Reviewer’s report

Title: Evaluating the impact of prediction models: lessons learned, challenges and recommendations

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Reviewer: David Prieto-Merino

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This paper discusses some problems in the implementation of an impact study. However, I feel the paper is good at exposing problems (some more or less obvious) but is not providing a clear set of recommendations / guides / suggestions on how to explore solutions.

The main message of the paper is that the effects observed from implementation studies are a consequence of a concurrency of three different kind of effects:

a) The precision of the prediction algorithm in the study population.

b) The actions that the physicians (and patients) might take after seeing the output of the model (and depending on whether these outputs are just probabilities or recommended actions).

c) The effectiveness of those actions to advert the undesirable predicted event.

The authors acknowledge that it is difficult to disentangle how much of the final overall observed effect in the implementation study is due to each of these three factors. So, for example, if an implementation of a risk score in a population does not seem to work is it because the prediction model is not accurate in that population? Or because the doctors are not reacting to the information? Or because the measures they take are ineffective? Or maybe because those measures are not effective in patients precisely scored with high risk by the model in that population?

All these reflections are important, but my worry is that the authors don't seem to provide any suggestions on how one might try to disentangle this, so the reader is left with a sense of impossibility of carrying this kind of studies. Can we try to disentangle these effects by exploring the data in our studies? What data and associations we need to look at?

In their example they have shown this situation, but they have not tried to disentangle the mechanisms by doing further analysis in the data. For example, did the doctors prescribed the treatment more often to patients that had certain characteristics in subcomponents of the risk score rather that looking at the overall score? (maybe to younger patients, or sicker or whatever). Was the drug less effective precisely in that kind of patients? Notice that these questions and analysis are beyond the simple original question of the trial and require a different kind of
analysis. Is about dissentingly the mechanisms that have operated in the decisions and effects by analysing the data.

Finally for the specific study presented here I do not understand how exactly was designed the second randomisation: Did the same 71 doctors in the same hospitals participate? (that might explain the higher rate of prescriptions in the second experiment even in the control group). Were the doctors randomised again or did they maintain the same groups as in the first randomisation? Did they know the results from first study? What do they mean by a "before-after" design? What were the "before" and the "after" groups? There fact that the control group in the second study has so much higher prescriptions suggests some sort of carry-over effect from the first study.

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