Author's response to reviews

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

Authors:

Peter Croft (p.r.croft@keele.ac.uk)
Douglas G Altman (doug.altman@csm.ox.ac.uk)
Jonathan Deeks (j.deeks@bham.ac.uk)
Kate M Dunn (k.m.dunn@keele.ac.uk)
Alastair Hay (alastair.hay@bristol.ac.uk)
Harry Hemingway (h.hemingway@ucl.ac.uk)
Linda LeResche (leresche@uw.edu)
George M Peat (g.m.peat@keele.ac.uk)
Pablo Perel (Pablo.Perel@lshtm.ac.uk)
Steffen E Petersen (s.e.petersen@qmul.ac.uk)
Richard Riley (r.d.riley@bham.ac.uk)
Ian Roberts (Ian.Roberts@lshtm.ac.uk)
Michael Sharpe (michael.sharpe@psych.ox.ac.uk)
Richard Stevens (richard.stevens@phc.ox.ac.uk)
Danielle AWM Van Der Windt (d.van.der.windt@keele.ac.uk)
Michael Von Korff (vonkorff.m@ghc.org)
Adam Timmis (adamtimmis@mac.com)

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Author's response to reviews: see over
Dr Lin Lee, PhD  
Senior Editor  
BMC Medicine  

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Dear Dr Lee  

Thank you for your email of 14th October 2014 and for the invitation to amend and resubmit our paper “The science of clinical practice: disease diagnosis or patient prognosis?” as an ‘Opinion’ piece  

Thank you also to both referees for their very helpful and clear suggestions as to how the article can be improved. We outline our responses and changes in detail below.  

The Editors  

“As you can see, both reviewers find this to be a very interesting debate, but Reviewer 1 has suggested this requires major re-write to ensure the article is balanced and the conclusions are strong. We would be in agreement with this suggestion.  

The reviewers have also highlighted that the subject of your debate may be a potentially contentious area. With this in mind, I was wondering if you would consider changing the article type to an 'Opinion' …rather than having this as a 'debate'”.  

We are happy to resubmit the amended article as an ‘Opinion’ piece.  

In our detailed response to referees below, we have outlined how we have reorganised and changed the article to take account of the concerns of the referees.  

In responding to Reviewer 1’s suggestion of a major re-write, we have also taken account of Reviewer 2’s positive view of the written quality of the original version. We have therefore attempted to ensure the latter is retained in responding to the former.  

Reviewer 1  

Point 1: I am very sympathetic to the authors’ overall position. However I do not think they make their case well. First I find the structure of the article to be questionable. In place of a linear argument, the authors give a number of examples, each followed by a brief discussion. The examples seem to follow no particular order, and the discussion following each example tends to be somewhat general, rather than strictly to the case in question. ……..The authors do discuss different aspects of why diagnosis is problematic…but these aren’t presented in a clear and logical
framework......In my view the article needs to be drastically restructured with the arguments more systematically presented.

We are grateful to referee 1 for making us re-think the precise logical steps and order of our argument, and have re-structured and revised the article to meet the referee’s concerns about this. Specifically

1. We have re-ordered the material from the original version to provide a more explicitly linear argument and have provided new sub-headings to support this framework. (These changes have also been informed by referee 2’s comments – see below). The argument is ordered around the ‘opinion’ that prognosis can provide an alternative framework to diagnosis. The progression of the argument is now as follows (new sub-headings in bold, accompanied here by a brief précis of each sub-heading argument):

   a. **A useful diagnosis is defined by patient prognosis** (pages 6-9)
      The extent to which diagnoses are important and useful is defined by prognosis (page 6-8), but evidence about this is often lacking (page 8-9).

   b. Furthermore **Prognosis identifies overdiagnosis** (pages 9-10)
      Many diagnoses and diagnostic procedures carry no benefit or may even be harmful (overdiagnosis). This translates to a need to give primacy to evidence about patient prognosis in clinical practice.

   c. However **Patient prognosis is determined by more than disease diagnosis** (pages 10-13)
      Patient prognosis is not only about evaluating whether diagnosing disease is useful or not, but about incorporating a much wider range of information than can be supplied by diagnosis alone.

   d. Other problems arise because diagnosis assumes disease is present or absent: Not ‘have you got it or not?” but “how much have you got?” (pages 13-14)
      Diagnosis of a disease state is often created by cut-offs applied to what are in reality continuous measures of risk of future outcomes. Such risk measures are better handled in a framework of patient prognosis.

   e. And finally in any framework for clinical practice there are **The pros and cons of labelling people** (pages 15-17)
      Diagnosis has important functions in society apart from determining pathology-targeted treatment, notably the legitimising of illness. Prognosis can provide a framework for these functions which is more usefully focused on patient outcomes.

   f. **In conclusion Prognosis provides a natural framework for modern clinical practice** (pages 17-18).
      New developments in medicine (stratified care and personalised medicine) fit a prognostic framework.
2. In acknowledgement of referee 2’s strong endorsement of the original paper’s style, we have retained our use of clinical examples. We feel this style of using examples is now more justifiable in the context of the paper being an ‘Opinion’ piece, i.e. the examples are there to illustrate different stages of the argument. However we have edited and tightened the text relating to each labelled example in order to respond to referee 1’s concerns that the arguments should be more focused (so for example COPD has been removed).

Point 2: ...the authors fail to distinguish between rather different aspects of the problem. I was particularly worried by their statement that the argument of my own paper is “the diagnostic model is inappropriate for many chronic diseases because it ignores their underlying variability and concerns the hunt for one arbitrary disease state in each sick person.” I barely recognise this characterisation. If there was one key point of the paper, it was that many of what we currently call diseases cause no symptoms and are merely risk factors for some future event such as a heart attack.

We accept this is reasonable criticism. We used one particular aspect of the author’s paper to build a much wider point, rather than highlighting one of the key points of that paper (asymptomatic risk factors are being called diseases). We agree the latter should be a more prominent component of our own argument - this is supported also by referee 2 having a similar criticism (see below). We have therefore amended as follows:

1. In the **Background**, last paragraph (page 5-6): We have added the phrase “well people classified as having a risk-based condition” to the specification of groups for whom a prognostic model might be relevant; and added the phrase “to promote incorporation of quantitative estimates of future outcomes into shared decision-making with patients in clinical practice (6)” to the potential of a prognostic model, reference 6 being a first reference to the reviewer’s paper.

2. Under the sub-heading **“Not “have you got it or not?” but “how much have you got?””**, on page 14 top paragraph, we have rewritten our account of the referee’s paper as follows: “Vickers et al (6) highlight that many such risk variables are artificially dichotomised and treated as disease states rather than as sources of information about probability of future events which provide a quantitative estimate of individual risk for particular outcomes”

3. In first paragraph under **the summary section** on page 18, we have added a further phrase and reference to the referee’s paper as follows: “This extends calls for a risk-centred approach to many syndromes and chronic conditions (6)......”
Reviewer 2

We are grateful for the reviewer's introductory comments on the style, importance and citation potential of the paper.

Point 1: My most important suggestion is that the authors include a few explicit words about the potential downsides/limitations of the shift they are advocating…the current lack of such a suitable caveat is notable.

We accept this point, and have added a number of reflections throughout the paper on potential downsides, hazards and limitations of the prognostic approach, although we have done this in the context of this now being an ‘Opinion’ piece rather than a debate. Specifically

1. The **Background** has new final sentence (top of page 7): “We also discuss potential downsides and limitations of a shift to prognosis-based clinical practice”.

2. First subheading (**a useful diagnosis is defined by patient prognosis**) has new final paragraph (page 9):

   “This demand for prognostic evidence of improved outcomes when evaluating new diagnostic information poses substantial challenges of feasibility for the necessary research, especially for studies of long-term impact and cost. This is a limitation on the prognostic model. Information science, and its expanding reservoir of data linked to patient outcomes, will need to drive novel methods to address these questions, such as modelling of long-term outcomes by combining data from cross-sectional diagnostic and short-term effectiveness studies”.

3. Fourth subheading (**Not ‘have you got it or not?’ but ‘how much have you got?’**) final paragraph is now couched as a caveat (page 14):

   “A potential downside of the prognostic approach is whether clinical models in the real world can incorporate the continuous nature and variability of risk of future avoidable outcomes into decision making. ……Evidence about the clinical usefulness of such new categorisations is essential - prognostic classification for its own sake should not replace diagnosis for its own sake (29)”.

4. Fifth subheading (**The pros and cons of labelling people**) has new final paragraph with a new reference (page 16-17):

   “A hazard of applying a prognostic model in clinical practice relates to the very thing it is designed to reduce, namely over-medicalization of daily life. We have discussed how excessive diagnostic zeal in the absence of improved outcomes for the patient, and the wish to find a pathology to explain every symptom, and the application of diagnostic labels to asymptomatic risk factors, may all lead to ineffective and inefficient care, and harmful side-
effects for the patient. The potential for a prognostic model of care to solve these problems has to be weighed against the possibility that such a model may create its own version of over-medicalization. Aronowitz points to healthy individuals locked rather fearfully into long-term surveillance of risk markers, believing this is the way to ensure continuing good prognosis, even if their risk of death and other adverse outcomes is low (34). The anxieties, and unnecessary and inefficient health care, and commercial and professional interests involved look remarkably similar to those associated with unevidenced diagnostic excess. The resolution lies in demanding high quality evidence of what is and is not useful for improving outcomes, i.e. pursuit of the best prognostic evidence as the scientific basis for resisting excessive medicalization.

5. The **conclusion** has a new ending (page 19):

“However prognosis must not be seen as a panacea for all the problems we have discussed in relation to diagnosis. There must be continuing debate about the benefits, value, limits, harms and costs of medicalization and medical care”.

**Discretionary Point 2:**

We agree and referee 1 raised a similar point. We have added the relevant phrase as detailed in our response 1 to referee 1’s point 2 above.

**Discretionary Point 3:**

We agree and have therefore introduced and more heavily acknowledged the topic of overdiagnosis as an important component of our argument and made the following alterations:

1. Introduced the term ‘overdiagnosis’ (with reference) in the Background section
2. As part of our general restructuring in response to referee 1, we have introduced a new sub-heading “prognosis identifies overdiagnosis”. The text under this sub-heading has been changed to include a definition of overdiagnosis and to incorporate more of our original argument under the umbrella of this term. The reference to the breast cancer screening review now includes the referee’s suggested amendment.

**Discretionary Point 4:**

We agree and this also aligns with referee 1’s second point. The text has been changed.

**Discretionary Point 5:**

We accept our original wording was ambiguous and have made the amendments suggested by the referee.
Discretionary Point 6:

We have used all of the suggestions made under this point to inform the detail and the wording of our changes in response to the referee’s general point 1 (see above) about lack of caveats in the paper.

We hope and believe these changes have made for a more logically structured and balanced paper, whilst retaining our original ambition to provide clinical examples of the main points of our argument.

Yours sincerely

Peter Croft