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

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Author’s response to reviews: see over
Authors’ response to reviews of resubmission

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Author’s response to reviews: see over
Dear Dr Lee

Thank you for your email of 10th December and for the invitation to respond to the peer reviewers’ concerns and to submit a revision of our Opinion piece (a resubmission of the original ‘Debate’) “The science of clinical practice: disease diagnosis or patient prognosis?”

Thanks also once again to both referees for positive views on the resubmitted Opinion piece and clear suggestions as to how the article can be further improved. We outline our responses in detail below.

The Editors

We are happy to address all the referee comments as you request, and have made amendments in the relevant places. Please note we have also amended the conclusions to reflect some of these comments as well, and have included two new references as part of our response to the comments.

Referee 1

General point: “Encouragement to make clarity and coherence and argument-flow key priorities”

Response: We have made amendments in the paper on all specific comments raised but kept them as brief as possible to meet this first comment from referee 1. Most of referee 1’s specific points below are about making the language clearer anyway and so we hope (and certainly believe) that clarity and coherence have been improved/maintained.

Discretionary point 1 “In the final paragraph of the section on overdiagnosis………given there is a reasonable estimate of overall breast cancer benefit, I would soften the sentence and change it to something like this….

There is debate about breast cancer screening for example, and about how much outcomes such as premature cancer mortality are reduced by the programme and to what extent the nature and rate of adverse consequences of screening are acceptable, i.e. how population prognosis changes as a result of a screening programme (19)”

Response: We have altered the paragraph in line with the reviewer’s suggested rewrite in order to better reflect the content of the article we were referencing.

It now reads:

“There is debate for example about how much breast cancer screening programmes reduce outcomes such as premature mortality and to what extent the nature and rate of adverse consequences are acceptable, i.e. how population prognosis changes as a result of a screening programme (20)”:
Discretionary point 2: “In the 3rd paragraph after the subheading ‘patient prognosis is determined by more than disease diagnosis’, the following is not quite clear enough, too complex…..

"Modelling an individual's prognosis can incorporate and organise information from a range of continuously distributed or categorical prognostic factors, which include but extend widely beyond diagnostic information and treatment responsiveness."

Response: We agree. The sentence now reads:

“Modelling an individual's prognosis can draw on the full range of relevant and available information - clinical and non-clinical”.

Discretionary point 3: “Last paragraph before sub-head “The pros and cons of labelling”….consider a new sentence …raising or hinting at the challenges of this new…paradigm within the reality of general practice”

Response:

We are pleased the referee feels the paper has greatly improved with the acknowledgement of downsides – we also feel it has improved and our thanks to the referee for suggesting the addition.

We now also take his point that the challenges of implementing this need to be acknowledged. We have added a brief paragraph as follows:

“There are practical challenges to introducing an information-rich prognosis framework for a real-world clinical practice already struggling with volumes of guidelines, decision-aids and protocols of care. Technological and statistical advances to make calculation and presentation of prognostic information more accessible, and research into ways in which health care professionals and patients can better assimilate, use and share prognostic information, could help to meet these challenges”

Please note that we have also added a sentence in the revised paragraph responding to discretionary point 5 below (the sentence is highlighted in yellow) which covers another of the challenges, namely how to engage patients with the new model. We have added a new reference to accompany this point (reference 38)

Discretionary point 4: Second last paragraph in section on labelling. In comment on patients, consider “some patients may be more interested…”

Response: We like this more cautious language to express lack of an explicit evidence base on this point, and so we have altered the wording exactly as the referee has suggested.

Discretionary point 5: “1st paragraph under “prognosis provides a natural framework for modern clinical practice”. I don’t understand what you mean by “Data on outcomes among consulters”, and the natural flow of argument seems to be cut in the jump to the single-line paragraph on stratified care….the reader may need a gentle reminder of what you mean by ‘stratified care’. I think the first and second paragraph need to be a little clearer and stronger.”

Response: We agree that this did not flow. We have rewritten the first paragraph, deleting the phrase “data on outcomes among consulters”, and amending and sharpening up the other
sentences. We have deleted the single-line second paragraph, and inserted the phrase ‘stratified care’ into an appropriate point in the example as a means to more clearly define what we mean by it. The first paragraph now reads:

“Disease diagnosis is a crucial component of modern medicine but fails to provide a sufficient framework for a modern clinical practice which must incorporate variability in individual patient risk of different outcomes, influences on patient outcome which extend beyond disease, and avoidance of harm. Prognosis provides such a framework. Clinicians often think in terms of prognosis, especially the primary care physician who may start by judging if the patient is going to get better or not (36). Decisions about individual patients in primary care are informed by available evidence about likely future outcomes, and a clinician’s own judgement on likely outcome has prognostic value and helps to guide decision-making (37). Shared exploration and understanding between clinician and patient of which outcomes are wanted or needed, achieved through patients being able to voice their own priorities and goals for care and treatment in the consultation, supports a prognostic framework for the clinical encounter, particularly for the patient with long-term conditions and multimorbidity (38)”

Referee 2

Thank you for the generous and positive response to the rewrite – and for the suggestions that guided the rewrite.

**The referee has one concern** “There is one error that does need to be addressed. (In the example) on page 9, the authors appear to assume that all prostate cancer is benign…this is misleading….the authors should instead refer to risk stratification by stage and grade…the example should refer to expected outcome with and without treatment….”

Response: It was certainly not our intention to suggest that all prostate cancer was benign and so it is clear that we did not express this argument well. We are happy to amend it along the lines suggested by the referee and have also incorporated the new reference he suggests as support.

The example now reads, with the changed sentence highlighted in yellow:

Example: A patient presenting with mild urinary symptoms has prostate cancer diagnosed by a test and histopathology. **The grading of his cancer places him at one end of the spectrum of risk of future poor outcome, with a low probability that he will die prematurely and evidence that surgical treatment would not alter this probability (18). Furthermore, if surgically treated, there is a risk of undesirable outcomes such as reduced genito-urinary function. The evidence base to inform clinical, personal and policy decisions needs to show how use of diagnostic tests to identify and classify prostate cancer links to outcomes with and without treatment (8, 9), i.e. decisions should be informed by evidence about patient prognosis. We cannot assume the pursuit of diagnosis and disease is beneficial in the absence of evidence about future outcomes”

We look forward to hearing from you

Yours sincerely

Peter Croft