Reviewer’s report

Title: Exploratory trials, confirmatory observations: a new reasoning model in the era of patient-centered medicine

Version: 2 Date: 29 March 2011

Reviewer: Robyn Bluhm

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Review of Sacristan: “Exploratory trials, confirmatory observations…”

Major Compulsory Revisions: None

Minor Revisions and comments:

p. 2 – line one of background section: “The prevailing view…is that observations” – should “observations” be “observational studies”

p. 2 – Discussion “…approach to drug R & D” – spell out this abbreviation.

p. 4 – “RCTs were not developed for the purpose of defining individual treatment” – should “defining” be “determining”?

p. 5, first full paragraph: Clarify the relationship between the material in the brackets to what comes before the brackets – are these meant to be examples?

p. 5, last full paragraph: “i.e. RCTs” – but nonrandomized studies can also be controlled. Change “i.e.” to “particularly” or something similar

p. 6, second paragraph – Why is the word “trialists” in italics?

p. 7, first paragraph, last full line – “Dilutional” should probably be “diluting” in this context.

p. 7, second paragraph, line 4: typo – should be “real world”

p. 7, second paragraph, fourth line from bottom: “large sample size equates to a higher level of scientific evidence” – does anyone actually claim this? Is there a hierarchy of evidence that explicitly ranks large trials over small ones?

p. 10 “..the unexpected can signal a new ‘truth’” – what does this mean?

p. 10, second line from bottom: change “He” to “She” (in reference to Cartwright)

p. 11, middle of the page: “until shown to be valid or not by the particular reality of the individual patient or subgroup of patients” – reality is not the best word choice here. Change to reflect something like “circumstances of individual patients…” or “observations of individual patients…” – whichever is truer to your meaning.
p. 13, last full paragraph “to assess how and in particular types of patients interventions are applied in clinical practice” – is there a word missing here?

p. 13, PCR – should this be PCM? (Same on p. 14)

p. 15, first paragraph – “Thoroughly interrogating patients” – interrogation is the wrong word to use here – it sounds rather hostile. Perhaps “Having a thorough discussion with patients” would be a good substitute.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests'