Response to Bjorn Hofmann: Clarifying overdiagnosis without losing conceptual complexity

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We thank Hofmann for his thoughtful engagement with our analysis of overdiagnosis.[1-2] Here we address three of the main criticisms and challenges he raises for our account, but first we address his worry that our two types of overdiagnosis are not exhaustive or mutually exclusive, and hence lack conceptual clarity. We beg to differ. As far as we are aware, between them misclassification overdiagnosis (MCOD) and maldetection overdiagnosis (MDOD) are exhaustive in that they encompass all forms of overdiagnosis currently identified. The two types of overdiagnosis are not mutually exclusive in all cases; however, we do not see this as conceptually problematic. Our typology tracks two factors that underlie overdiagnosis: broadening of diagnostic criteria leading to expansion of the boundaries of diseases (MCOD) and failure of currently accepted gold standard tests to accurately identify cases of disease (MDOD). Identifying and analysing these factors increases our understanding of the phenomenon of overdiagnosis.

Hofmann claims that: "Overdiagnosis is a problem of lack of knowledge, i.e., an epistemological problem." [2, p.1] We agree that lack of knowledge is a key issue in overdiagnosis. Our category of maldetection overdiagnosis (MDOD) refers directly to this epistemological feature. MDOD picks out the group of

overdiagnosed conditions that arise primarily from screening or as incidental findings in the course of unrelated investigations. With these conditions, it is not possible at the point of diagnosis, given current 'gold standard' tests, to discriminate between those that will progress in a recognised disease trajectory, and those that will not. The latter are the overdiagnosed cases. Screening detected and incidentally identified conditions, many of which are cancers, contribute significantly to the problem of overdiagnosis.

However, as well as lack of knowledge about which identified cases of early cancer will or will not progress, the phenomenon of overdiagnosis highlights a different problem to do with the boundaries of disease. We take this to be an ontological problem, because it raises questions about the nature of disease entities. On our account, misclassification overdiagnosis (MCOD) picks out a group of overdiagnosed conditions where there is a mismatch between the phenomena currently included in the definition of a specific disease (e.g., degree of glucose intolerance in gestational diabetes, level of bone density in osteoporosis) and the phenomena that are the disease-making features of that disease. Of course, this begs the question as to how one defines disease; in our paper we asked readers to assume a naturalistic account based on dysfunction. In our view, MCOD arises because the criteria taken to delineate the boundaries of specific diseases are shifted; there is a redefinition of the pathognomic features of those diseases. The current definition of chronic kidney disease no longer tracks the phenomenon of renal failure but instead, identifies a much larger cohort of people with normal kidney function. Some of those identified

may have or will progress to renal failure, but most will not; they are the overdiagnosed.

We believe that it is useful to identify this aspect of overdiagnosis. Diagnosis is premised on there being something (an ontological entity - a particular disease) that is being picked out by the diagnostic criteria. With MCOD, this process fails in predictable ways as new diagnostic criteria for the disease in question now include much normal variation. In the final analysis, the shifting of disease boundaries does lead to an epistemological problem in that we do not know which of the many people identified by the new criteria will turn out to have disease-signifying dysfunction. Nonetheless, this form of overdiagnosis (MCOD) arises in a different manner to that of MDOD, and we believe that this is a worthwhile distinction to make. To know whether a condition is correctly identified as an instance of a particular disease, we need to know first, what counts as an instance of that disease; and second, how to identify accurately when instances of that disease occur. Failures at either of these steps can lead to overdiagnosis; therefore we believe that overdiagnosis involves both ontological and epistemological elements.

Our account draws upon a distinction between harmful and non-harmful cases of disease. In so doing, we are consistent with much of the literature which characterizes the key feature of overdiagnosis to be the identification of non-harmful or inconsequential disease.[3-5] Hofmann claims that disease just is harmful, and that any condition that is not harmful is not disease, but some kind of indicative phenomena, without explaining how he sees the relationship

between indicative phenomena and disease. We defend our use of the term 'harmful disease' in the paper [1] and will not repeat those arguments here. However, we think that Hofmann is not correct when he claims that only harmful conditions are diseases. It is not possible to make sense of the concept of overdiagnosis, for example of lung cancer, without the finding that some people with this disease will never suffer from the expected symptoms or death.[6] Lung cancer is a disease that causes harm, but nonetheless, there are some patients, identified according to our best diagnostic criteria, in whom this disease does not cause harm. Maldetection overdiagnosis picks out a subpopulation of people with a certain disease who evade the expected natural history of that disease – who have a non-harmful instance of the disease. It is unclear how Hofmann's account might work if disease diagnosis is withheld until certain harmful features are present.

Our use of the term 'harmful disease' does not contribute to the problem as we are not seeking to expand the criteria of specific diseases to intentionally include non-harmful cases. Rather, we identify that the problem of (maldetection) overdiagnosis arises because it is not possible antecedently to sort the harmful from the harmless cases.

Hofmann claims that overdiagnosis and medicalization are "quite different concepts" and that our view that MCOD and medicalization are linked is wrong. We agree that many instances of overdiagnosis are distinct from medicalization but maintain that some cases of overdiagnosis are also medicalization. Hofmann himself argues that the two concepts share many features and are evolving in

ways that may blur the distinction between them.[7] He distinguishes medicalization from overdiagnosis in terms of the phenomena of interest, claiming that overdiagnosis concerns phenomena that are already characterised in biomedical terms, that is they are already medical matters. In contrast, medicalization concerns conditions that are non-medical which become classified as medical matters. This analysis relies on there being a clear boundary between biomedical phenomena that are already medical matters, and everything else. For some conditions this assumption holds good – DCIS is already a medical matter, and we do not claim that overdiagnosis of breast cancer is medicalization. But some conditions that are considered to be medical matters occur on a spectrum that blurs with what we take to be social phenomena (non-medical matters). Hofmann refers to the medicalization of grief through its inclusion in DSM-V.[7] We consider including grief in DSM-V to be misclassification overdiagnosis. There is a spectrum from (non-medical) grief understood in social and behavioural terms, through to depression and major depression. Grief and depression share some features in their phenomenology; it is a matter of degree when the symptoms of grief blur into those of depression. When a condition such as grief becomes included in DSM-V by lowering the threshold at which symptoms of grief are taken to be symptoms of disease, this is simultaneously misclassification overdiagnosis *and* the medicalization of grief.

Finally, we find Hofmann's notion of a "diamond standard test" intriguing. Undoubtedly it would be ideal to have diagnostic tests of such prognostic sophistication and accuracy that all and only those diagnosed experience the signs, symptoms and sequelae characteristic of the identified disease. Such an

entity would provide the benchmark against which current gold standard tests might be measured regarding sensitivity, specificity, and predictive values; and would resolve the problem of overdiagnosis. In the absence of diamond standard tests, we must continue to try and unravel overdiagnosis, based upon our current, admittedly problematic diagnostic methods. Like Hofmann, we share the goal of overcoming overdiagnosis so that we can accurately distinguish disease from 'indicative phenomena'. We differ from Hofmann as we take this quest to entail ontological as well as epistemological challenges, but look forward to continuing the debate.

1. Rogers W.A and Mintztker Y. (2016) Getting clearer on overdiagnosis. *J. Eval. Clin. Pract.,* 22, 580-580.
2. Hofmann, B. (2016) Conceptual overdiagnosis. A comment on Wendy Rogers and Yishai Mintzker's article "Getting clearer on overdiagnosis". *J. Eval. Clin. Pract.*, doi: 10.1111/jep.12652.
3. Gøtzsche, P. C., & Jørgensen, K. J. (2013). Screening for breast cancer with mammography. *The Cochrane Database of Systematic Reviews*, *6*, CD001877. https://doi.org/10.1002/14651858.CD001877.pub5
4. Moynihan, R., Doust, J., & Henry, D. (2012). Preventing overdiagnosis: how to stop harming the healthy. *BMJ*, *344*, e3502.
5. Welch, H. G., & Black, W. C. (2010). Overdiagnosis in cancer. *Journal of the National Cancer Institute*, *102*(9), 605–13.

6. Patz, E. F., Pinsky, P., Gatsonis, et al. (2014). Overdiagnosis in low-dose computed tomography screening for lung cancer. *JAMA Internal Medicine*, *174*(2), 269–74.
7. Hofmann, B. (2016). Medicalization and overdiagnosis: different but alike. *Medicine, Health Care, and Philosophy*, *19*(2), 253–64.