence?

How far and how should health economics be involved?

This is an easy job
What to do when there is no evidence?

If we have guidelines, how will we measure/monitor the adherence to them?

How far and how should health economics be involved?

This is an easy job
If we have guidelines, how will we measure the adherence to them?
Measuring quality

* Measures vs indicators

Direct measuring of a physical concept eg body weight

Some representation that reflects another entity

* Structures vs procedures vs outcomes

How many nurses, is there a CT scan etc

Hepatitis B vaccination
Hand washing etc
% of patients having a bone densitometry
How many patients receive a statin

Number of bacteraemias in the HD unit
Cardiovascular deaths/year

Type of outcomes:
- clinical outcomes
- Clinical correlates
- surrogate markers
Measuring quality

* Aim of the quality measurement

- Performance monitoring (eg registries; cave confounding, cave cherry picking)
- Formative monitoring: to improve quality
- Summative monitoring
  - evidence based
  - measurable in a reliable way
  - direct relation with hard outcome
  - no negative/undesired influence on behavior (eg the fistula first debacle)
Quis custodiet ipsos custodies?