PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Overdiagnosis across medical disciplines: a scoping review
AUTHORS	Jenniskens, Kevin; de Groot, Joris; Reitsma, Johannes; Moons, Karel; Hooft, Lotty; Naaktgeboren, CA

VERSION 1 – REVIEW

REVIEWER	Jenny Doust Centre for Research in Evidence Based Practice, Bond University, Gold Coast, Australia
REVIEW RETURNED	26-Jul-2017

GENERAL COMMENTS	The authors have provided a comprehensive overview of the literature published on the topic of overdiagnosis to date. The findings will assist researchers working in this area to understand the type of studies being produced and where there are potential gaps in research. The main limitation of the study is the search terms seem to be limited. For example, studies examining “incidental findings” would not have been found using the search terms as listed. More extensive piloting of the search terms would have given more confidence that the review was able to adequately provide a complete overview of the current literature, particularly in an area which is relatively new and considerable variation in terms used under the umbrella of overdiagnosis exists. This limitation is dicussed in the second point of the discussion, but needs further expansion. Several authors are using the term overdiagnosis for clinical contexts where the patient has a disease but it is misdiagnosed as another condition. For example, there are several studies of the overdiagnosis of asthma and malaria that use the term in this way. These are closer to false positive diagnoses, and therefore conceptually different to the way that overdiagnosis is generally being used. Did the authors find this in this study? Were these studies included in the overview? This distinction needs to be included in the methods of the review and it would be helpful to include a sentence describing if these were included, how many were found in the results. In Table 1, the columns do not add to the total. I presume that there is a column missing of papers that were in a specific clinical field not included in the 4 previous columns. This missing column should be included in the table. Minor issues: P6 2nd last para: these are criteria are described below P9 under screening subheading: screening in 42% of studies P10 line 269: 3% of all 1457 publications (the decimal place is not necessary)

REVIEWER	Bjørn Hofmann NTNU Gjøvik and University of Oslo I am a researcher in the conceptual and philosophical aspects of overdiagnosis
REVIEW RETURNED	26-Jul-2017

GENERAL COMMENTS	This is an impressive and important work that is of interest to many readers. It is well structured and well written. The results give a valuable overview over the field. Some points for improvement: The manuscript refers to several categories to describe itself: "systematic analysis," "systematic overview," "systematic review," and "scoping review." Good arguments can be given for the study being each of these. However, they may not be the same. Hence, the authors should clarify what type of study this is. There are of course many ways to perform this search. Some relevant synonyms have been included, while others have not (overtesting, overutilization). The authors have addressed this in the Discussion. However, some targeted synonyms, such as pseudodisease, are not included. While it is far from clear that including such synonyms would have given other results, it could improve the study to comment on this in the discussion. (Other relevant synonyms can be found in DOI: 10.1007/s10654-014-9920-5). A curious and interested reader would very much like to know the (range of) estimated overdiagnoses for specific diseases that are identified by the literature search. Such information would add value to the manuscript. Minor details: The authors claim that the definition of overdiagnosis as "a 'disease'' in an individual, that will never go on to cause symptoms or early death" implies that "overdiagnosis can occur only in asymptomatic individuals" and that "overdiagnosis in most mental disorders is impossible." However, the or-clause in the definitions allows for asymptomatic cases, e.g. in diseases with sudden death. This may not be relevant for very many cases, but it might be worth noting. When referring to drivers of overdiagnosis, the authors refer to: Paris J, Bhat V, Thombs B. Is Adult Attention-Deficit Hyperactivity Disorder Being Overdiagnosed? Can J Psychiatry. 2015;60(7):324-8. Here other references may appear more relevant, e.g., Brownlee S. Overtreated: why too much medicine is making us sicker and poorer: Bloomsbury, 2007. Moynihan RN, Cooke GP, Doust JA, Bero L, Hill S, Glasziou PP. Expanding disease definitions in guidelines and expert panel ties to industry: a cross-sectional study of common conditions in the United States. PLoS Med2013;10:e1001500. http://www.bmj.com/content/358/bmj.j3314 http://www.bmj.com/content/350/bmj.h705 http://www.bmj.com/content/357/bmj.j2102 The authors write "Other work by Hofmann et al takes a more sociological and philosophical point of view. In their most recent publication, they use indicative, measurable and observable phenomena to describe the different stages in which a phenomenon develops into a clinical manifestation. (16)" The referred work does only have one author. In general I think this is a very nice contribution to the field. I have tried to indicate how the work could be improved even further.

REVIEWER	Stacy Carter The University of Sydney Australia
REVIEW RETURNED	03-Aug-2017

GENERAL COMMENTS	Thanks for the opportunity to review this paper. In general I thought it was a piece of work worth doing, and most of the decisions made seemed reasonable. My main concern is whether the search string was comprehensive enough (it seems very short, and was applied only in one database). The string seems to miss terms that have been commonly used in the past, like inconsequential disease/diagnosis, and there's no snowball searching based on the reference lists of included papers. The authors themselves note that they missed relevant papers from the genetics literature, and PubMed doesn't index all of the relevant literatures (e.g. some of the definitions work has been published in the philosophy of medicine literature, which isn't always indexed in PubMed). There's not much discussion of how the authors came to the search string they did. A lot rests on the searching, and the conclusions reached are mostly conclusions about the distribution of the literature, so it seems important to be able to justify the search strategy. I'm not sure what the appropriate response to this is. Of course to expand the search means going right back to the beginning of the project, which may not be justified given that the paper as it stands provides a useful overview, and it's not seeking to produce a meta-analysis. I would suggest a couple of possible approaches. First, I would reframe the paper as reporting on a scoping review, rather than a systematic review. See, e.g.: http://www.tandfonline.com/doi/abs/10.1080/1364557032000119616 http://onlinelibrary.wiley.com/doi/10.1002/jrsm.1123/full https://implementationscience.biomedcentral.com/articles/10.1186/1748-5908-5-69 Second, it would be helpful to do some additional searching using other keywords that would hopefully show that you haven't missed anything important, and to provide this information as supplementary material. If you find that you have missed important sections of the literature, it substantially weakens the claims you can make, because a lot of your claims focus on quantifying the proportions of the literature that have different characteristics, and this is highly dependent on the denominator you use. So there's a possibility you might have to code some additional papers and re-run your analyses if you can't adequately deal with any missing papers via additional justification of your existing strategy. My only other comment is that the paper is very descriptive. This is in part because of the nature of the task, but it would be useful to see a more interpretive discussion. Given that you've read so much of the literature now, can you provide any more reflections on lessons for those working on overdiagnosis? What should we do less of or more of? What remains unresolved and needs more attention? What systematic problems do you see?

	Apart from this, I can't see much to criticise. Although very descriptive, the overview it provides will be a helpful way in for people unfamiliar with the literature, and may also provide a helpful big picture view for those working in one corner of overdiagnosis research, unaware of what others are doing. With respect to the questions I answered 'no' to above -- if there had been a 'more information required' button I would have used that instead. To clarify: Re: Study Design -- this is in relation to the adequacy and justification of the search strategy Re: Limitations--this is also with regard to the search strategy, which at least, I think, requires a little more justification Re: Supplementary reporting--I note the PRISMA chart included, but there's no mention of registration of the systematic review. This again could be dealt with by locating this study as a scoping review rather than a systematic review, which I think would be accurate. P10 L44-45, 'without any significant *rise* in the mortality rate' I think is a typo. Usually we would conclude that overdiagnosis may be occurring if there is widespread testing, incidence is rapidly increasing, but mortality rates are not *decreasing* (i.e. because the detection of more early stage disease should prevent later stage disease and disease specific mortality and so reduce the disease specific mortality rate).

VERSION 1 – AUTHOR RESPONSE

Review 1

Reviewer Name: Jenny Doust

Institution and Country: Centre for Research in Evidence Based Practice, Bond University, Gold Coast, Australia Please state any competing interests or state 'None declared': None declared

Comment: The authors have provided a comprehensive overview of the literature published on the topic of overdiagnosis to date. The findings will assist researchers working in this area to understand the type of studies being produced and where there are potential gaps in research.

Response: We would like to thank Reviewer 1 for the overall positive reception of our manuscript.

Comment: The main limitation of the study is the search terms seem to be limited. For example, studies examining "incidental findings" would not have been found using the search terms as listed. More extensive piloting of the search terms would have given more confidence that the review was able to adequately provide a complete overview of the current literature, particularly in an area which is relatively new and considerable variation in terms used under the umbrella of overdiagnosis exists.

Response: We acknowledge that this was a limitation of our review. We used terminology mentioned by the reviewers and from the paper by Hofmann (DOI: 10.1007/s10654-014-9920-5) to pilot the number of additional search hits. As a result, we included terms related to overtesting, overmedicalisation, pseudodisease, inconsequential disease, and quaternary prevention. The search terms inconsequential diagnosis, lanthanic disease, and diagnostic creep did not yield any additional hits.

The extended and updated search (see paper) resulted in 1094 additional papers, of which in 394 overdiagnosis was a dominant theme. These articles were all scored in the same way as papers from the original search and the numbers in the table and figure were updated accordingly. Changes across all clinical fields and scoring criteria in this table and figure did not exceed 5%, and the overall conclusions did not change meaningfully. The extension of our search did not yield extra studies on incidental findings. Incidental findings are apparently not addressed in combination with the terminology that we used relating to overdiagnosis.
Search items resulting in >2000 extra hits (e.g. overtreatment, medicalisation, incidental findings) were excluded, as additional scoring was not deemed feasible within a short timeframe.

This limitation is discussed in the second point of the discussion, but needs further expansion. Several authors are using the term overdiagnosis for clinical contexts where the patient has a disease but it is misdiagnosed as another condition. For example, there are several studies of the overdiagnosis of asthma and malaria that use the term in this way. These are closer to false positive diagnoses, and therefore conceptually different to the way that overdiagnosis is generally being used. Did the authors find this in this study? Were these studies included in the overview? This distinction needs to be included in the methods of the review, and it would be helpful to include a sentence describing if these were included, how many were found in the results.
Indeed we did find a significant number of articles which apparently use the word overdiagnosis to refer to misdiagnosis. This occurred frequently in asthma and malaria, but also in COPD and a number of mental disorders. We refer to the inclusion of these studies in our methods section by stating: “Studies with overdiagnosis as a dominant theme were included regardless of which definition of overdiagnosis the authors adopted.” Hence these studies are included in the review. Unfortunately we did not score this separately in our assessment. We have however addressed this issue by including additional text in the results section on overdiagnosis context, pointing out disease areas in which it was found most often.
“Several articles estimated overdiagnosis in symptomatic conditions, such as incorrect diagnosis by untrained clinicians in patients presenting with malaria-like symptoms, leading to false-positives and unnecessary treatment. (26, 27) This should rather be considered misdiagnosis (incorrect diagnosis of a symptomatic person with a condition they do not have (1)) due to inaccuracy of clinical tests used in practice leading to false-positives, incorrect disease labels, and overtreatment.”
“Common topics included application of DSM for bipolar disorder, depression and ADHD, (35, 36) and physician diagnosis of COPD asthma, which were related to misdiagnosis rather than actual overdiagnosis. (37-39)”

Comment: In Table 1, the columns do not add to the total. I presume that there is a column missing of papers that were in a specific clinical field not included in the 4 previous columns. This missing column should be included in the table.

Response: We have added a column to Table 1 in which all the other ICD-10 clinical fields are combined. The numbers of columns 3 – 8 now add up to the total number of articles.

Minor issues:
P6 2nd last para: these are criteria are described below
P9 under screening subheading: screening in 42% of studies
P10 line 269: 3% of all 1457 publications (the decimal place is not necessary)

Response: We thank the reviewer for her careful attention and have made all these changes.

Reviewer: 2
Reviewer Name: Bjørn Hofmann
Institution and Country: NTNU Gjøvik and University of Oslo Please state any competing interests or state 'None declared': I am a researcher in the conceptual and philosophical aspects of overdiagnosis

Comment: This is an impressive and important work that is of interest to many readers. It is well structured and well written. The results give a valuable overview over the field.

Response: We would like to thank Reviewer 2 for his valuable feedback and kind words.

Some points for improvement:
The manuscript refers to several categories to describe itself: "systematic analysis," "systematic overview," "systematic review," and "scoping review." Good arguments can be given for the study being each of these. However, they may not be the same. Hence, the authors should clarify what type of study this is.

Response: We agree with the reviewer that there should be consistency in the category into which this paper falls. After deliberation we now consequently use the term scoping review instead of systematic review throughout the paper

Comment: There are of course many ways to perform this search. Some relevant synonyms have been included, while others have not (overtesting, overutilization). The authors have addressed this in the Discussion. However, some targeted synonyms, such as pseudodisease, are not included. While it is far from clear that including such synonyms would have given other results, it could improve the study to comment on this in the discussion. (Other relevant synonyms can be found in DOI: 10.1007/s10654-014-9920-5).

Response: As also stated above to a similar comment raised this important issue was raised by Reviewer 1. We acknowledge that this was a limitation of our review. Please find our detailed response and how we extended our search above. (lines 43-57)

Comment: A curious and interested reader would very much like to know the (range of) estimated overdiagnoses for specific diseases that are identified by the literature search. Such information would add value to the manuscript

Response: Our data extraction was based on broad ICD-10 domains (not disease specific) and at what the context of overdiagnosis was (not the absolute percentage of overdiagnosis provided in papers). We fully recognize that this suggestion would be a valuable addition, but it will be labor-intensive to retrospectively determine this for all 'overdiagnosis estimation' papers. Also overdiagnosis estimates depend on study characteristics and on the methods used for quantification. Performing such an assessment would require more in depth analysis on study design, type of methods used and risk of bias assessment.
Our database does however provide us with the ability to search for keywords in title and abstracts in order to filter out specific diseases that are of interest. Prompted by the reviewer's comment we have now provided a sentence stating that other researchers are free to contact us for any subset of articles, including those providing overdiagnosis estimates.

Minor details:
The authors claim that the definition of overdiagnosis as “a ‘disease'' in an individual, that will never go on to cause symptoms or early death” implies that “overdiagnosis can occur only in asymptomatic individuals” and that “overdiagnosis in most mental disorders is impossible.” However, the or-clause in the definitions allows for asymptomatic cases, e.g. in diseases with sudden death. This may not be relevant for very many cases, but it might be worth noting.

Response: We have adjusted the sentence following the definition into: “Using this definition, overdiagnosis in most mental disorders is impossible, as virtually all of these deal with symptomatic individuals, and do not typically lead to early death.”

When referring to drivers of overdiagnosis, the authors refer to: Paris J, Bhat V, Thombs B. Is Adult Attention-Deficit Hyperactivity Disorder Being Overdiagnosed? Can J Psychiatry. 2015;60(7):324-8. Here other references may appear more relevant, e.g., Brownlee S. Overtreated: why too much medicine is making us sicker and poorer: Bloomsbury, 2007. Moynihan RN, Cooke GP, Doust JA, Bero L, Hill S, Glasziou PP. Expanding disease definitions in guidelines and expert panel ties to industry: a cross-sectional study of common conditions in the United States. PLoS Med2013;10:e1001500. http://www.bmj.com/content/358/bmj.j3314 http://www.bmj.com/content/350/bmj.h705 http://www.bmj.com/content/357/bmj.j2102
Thank you for the suggestions of references. We have added several references that we found prompted by this comment of the reviewer, including a recent one by Pathirana, Clark and Moynihan. We were only unable to obtain the book by Brownlee and were hence unable to verify this reference.

The authors write “Other work by Hofmann et al takes a more sociological and philosophical point of view. In their most recent publication, they use indicative, measurable and observable phenomena to describe the different stages in which a phenomenon develops into a clinical manifestation. (16)” The referred work does only have one author.
We thank the reviewer for his careful reading. We deleted et al.

In general I think this is a very nice contribution to the field. I have tried to indicate how the work could be improved even further.
We are grateful for the reviewer’s constructive suggestions which have enabled us to improve our manuscript.

Reviewer: 3
Reviewer Name: Stacy Carter
Institution and Country: The University of Sydney, Australia Please state any competing interests or state ‘None declared’: None declared

Comment: Thanks for the opportunity to review this paper. In general I thought it was a piece of work worth doing, and most of the decisions made seemed reasonable.

Response: The comments and constructive feedback provided by Reviewer 3 were appreciated and well received by the authors, and we would like to thank her for her feedback on the manuscript.

Comment: My main concern is whether the search string was comprehensive enough (it seems very short, and was applied only in one database). The string seems to miss terms that have been commonly used in the past, like inconsequential disease/diagnosis, and there's no snowball searching based on the reference lists of included papers. The authors themselves note that they missed relevant papers from the genetics literature, and PubMed doesn't index all of the relevant literatures (e.g. some of the definitions work has been published in the philosophy of medicine literature, which isn't always indexed in PubMed).
There's not much discussion of how the authors came to the search string they did. A lot rests on the searching, and the conclusions reached are mostly conclusions about the distribution of the literature, so it seems important to be able to justify the search strategy.

Response: As was also commented by the other two reviewers, we fully agree that we had to update our search query. We did search PsychoInfo (March 2016) and found 800 papers, virtually all of which were duplicates compared to the ones found on PubMed. Furthermore, a significant number of relevant ethical and philosophical papers were found on Medline, in journals such as the Journal of Medical Ethics and Medicine, Healthcare, and Philosophy. Although we recognize that these are do not comprise of all the literature on these subjects, they are at least to some degree represented in our dataset.

Additional measures taken to address the issue of comprehensiveness are now discussed in the section below. (lines 43-57)

I would suggest a couple of possible approaches.
First, I would reframe the paper as reporting on a scoping review, rather than a systematic review. See, e.g.:
http://www.tandfonline.com/doi/abs/10.1080/1364557032000119616
http://onlinelibrary.wiley.com/doi/10.1002/jrsm.1123/full
https://implementationscience.biomedcentral.com/articles/10.1186/1748-5908-5-69

Response: We agree that a scoping review would be more appropriate to align with the contents of the manuscript. The term systematic was replaced with scoping throughout the paper.

Comment: Second, it would be helpful to do some additional searching using other keywords that would hopefully show that you haven't missed anything important, and to provide this information as supplementary material. If you find that you have missed important sections of the literature, it substantially weakens the claims you can make, because a lot of your claims focus on quantifying the proportions of the literature that have different characteristics, and this is highly dependent on the denominator you use. So there's a possibility you might have to code some additional papers and re-run your analyses if you can't adequately deal with any missing papers via additional justification of your existing strategy.

Response: As also stated above to a similar comment raised this important issue was raised by Reviewer 1 and 2. We acknowledge that this was a limitation of our review. Please find our detailed response and how we extended our search above. (lines 43-57)

Comment: My only other comment is that the paper is very descriptive. This is in part because of the nature of the task, but it would be useful to see a more interpretive discussion. Given that you've read so much of the literature now, can you provide any more reflections on lessons for those working on overdiagnosis? What should we do less of or more of? What remains unresolved and needs more attention? What systematic problems do you see?

Response: Reflection on this would indeed be a valuable addition to the paper. We have added this now in the final paragraph on relevance to current practice and implications for further research in the discussion section.
“A lack of consensus on what is called overdiagnosis hampers communication between researchers, physicians, patients, and policy makers. The use of overdiagnosis to describe misdiagnosis will dilute its actual meaning, result in linguistic confusion, and counterproductive discussion, and should thus be avoided.”

Comment: Apart from this, I can’t see much to criticise. Although very descriptive, the overview it provides will be a helpful way in for people unfamiliar with the literature, and may also provide a helpful big picture view for those working in one corner of overdiagnosis research, unaware of what others are doing.

Response: We would like to thank Reviewer 3 for these kind words and appreciation of the paper.

With respect to the questions I answered 'no' to above -- if there had been a 'more information required' button I would have used that instead.

Comment:
To clarify:
Re: Study Design -- this is in relation to the adequacy and justification of the search strategy
Re: Limitations--this is also with regard to the search strategy, which at least, I think, requires a little more justification

Response: These comments were addressed above

Re: Supplementary reporting--I note the PRISMA chart included, but there's no mention of registration of the systematic review. This again could be dealt with by locating this study as a scoping review rather than a systematic review, which I think would be accurate.
The study is now referred to as a scoping review. As there is no formal alternative to PRISMA for scoping reviews, this chart will stay included with the article.

P10 L44-45, 'without any significant *rise* in the mortality rate' I think is a typo. Usually we would conclude that overdiagnosis may be occurring if there is widespread testing, incidence is rapidly increasing, but mortality rates are not *decreasing* (i.e. because the detection of more early stage disease should prevent later stage disease and disease specific mortality and so reduce the disease specific mortality rate).

Response: This typo is now corrected

VERSION 2 – REVIEW

REVIEWER	Jenny Doust Bond University, Australia
REVIEW RETURNED	30-Oct-2017

GENERAL COMMENTS	Agree with all revisions and think the paper adds a valuable and original contribution to the field. One small last point is that some of the studies estimating overdiagnosis in non-screening contexts may involve symptomatic individuals, and therefore may be using the broader definition of overdiagnosis such as that proposed by Carter et al. Therefore not all the paper describing overdiagnosis in symptomatic individuals will be misdiagnosis.

REVIEWER	Björn Hofmann Norwegian University of Science and Technology at Gjövik and University of Oslo, Norway
REVIEW RETURNED	30-Oct-2017

GENERAL COMMENTS	I have reviewed this study before, and the authors have taken the constructive comments from all reviewers into careful considerations and significantly improved the manuscript.

REVIEWER	Stacy Carter The University of Sydney
REVIEW RETURNED	25-Oct-2017

GENERAL COMMENTS	The authors have done considerable additional work to respond to the last round of reviews, including a new round of searches with additional terms. I still would have liked to have seen a wider range of data bases included, and I think some of the topic summaries (e.g. on definitions of overdiagnosis) could perhaps be refined further. However I think it's reasonable to accept at this point. The methods are clear enough that the reader can decide for themselves how to interpret the findings.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Jenny Doust
Institution and Country: Bond University, Australia
Please state any competing interests or state 'None declared': None declared
Please leave your comments for the authors below

Comment: Agree with all revisions and think the paper adds a valuable and original contribution to the field.

Response: We would like to thank Reviewer 1 for her constructive comments on and positive reception of our work.

Comment: One small last point is that some of the studies estimating overdiagnosis in non-screening contexts may involve symptomatic individuals, and therefore may be using the broader definition of overdiagnosis such as that proposed by Carter et al. Therefore not all the paper describing overdiagnosis in symptomatic individuals will be misdiagnosis.

Response: We think that her comment was triggered by the following sentences: (page 12, subheading 'Overdiagnosis definitions')

… "However, not all studies follow this definition, but rather describe overdiagnosis as a diagnosis of a "disease" in an individual, that
will never go on to cause symptoms or early death. Using this definition, overdiagnosis in most mental disorders is impossible, as virtually all of these deal with symptomatic individuals, and do not typically lead to early death."

The goal of this section was to highlight the differences between definitions of overdiagnosis in which the starting point is asymptomatic individuals and definitions that are broader and may include scenarios with symptomatic individuals. We improved the section as follows:
… "However, not all included studies give a clear definition, but implicitly use the definition of overdiagnosis as a diagnosis of a "disease" in an asymptomatic individual, that will never go on to cause symptoms or early death. This definition is particular to the screening-context, but does not apply to a large portion of the studies found in this review that are on testing of symptomatic individuals, for example those with mental disorders."

Added as well to the end of the paragraph is the sentence:
… "Which definition researchers use for overdiagnosis needs to be reported completely to be able to judge the applicability of the results."

Reviewer: 2
Reviewer Name: Björn Hofmann
Institution and Country: Norwegian University of Science and Technology at Gjövik and University of Oslo, Norway
Please state any competing interests or state 'None declared': None declared.
Please leave your comments for the authors below

Comment: I have reviewed this study before, and the authors have taken the constructive comments from all reviewers into careful considerations and significantly improved the manuscript.

Response: We would like to thank Reviewer 2 for his kind words and positive response.

Reviewer: 3
Reviewer Name: Stacy Carter
Institution and Country: The University of Sydney
Please state any competing interests or state 'None declared': None declared
Please leave your comments for the authors below

Comment: The authors have done considerable additional work to respond to the last round of reviews, including a new round of searches with additional terms. I still would have liked to have seen a wider range of data bases included, and I think some of the topic summaries (e.g. on definitions of overdiagnosis) could perhaps be refined further. However I think it's reasonable to accept at this point. The methods are clear enough that the reader can decide for themselves how to interpret the findings.

Response: We would like to thank Reviewer 3 for her feedback and positive response. We acknowledge that more comprehensive searches are possible, but it is unlikely that meaningful changes in results would have occurred in our scoping review. We do mention the search in a single database as a potential limitation.
The variation in overdiagnosis definitions is discussed at multiple places, including the introduction, results and discussion section. In our scoping review it was not possible to fully elaborate on the various aspects of the definitions of overdiagnosis and frameworks that have been constructed. However, our review does highlight that there are discrepancies between overdiagnosis definition, and that both readers and researchers need to be aware of this variation. In particular, we urge future researchers to be specific about their interpretation and meaning of overdiagnosis.

VERSION 3 – REVIEW

REVIEWER	Jenny Doust Bond University
REVIEW RETURNED	08-Nov-2017

GENERAL COMMENTS	Great work

REVIEWER	Bjørn Hofmann NTNU and University of Oslo, Norway
REVIEW RETURNED	06-Nov-2017

GENERAL COMMENTS	The authors have addressed the comments and suggestions well.