Types of questions.
Framing a question: PICO question

Jesús López Alcalde
Public Health Policy Support Unit
Institute for Health and Consumer Protection
(JRC-IHCP)

Outline

- Guideline as a list of questions to answer
- Types of questions
- Question formulation: the PICO format
- Exercise

Guideline as a list of questions to answer

"[...] knowledge is information in action, information focused in results" 

Peter F. Drucker

Take home message:
Guidelines formulate questions which lead to actions

Outline

- Guidelines as lists of questions to answer
- Types of questions
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Types of questions

Background questions

- Definition: What is Chronic Obstructive Pulmonary Disease (COPD)?
- Mechanism: What is the mechanism of action of beta-agonists?

Foreground questions

- Effects interventions: In patients with COPD, do beta-agonists improve survival?
- Validity of diagnostic tests

Background question

What is contact investigation in tuberculosis?

Foreground question

What proportion of people who have contact with cases of TB are correctly diagnosed with the Mantoux test?

Exercise: Type of question (Background/Foreground)

<table>
<thead>
<tr>
<th>Question</th>
<th>Type of question</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is contact investigation in tuberculosis?</td>
<td>Recommendation</td>
</tr>
<tr>
<td>What is avian influenza?</td>
<td>Recommendation</td>
</tr>
<tr>
<td>What effect do antivirals have on reducing mortality?</td>
<td>Recommendation</td>
</tr>
<tr>
<td>Is this antiviral safe?</td>
<td>Recommendation</td>
</tr>
<tr>
<td>What proportion of people who have contact with cases of TB are correctly diagnosed with the Mantoux test?</td>
<td>Recommendation</td>
</tr>
</tbody>
</table>

Types of question: other classification

How common is the problem?

Is this diagnostic test accurate?

What will happen if we do not add a therapy?

What are the benefits of this intervention?

What are the harms associated to this intervention?

Exercise: Type of question

<table>
<thead>
<tr>
<th>Question</th>
<th>Type of question</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. What is the sensitivity and specificity of mammography for screening of breast cancer?</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>2. Do centrally organised screening programmes reduce breast cancer mortality?</td>
<td>Efficacy/Effectiveness</td>
</tr>
<tr>
<td>3. Does the increase of tobacco taxes reduce lung cancer mortality?</td>
<td>Efficacy/Effectiveness</td>
</tr>
<tr>
<td>4. Does breast cancer screening based in mammography cause anxiety in women?</td>
<td>Safety/Concerns</td>
</tr>
<tr>
<td>5. What are the effects of intercessory prayer as an additional intervention for people with health problems already receiving routine health care?</td>
<td>Efficacy/Effectiveness</td>
</tr>
</tbody>
</table>

This workshop will focus on recommendations about the effects of interventions

GRADE does not provide a formal structure for evaluating the quality of evidence underlying questions of prognosis.

A hard moment: select the questions to answer in the guideline

“I am rather like a mosquito in a nudist camp; I know what I ought to do, but I don’t know where to begin” - Stephen Bayne

Please, select good questions!
What is a good question? Please, answer

- There is controversy around the answer
- There is doubt around the answer
- Want to confirm the present answer
- It will determine research in future
- Will improve care, cost, quality of life

Questions in guidelines...

...should be practice driven
...should NOT be evidence driven

Outline

- Guidelines as list of questions to answer
- Types of questions
- Question formulation: the PICO format
- Exercise

Framing a foreground question

Example: Should we recommend the use of antiplatelet agents in people with vascular disease?

**P**opulation

Question: Should we recommend the use of antiplatelet agents in people with vascular disease?

Decide how broadly the patients will be defined

Options for the population's definition:
- only patients with myocardial infarction;
- patients with myocardial infarction and stroke;
- patients with any vascular disease (cerebro-, cardio-, or peripheral vascular disease), etc.

**I**ntervention

**C**omparison

**O**utcomes

Example

A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). Lancet 1997;349:1329-39

Antiplatelet agents differ in effectiveness in those with peripheral vascular disease vs. those with myocardial infarction

**P**opulation:

Patients with any vascular disease (cerebro-, cardio-, or peripheral vascular disease).

**I**ntervention

**C**omparison

**O**utcomes

It may be inappropriate
Please, consider “everyday patients”, not “ideal patients”.

What proportion of everyday depressive patients would be excluded from antidepressant efficacy trials?

66% of everyday depressive patients would be excluded.

Example: Should we recommend the use of mozzarella versus Parmigiano in pizzas?

POPULATION: Pizza
INTERVENTION: Mozzarella
COMPARISON: Parmigiano
OUTCOMES: Customer’s satisfaction

Take home message: If different kinds of mozzarella differ in taste, a single estimate across the mozzarelas will not well serve the decision-making needs of customers.

What kind of Comparators can we find? Please, suggest

- Doing nothing
- Placebo (an inactive substance)
- “Sham intervention” (an inactive procedure)
- Other active intervention
- The same intervention but with different dose, administration route, etc.

One important comment about Comparators:

Test your intervention against something meaningful!!

On the contrary you will do marketing, not research.

PI CO question: the Intervention

Question: Should we recommend the use of antiplatelet agents for vascular disease?

The panel must decide how broadly the intervention will be defined.

Options to define the intervention:
- All antiplatelet agents;
- Any dose of a specific antiplatelet, aspirin;
- A relatively narrow range of doses of aspirin, etc.

PI CO question: the Comparator

There may be multiple comparators to an intervention

Specify the comparator explicitly!

When multiple agents are involved, guideline developers should specify whether the recommendation is suggesting that all agents are equally recommended or that some agents are recommended over others.
Examples of meaningless comparators

- A comparator known to be useless
- A comparator known to be useful but in the trial is used in a useless way (for example, at a low or high dose)

"One thing that's likely to make your new treatment look good is testing it against something that doesn't work very well; this might sound absurd, or even cruel..."

Ben Goldacre, 2012: Bad Pharma: How Medicine is Broken, and How We Can Fix It

Example of meaningless comparison

<table>
<thead>
<tr>
<th>Amitryptiline (new antidepressant)</th>
<th>Versus</th>
<th>Paroxetine (old antidepressant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apparently free of side effects like drowsiness</td>
<td>Old drug known to make people sleepy</td>
<td>Normally given by night</td>
</tr>
</tbody>
</table>

Outcome: daytime sleepiness

Ben Goldacre, 2012: Bad Pharma
Safer 2002.

Nerv Ment Dis
190:583–592, 2002

A guideline question often involves another specification:

The SETTING where the recommendation is intended

High income environment
Middle income environment
Low income environment

Should we recommend the use of antibiotics for children with otitis media?

Low risk of mastoiditis
High risk of mastoiditis

Framing a foreground question

Example: Should we recommend the use of antiplatelet agents for vascular disease?

P - POPULATION
I - INTERVENTION
C - COMPARISON
O - OUTCOMES

+ SETTING

Please, consider the context!

Evidence of the importance of the context: a dramatic document

Take home message: When defining P, I and C...

- The magnitude of the effect on the key outcomes should be similar across the range of patients and interventions considered by the question
- Consider the context where the recommendation will be applied
Background
• Anticoagulants (blood thinners) may improve the survival of patients with cancer
• This benefit could be related to the prevention of blood clots and to a direct antitumor effect (in addition to preventing blood clots)

The "general" question: Should I give blood thinners in patients with cancer?

Instructions:
• Read Section 0: "Background on anticoagulants" (5 min)
• Form groups and select someone to report back (3 min)
• Specify P, I and C of the clinical question (10 min)
• Report back to the whole group (2 minutes)
• Question suggested by the facilitator

Exercise: Define Population, Intervention and Comparator (30 min)

Population
Patients with cancer with no indication for prophylactic anticoagulation (e.g., peripherally) or for therapeutic anticoagulation (e.g., for the treatment of deep vein thrombosis)

Intervention
Parenteral anticoagulants, in particular, unfractionated heparin (UFH), low molecular weight heparin (LMWH), and fondaparinux (synthetic heparin)

Comparator
Placebo or no intervention

Outcome
See next session!!!