The notion of PICO for synthesis: planning the grouping of studies for meta-analyses and other syntheses

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Declaration of interest

I am employed by Cochrane Australia (CA), School of Public Health and Preventive Medicine, Monash University. CA is funded by the Australian Government through the National Health and Medical Research Council (NHMRC) to support the conduct and use of systematic reviews, research translation, and methodological development in evidence synthesis.

I am the director of the Melbourne GRADE Centre.

I have received funding from the NHMRC and other government funders to undertake commissioned systematic reviews and methodological review of systematic reviews and guidelines.

I am co-author on four chapters of the new Cochrane Handbook.
Defining the criteria for including studies and how they will be grouped for the synthesis

Joanne E McKenzie, Sue E Brennan, Rebecca E Ryan, Hilary J Thomson, Renée V Johnston, James Thomas

3.1 Introduction

One of the features that distinguishes a systematic review from a narrative review is that systematic review authors should pre-specify criteria for including and excluding studies in the review (eligibility criteria; see MECIR Box 3.2.a).

When developing the protocol, one of the first steps is to determine the elements of the review question (including the population, intervention(s), comparator(s) and...
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Origins of PICO for synthesis

2011
Madrid methods symposium. Jo McKenzie first aired the ideas on ‘other synthesis methods’ (Chapter 12).

2015
One chapter becomes two

2016
Julian and Tianjing added a subheading. ‘Articulating the PICO for synthesis’

2017
We were still at a loss as to what to write about PICO for synthesis (without copying the chapter on eligibility criteria), but managed 9207 words + 17 pages of tables

2018
Editors. silence ...

2018
GoTo meeting.
We heard James say: “Some useful stuff here. We like the work on PICO for synthesis. WE’VE PUT THAT BIT IT IN CHAPTERS 2 & 3 …”.

2019
One chapter ends up as four. PICO for synthesis was born.

... and Jo, how is the second chapter progressing?
Three levels of PICO

1. **Review PICO** (planned at protocol stage) on which *eligibility of studies* is based [Chapters 2 and 3]

2. **PICO for each synthesis** (planned at protocol stage) which defines *the question that each synthesis aims to answer*. [Chapters 2 and 3]

3. **PICO of included studies** (determined at the review stage) which defines the questions investigated in the included studies [Chapter 9]
The questions we ask

**P**

Does exercise increase bone density in postmenopausal women?

**I**

What is the effect of psychosocial interventions for supporting women to stop smoking in pregnancy?

**C**

What is the comparative efficacy and acceptability of different psychological therapies for panic disorder?
PICO characteristics of studies identified by the search

Which of these studies are ‘eligible’ for the review?

PICO for the review (i.e. the criteria for including studies)
Does exercise increase bone density in postmenopausal women?
Does exercise increase bone density in postmenopausal women?

**The questions we answer**

1. Does exercise increase bone density in postmenopausal women?
2. Does dynamic weight bearing, high force exercise increase bone density?
3. Does dynamic weight bearing, low force exercise increase bone density?
4. Does non-weight bearing, high force exercise increase bone density?
5. Does non-weight bearing, low force exercise increase bone density?
What are the intervention characteristics (criteria) that differentiate each group?

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td><strong>DWB-HF</strong></td>
</tr>
<tr>
<td>16</td>
<td><strong>DWB-HF</strong></td>
</tr>
<tr>
<td>3</td>
<td><strong>DWB-LF</strong></td>
</tr>
<tr>
<td>1</td>
<td><strong>NWB-HF</strong></td>
</tr>
<tr>
<td>10</td>
<td><strong>NWB-HF</strong></td>
</tr>
<tr>
<td>1</td>
<td><strong>NWB-LF</strong></td>
</tr>
<tr>
<td>17</td>
<td><strong>NWB-LF</strong></td>
</tr>
</tbody>
</table>
Which of these studies are ‘eligible’ for each synthesis?
Does dynamic weight bearing, low force exercise increase bone density?

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Exercise</th>
<th>Means (95% CI)</th>
<th>Control</th>
<th>Means (95% CI)</th>
<th>Mean Difference</th>
<th>95%CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bravo 1996</td>
<td>61</td>
<td>0.27 (0.08)</td>
<td>63</td>
<td>0.59 (0.06)</td>
<td>-0.32 (0.06)</td>
<td>11.5</td>
<td>0.05 [0.01, 0.09]</td>
</tr>
<tr>
<td>Chen 2004</td>
<td>44</td>
<td>-0.34 (-0.86)</td>
<td>40</td>
<td>-1.8 (2.93)</td>
<td>1.5 (2.93)</td>
<td>3.8</td>
<td>0.06 [0.01, 0.12]</td>
</tr>
<tr>
<td>Brismeh 1997</td>
<td>40</td>
<td>-0.35 (0.18)</td>
<td>46</td>
<td>-2.75 (0.73)</td>
<td>2.4 (0.73)</td>
<td>0.5</td>
<td>0.06 [0.01, 0.12]</td>
</tr>
<tr>
<td>Lau 1992</td>
<td>11</td>
<td>-0.6 (-0.38)</td>
<td>12</td>
<td>1 (0.58)</td>
<td>-1.6 (0.58)</td>
<td>2.3</td>
<td>0.04 [-0.05, 0.15]</td>
</tr>
<tr>
<td>Lloyd 1995</td>
<td>45</td>
<td>1.53 (1.54)</td>
<td>70</td>
<td>3.13 (6.53)</td>
<td>-1.6 (6.53)</td>
<td>0.2</td>
<td>0.04 [-0.05, 0.15]</td>
</tr>
<tr>
<td>Total (59%) CI</td>
<td>243</td>
<td>242</td>
<td>242</td>
<td>242</td>
<td>100.0</td>
<td>-1.20 [4.41, 2.05]</td>
<td></td>
</tr>
</tbody>
</table>

Interpretation: "Total + 0.019 (95% CI: 0.019; 0.049) = 0.039 (95% CI: 0.019; 0.049)
Test for overall effect: Z = 0.72 (P = 0.47)
Test for subgroup differences: Not applicable"
Should we pre-specify our PICO for each synthesis?

Ideally, yes!

(new guidance in 2019 Cochrane Handbook)
training.cochrane.org/handbook

... almost always some important variants (dose, duration of treatment ...
Why specify PICO for synthesis?*

- Minimise bias & increase reproducibility
- Improve interpretation
- Increase utility

*Cochrane Handbook, Chapter 3, Table 3.2.b
Why specify PICO for synthesis?

| Minimise bias & increase reproducibility | The way in which studies are grouped for synthesis influences findings. A decision to include a study (or not) in a given MA (or other synthesis) will change the result, and possibly the conclusion.
Careful planning of groups may help
• avoid decisions influenced by the findings of individual studies
• increase the reproducibility of findings |
| Improve interpretation | Provides a ‘standardised’ terminology for interventions and outcomes that
• overcomes the varied descriptions used by study authors
• enables comparison and synthesis of PICO characteristics across studies
• provides a consistent language for reporting that aids interpretation |
| Increase utility | Helps ensure that we
• make best use of available data
• produce a review focused on questions relevant to decision makers (especially if involved in planning ..) |

*Cochrane Handbook, Chapter 3, 3.2.3*
A process for planning PICO for each synthesis*

1. Identify intervention characteristics that may modify the effect of the intervention
2. Label and define intervention groups (+ define levels for group based on ‘how much’)
3. Check whether there is an existing system for grouping
4. Plan how the groups will be used in synthesis and reporting
5. Decide how to group interventions with multiple components or co-interventions
6. Build in contingencies by specifying both specific and broader intervention groups

*Suggests steps and the decision points at each step

- Aim is to capture the ‘behind the scenes’ work
- Not intended to be prescriptive, may be iterative, and some steps may be concurrent
- Includes principles for developing a flexible plan, that maximises the potential to synthesise

*Cochrane Handbook, Chapter 3, Tables 3.2.b and 3.2.c
A process for planning intervention groups for synthesis*

1. Identify intervention characteristics that may modify the effect of the intervention
2. Label and define intervention groups (+ define levels for group based on ‘how much’) 
3. Check whether there is an existing system for grouping 
4. Plan how the groups will be used in synthesis and reporting
5. Decide how to group interventions with multiple components or co-interventions
6. Build in contingencies by specifying both specific and broader intervention groups

1. Identify intervention characteristics that may modify the effect of the intervention

Consider whether differences in interventions characteristics might modify the size of the intervention effect importantly. Content-specific research literature and expertise should inform this step.

The TIDieR Checklist – a tool for describing interventions – outlines the characteristics across which an intervention might differ (Hoffmann et al. 2014). These include ‘what’ materials and procedures are used, ‘who’ provides the intervention, ‘when and how much’ intervention is delivered. The iCAT-SR tool provides equivalent guidance for complex interventions (Lewin et al. 2017).

2a. Label and define intervention groups to be considered in the synthesis.

For each intervention group, provide a short label (e.g., supportive psychotherapy) and describe the core characteristics (criteria) that will be used to assign each intervention from an included study to a group.

Groups are often defined by intervention content (especially the active components), such as materials, procedures or techniques (e.g. a specific drug, an information leaflet, a behaviour change technique). Other characteristics may also be used, although some are more commonly used to define subgroups (see Chapter 10, Section 10.11.5); the purpose or theoretical underpinning, mode of delivery, provider, dose or intensity, duration or timing of the intervention (Hoffmann et al. 2014).

In specifying groups:
- focus on ‘clinically meaningful groups that will inform selection and implementation of an intervention in practice;

**Exercise interventions** differ across multiple characteristics, which vary in importance depending on the review.

In a review of exercise for osteoporosis, whether the exercise is weight-bearing or non-weight-bearing may be a key characteristic, since the mechanism by which exercise is thought to work is by placing stress or mechanical load on bones (Howe et al. 2011).

Different mechanisms apply in reviews of exercise for knee osteoarthritis (muscle strengthening), falls prevention (gait and balance), cognitive function (cardiovascular fitness). The differing mechanisms might suggest different ways of grouping interventions (e.g. by intensity, mode of delivery) according to potential modifiers of the intervention effects.

In a review of psychological therapies for coronary heart disease, a single group was specified for meta-analysis that included all types of therapy. Subgroups were defined to examine whether intervention effects were modified by intervention components (e.g. cognitive techniques, stress management) or mode of delivery (e.g. individual, group) (Richards et al. 2017).

In a review of psychological therapies for panic disorder (Pompoli et al. 2016), eight types of therapy were specified:
1. psychoeducation; 
2. supportive psychotherapy (with or without a psychoeducational component); 
3. physiological therapies; 
4. behaviour therapy; 
5. cognitive therapy; 
6. cognitive behaviour therapy (CBT); 
7. third-wave CBT; and

*Cochrane Handbook, Chapter 3, Table 3.2.b
A process for planning outcome groups for synthesis

1. Fully specify outcome domains
2. Determine whether there is an existing system for identifying and grouping important outcomes
3. Define the outcome time points
4. Specify the measurement tool or measurement method
5. Specify how multiplicity of outcomes will be handled
6. Plan how the specified outcome domains will be used in the synthesis
7. Build in contingencies by specifying both specific and broader outcome domains

*Cochrane Handbook, Chapter 3, Table 3.2.c*
Thank you!