Reviewer’s report

Title: The science of clinical practice: disease diagnosis or patient prognosis? Evidence about “what is likely to happen” should shape clinical practice

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Reviewer: R Moynihan

Reviewer’s report:

1. General comment

This is an exceptionally well-written paper which describes and advocates a potentially major shift in medical thinking. I found it fascinating and educative and suspect it will be very well-cited. I think the paper is easily ready for publication, and my revision suggestions are minor.

My most important suggestion is that the authors include a few explicit words about the potential downsides/limitations of the shift they are advocating. While the emotional tenor of the paper’s language is admirably under-stated, the current lack of such a suitable caveat is notable. For example, addressing the uncertainties and flaws inherent in risk-prediction models is presumably one of several challenges ahead as we move more to a prognosis-based approach. Given the likely audience for this paper, I think the addition of such a caveat will only strengthen its value.

My second suggestion is to the editors: perhaps you might consider commissioning an informed critique of (or response to) this proposal - to help underscore the importance and magnitude of what is being proposed, but also to add a sense of caution and criticism to the considerable enthusiasm for change that is flowing through the paper. Something along the lines of “The Limits of Medical Prognosis” - perhaps written by a researcher from a “social and environmental determinants of health” perspective. (eg Professor Fran Baum - though I have no knowledge of whether she would be interested)

• Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

2. Page 5, Paragraph 2: where you say “patients with long-term illness” - I think you need to add words that reflect the fact that many well people are currently classified as having risk-based conditions. I’d suggest something like ..“For many others, notably patients with long-term ill-health, well people classified as having a risk-based condition, and persons in screening programmes….”

3. I was surprised (not surprisingly) that there was no mention of the problem of overdiagnosis, but presumably this was a deliberate decision by authors. I think mention could be made of the problem early in the article, when discussing the downsides/limitations of current diagnostic practice. I also think there is a very
important omission when the benefits and harms of breast cancer screening are mentioned - on page 14 top paragraph overdiagnosis should be listed as a key adverse consequence, as was stated in the cited Lancet article by Marmot et al.

4. Further to my point 2 above, on page 11 in the last paragraph which is the example, you use the word disease (and have blood sugar, kidney function, blood pressure in brackets) I think you might more accurately refer to these as risk-based conditions, or somesuch, rather than disease.

5. On page 12, bottom paragraph, in the sentence “These shifts….” you rightly mention various factors driving shifting diagnostic boundaries, but it strikes me that you undercut that sentence in the next sentence which starts “Such shifts are fuelled by….” Having written a lot about shifting diagnostic boundaries, my sense is that professional ambition and commercial interest are not motivated solely by a need to “organise medical knowledge” - they are forces which are often nakedly self-interested, and the current wording doesn’t reflect that reality.

6. As per my general comment above, I think the paper needs a few words--perhaps a few sentences, on the limitations of a prognosis-based approach, or a few words of caution about how we move from diagnosis to prognosis, as a key guiding principle in medicine. I suspect the authors will be able to come up with appropriate words, but one concern is that a shift from diagnostic thresholds to prognosis-based estimates of disease risks and treatment outcomes has the potential to extend medicalization and a form of constant medical-surveillance to all, all the time. The growing cultural phenomenon of the “quantified self”, driven by changing technology and enthusiasm for constant measurement of a range of health-related variables, is part of the context within which the papers advocacy of prognosis will emerge. While I think the paper makes many extremely insightful points, and I have considerable sympathy with much of what it advocates, painting prognosis as a panacea may not help generate informed debate about the limits, harms and costs of medicalization and medical care.

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