PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Treatment Outcomes for Eating Disorders in Sweden: data from the National Quality Registry
AUTHORS	Södersten, Per; Brodin, Ulf; Sjöberg, Jennie; Zandian, Modjtaba; Bergh, Cecilia

VERSION 1 – REVIEW

REVIEWER	Regan Bergmark, MD Gliklich Healthcare Innovation Scholar, Harvard Medical School, USA
REVIEW RETURNED	29-May-2018

GENERAL COMMENTS	Dear Authors, This study examines eating disorder remission rates in the Swedish eating disorders registry, which has more than half of the patients lost to follow up. Sweden has a large number of registries, often considered the gold standard for observational studies of a large population. Of note, I can review this manuscript from the standpoint of observational data utilization and outcomes in the registry context, but I do not specialize in eating disorders or psychiatry. A content expert in eating disorders should also review this manuscript. I believe the main focus of the paper comes out in the first paragraph of the discussion: "About 2600 patients were treated annually at the eating disorders clinics in Sweden in 2012-2016, fewer than half were followed-up, and the proportion of patients treated to remission decreased from one in five in 2012 to less than one in seven in 2016. However, remission rates which are more than three times higher have been publicized nationally. These estimates were derived by excluding patients lost to follow-up and patients followed-up at clinics that did not treat patients to remission." I found the methodology and results somewhat difficult to follow, primarily because the authors move back and forth between national data and data from three individual clinics, also between all clinics vs clinics than treat either more than 10 or more than 20 patients, or clinics that treat at least 1 patient to remission, and historical values. I would recommend simplifying. Can we compare the 2012-2016 data from the three clinics to their prior reported numbers? Is the objective to re-review the prior data without excluding so many patients? I believe the authors would benefit from re-framing the paper to focus on this central question of whether published remission rates are inaccurate due to exclusion of patients at clinics that did not treat patients to remission or patients lost to follow up. It may be useful to show how differences

	in the inclusion/exclusion criteria used historically change the "cure" rates of the modern sample. Another option for this paper is to focus on the loss-to-follow-up and remission rates in the studied time period (2012-2016) and then use the discussion to focus on the differences between the current time period and previously reported data. That approach would continue to allow the discussion to focus on how the historical data are reported and why exclusion of loss-to-follow-up patients and clinics without patients treated to remission would lead to overestimation of cure rates. In summary the data in this manuscript are important, highlighting known and unknown areas of outcomes for eating disordered patients in Sweden. They appropriately call attention to problems with the registry that may have led to inappropriate conclusions about treatment efficacy in the past. The authors have completed a number of analyses which crowd the paper and dilute the major points. It may be best to focus as I have described above. As I mentioned above, I do not have expertise in eating disorders. The manuscript should be reviewed by content experts in this area. For example, inclusion criteria, treatment guidelines as described in the Discussion section, what constitutes "remission," etc., should be reviewed by an expert in eating disorders. Likewise, a content expert should review how these follow up and remission/cure rates compare to other published data. Thank you for inviting me to review this manuscript. Congratulations to the authors on studying this important topic. Abstract: Please revise the abstract to make the methodology clearer. After reading the manuscript, I understood the abstract better, but I did not understand the abstract when reading it alone. As I mention, the multiple categories of data used obscure the main conclusions of the paper. It would be better to simplify as I described above. Introduction: Please refocus as mentioned above. Methods: In the introduction or methods section, could you provide more information about the registry data including: -how is "remission" defined by the registry? -can you provide any known details of data integrity/completeness or concerns thereof for this registry, aside from the follow up rates? -focus the methods on the areas of investigation you plan to concentrate on in this paper (see above) Results: Page 8 line 36-38: "the rate of remission at all clinics that followed-up their patients was less than 50% in 2012-2014, 29% in 2015 and 36% in 2016" - what is the explanation for these major differences (for your discussion)? I worry that these large differences do not reflect differences in care but in problems with the data quality in the registry. Discussion: I really like the first paragraph here, which focuses the reader on your main objectives and contextualizes your results. I would focus on the data quality in the registry and spend more time discussing

	why follow up is poor in this registry; because of the poor follow up %, I do not think you can make conclusions about clinical care quality. While couched in language highlighting the limitations of the follow up data, I am still concerned that the differences seen in remission rates are related more to registry data quality than to actual differences in care. Perhaps one of the main conclusions is that a concerted effort is needed at long term follow up, such that we can accurately estimate remission rates for healthcare policy planning and for patient counseling. Page 11 line 36-39 "In 2016, only four clinics treated 20 patients to remission, most clinics treated a small number of patients, followed-up a few, and treated only one patient in ten to remission." - please correct grammar (ie semicolon after remission?) Conclusions: Reframe to reflect the other changes made in the manuscript.

REVIEWER	Long Khanh-Dao Le Deakin Health Economics, School of Health and Social Development, Deakin University, Geelong, Victoria, Australia.
REVIEW RETURNED	29-Jul-2018

GENERAL COMMENTS	Thank you for inviting me to review an interesting manuscript. I am quite agreed with the authors that rates of remission for ED have been publically overestimated, misleading health care policies. Given that, evidence from national data is important to support for improving health care services. However, the manuscript needs improvement in method and discussion a lot to achieve a high-quality paper. I would suggest some points as following: - I am not sure whether other information regarding demographic variables, ED diagnosis... are available. If only number of people treated and remitted is available, I do not think it is a strong paper. Following this point, it is important to discuss about remission definition in this paper. Different definitions of remission would give different answers. And it is not appropriate to compare remission rate if the definition of remission was not taken in account (although I have seen the author discuss about this in the limitation). Furthermore, ED classification is also important. Remission for AN is quite different to remission for BN or BED or even ED subthreshold. Therefore, lack of these information, it is unclear for readers to have a better understanding. - The manuscript also needs further information regarding three clinics including Mando, SCA, and Capio. I am not sure whether remission data from these clinics came from Riksät? Also, the authors provided little information regarding treatment at these clinics and it is vague. For example, "Mando concentrates on normalizing the patients´ eating behaviour" -> what is the process for treatment? Please specify the full treatment if possible (I assume it is possible since we can retrieve these information from the clinic website??) - The number treated at each year is not clear for me that these patient is newly treated or people treated from previous year and did not remit? This point is related to the first point when the information is very limited. - Regarding treatment interventions, I think the author should discuss about the standard treatment for EDs within the Sweden context. It should put in both background and discussion. It would

	make the reader a little bit clear about the different remission rates across clinic. - The authors should also discuss and highlight an important point regarding the quality of clinics within the Sweden context. The clinics with low quality and did not adhere to the clinical guideline maybe a reason for low remission rate compared to Mando, as an example, which have many ED patients (maybe have better quality?). I think there are a lot of work for this manuscript but I hope this would improve this manuscript.

REVIEWER	Elise Berliner Agency for Healthcare Research and Quality, USA
REVIEW RETURNED	20-Aug-2018

GENERAL COMMENTS	The question addressed in this manuscript of real world outcomes measured in registries compared to other data sources and analyses is important. However, the methods need more description. Particularly, how is patient follow up done in the registry? On page 6, the methods state "in remission at follow-up one year after the start of treatment". Are patients called back after one year? What if a patient comes for follow-up at 13 months or later? How is that recorded in the registry? Can the authors follow patients for more than one year? Describing this correctly is extremely important to interpret whether the methods of analysis and conclusions are correct. For the comparison (reference 5), the authors state (page 12) "The combined rate of remission at these clinics was about 75% in on average one year of treatment", but the reference actually says that "estimated rate of remission for this therapy was 75% after a median of 12.5 months of treatment"; i.e. less than half the patients were in remission at the one year time point. The results from this reference are described correctly in the abstract: "27, 28, and 40% at one year of follow-up" (Page 2) which seems very consistent with the result in this paper: "on average 33% in 2012-2016 according to the Riksat calculation" (page 13). If the authors can clarify these issues, the other analyses (comparison of different clinics that use different methods, reason that remission rate at one year is apparently getting worse over time) will be very interesting. On a more minor note, it would be helpful if the authors could state how the registry defines "remission". Also, as this is secondary use of registry data, there likely are no human subject issues, but it would be helpful if the authors can make a statement about that in the methods.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1, Dr Regan Bergmark

I thank Dr Bergmark for her interesting review and for providing many helpful suggestions for revising the manuscript. It is a good idea to describe outcomes for all clinics first and outcomes at individual clinics second, and so I have attempted that task and also made an effort to simplify the text.

There are four aims, highlighted in green in the Introduction:

The first aim is to analyze the outcomes of eating disorders treatment in Sweden that have been reported in the National Quality Registry of Eating Disorders Treatment in Sweden.

The second aim is to examine the evidence basis for the national claims that outcomes of eating disorders treatment in Sweden are better than outcomes in the published literature.

The third aim is to analyze the outcomes at individual clinics, focusing on the three biggest clinics. Three clinics (Mandometer) have published their outcomes and these outcomes are compared with the outcomes reported by these clinics to the registry.

The fourth aim is to point out that outcomes of eating disorders treatment have been publicized as better than published outcomes not only in Sweden but also internationally. This may mislead policy makers.

I have added text, highlighted in yellow that briefly describes the treatments, including diagnostic procedures and the definition of “remission” (p 6, line 22 – p 8, line 20). Remission is defined according to the standard used in published papers, i.e., “no longer fulfilling and eating disorders diagnosis”, although there is no general consensus on this topic. Dr Bergmark is right in that procedures may differ amongst clinics and this is mentioned in the first paragraph of the Discussion (p 15), with a supporting reference (ref 19).

Abstract: Clarifications/simplifications are marked in yellow.

Introduction: The focus in now on “all clinics” first and then on “individual clinics” as suggested.

Methods: As mentioned above, patient characteristics and diagnostic procedures have been added (p 6, line 22 – p 8, line 20 and p 10, RESULTS and Table 1). Data on the completeness of the registry have been added (p 6, lines 29-40).

Results and Discussion: Some of the possible causes of the variability in outcomes are discussed on p 17, line 19 – p 18, line 14. Admittedly, some of this discussion may be somewhat speculative. Remission rates after CBT, the major treatment in Sweden as in most other countries, is lower that the remission rates after Mandometer (ref 7), and differences in outcomes are discussed on p 19, line 40 – p 20, line 12.

(Because the short form SCÄ is Swedish, it has been changed into the English SCED.)

I agree that the information in the registry cannot be used to say much about the quality of care in Sweden, but I think that the Mandometer treatment has been described adequately, including its outcomes. I think that this is a major result of the present study and an important result because outcomes of standard treatments have been publically overestimated in Sweden over a period of many years. This appears to be a general problem beyond the treatment of eating disorders in Sweden, and it is an important aim of the present study to make that point, which is made in the final paragraph “Implications for policy makers” (p 20, line 15- end).

Semicolon added as suggested.

I thank Dr Bergmark for her review. I am pleased to hear that she agrees with me that the data in the manuscript are important and I look forward to her additional advice for improving the manuscript, should she consider it necessary.

Reviewer 2, Dr Long Khanh-Dao Le

I am delighted to hear that Dr Long Khanh-Dao Le found the manuscript interesting and that he agrees with the conclusion that rates of remission for ED have been publically overestimated.

Text highlighted in green in the Introduction shows the aims of the study.

I have added new text, highlighted in yellow, as Dr Long Khanh-Dao Le wanted more information on the following topics:

Patient characteristics, including diagnostic procedures, the distribution of diagnoses, and definition of remission (p 6, line 22 - p 8, line 20, p 10, RESULTS and Table 1).

A sentence has been added to note that there is no information on the number of patients in remission related to the diagnosis in Riksät (p 11, lines 27-29). It would be difficult to obtain such measures because only a few units treated more than 20 patients to remission (Figure 3). However, Dr Long Khanh-Dao Le is right in that it takes longer to treat anorexic patients to remission compared to bulimic patients and EDNOS patients, and the fact that Mandometer has published data to support this point is mentioned on p 14, lines 46-48.

(Because the short form SCÄ is Swedish, it has been changed into the English SCED.)

The remission rates at SCED, Capio and Mando in Figure 5 are from Riksät. The Introduction of the manuscript makes the point that whereas Mandometer has published outcomes (p 5, line 52 – pp 6, line 3), the other clinics, including SCED and Capio, have not published their results (p 5, lines 33-40). The manuscript also makes the point that Mandometer reports to Riksät and so it is possible to compare Mandometer´s published outcomes with Mandometer´s outcome listed in Riksät.

The treatments at the Swedish clinics are briefly described (p 7, line 36 – p 8, line 20) and discussed, including the difference amongst standards of care and Mandometer (p 15, line 55 – p 16, line 18). As pointed out, Mandometer has been described many times already, and the description is therefore brief, several references to the previous descriptions are provided; another description might make the treatment over-published. Also, the manuscript deals with differences in outcomes rather than differences in treatments. The possibility that the differences in treatment explain differences in outcomes is discussed (p 19, line 40 – p 20, line 12).

Dr Long Khanh-Dao Le is right in that some of the patients that were treated might have been treated before. The proportion of patients treated before (4-5%) has been added (p 7, lines 10-12).

The “standard treatments for ED within the Swedish context” is now mentioned (p 7, line 36 – p 8, line 1). I agree that the remission rates after CBT, the major treatment in Sweden as well as the rest of the world, may depend on country-context, but the published literature indicates the outcomes of CBT are similar in different countries. Typically in RCTs on CBT for BN, and more recently AN, rates of remission average about 45% and rates of relapse within one year are more than 30% (ref 7). The only exception is the 1995 paper from Professor Christopher Fairburn in which the rate of remission from BN was 54% (Arch Gen Psychiatry 1995;52:302). But that study was a combination of two studies, one in which 44 and 36% of 25 patients went in remission after CBT and at follow-up 12 months later and another study in which 80 and 100% of 10 patients went in remission at these points in time. Because of the marked difference in outcomes of the same treatment in the two studies, the results of that study are difficult to interpret (detailed analysis in ref 7). CBT has been reported to have somewhat better outcome for EDNOS patients (reviewed in ref 7). Because of the problems with the description of outcomes after CBT, in particular the rates of relapse, the effects of CBT for EDs are open to doubt (ref 7). The details of all papers published on CBT were reviewed recently (ref 7) and I think therefore, that another discussion in the context of the present manuscript may not be necessary.

I have discussed possible explanations of the differences in outcomes (p 17, line 20 – p 18, line 14 and p 19, line 40 – p 20, line 12). Because remission rates for CBT have not improved significantly after this treatment was introduced in 1981 (refs 7, 45-47), it seems unlikely that adherence to clinical guidelines, all of which recommend the use of CBT, will increase remission rates.

I thank Dr Long Khanh-Dao Le for many useful suggestions and I look forward to any new suggestions that he might have after reviewing the revised version of the manuscript.

Reviewer 3, Dr Elise Berliner

I am happy that Dr Berliner also found the data in the manuscript important.

Riksät states that patients were followed-up one year after the start of treatment. As the first sentence of the Methods section now states, Riksät offers no information on whether the time of follow-up was exactly one year (p 6, lines 29-31). I agree that the registry should state this more precisely. A sentence to make the point has been added on p 12, line 28-29). I think that this weakness adds to the conclusion of the manuscript that outcomes of eating disorders treatments in Sweden have not been properly described.

There is no information on what happened to the patients after the assessment at one year (p 6, line 40). At the one year time of follow-up, some of the patients have completed their treatment, successfully or unsuccessfully, and others are still in treatment. In clinical trials, the term follow-up refers to patient examinations after completion the intervention, when there is an effect to follow-up. One point of the manuscript is to suggest that the one year time point of assessment in the registry should be replaced by a time-to-event analysis, which has long been used in survival analysis (p 19, lines 23-39). The manuscript also points out that because there is no longer term follow-up information there is no information on relapse, which is a major problem in the management of patients with eating disorders (p 19, lines 23-39). For these reasons the abstract concludes that “it is difficult to estimate the effects of eating disorders treatment in Sweden”. This conclusion is not stated equally clearly elsewhere in the manuscript, but the Discussion leaves no doubt that the description of outcomes of the treatment of ED in Sweden can be improved.

Remission is defined as “not fulfilling an eating disorders diagnosis” (p 2, line 9 and p 7, lines 7-9). This is the standard definition in most studies, although there is no general consensus on what criteria to use for remission.

Mandometer´s criteria for inclusion, exclusion, and remission, and the procedures for assessment during treatment at follow-up have been published many times, references are provided. For these reasons, the Mandometer treatment is described only briefly in the present manuscript (p 8, line 3 – 20 and p 15, line 55 – p 16, line 19).

(Because the short form SCÄ is Swedish, it has been changed into the English SCED.)

The rates of remission and relapse at Mandometer have been changed to “estimated”.

The final paragraph of the Method section clarifies that there are no human subject issues (p 10, lines 6-12).

I thank Dr Berliner for her thoughtful comments and for offering good advice. I am happy to undertake further modifications of the manuscript if needed.

VERSION 2 – REVIEW

REVIEWER	Regan Bergmark, MD Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School
REVIEW RETURNED	09-Oct-2018

GENERAL COMMENTS	To the Editor and Authors, Thank you for inviting me to re-review this manuscript. I apologize for my delayed reply. My general and section-specific comments are below. This paper is very nicely clarified, with sections re-written and the aims more straightforward. I do have a few small suggestions/requests for clarification. As I mentioned in my initial review, I focus on comparative observational data in the registry or health services research context, but have no clinical focus on eating disorders; an expert in that area should also review this paper if they have not already done so. I would be happy to review a revised version in the future if that would be helpful Comments to the authors, and by section: OVERVIEW AND GENERAL COMMENTS: I really appreciate the work the authors did to revise and restructure this manuscript. The aims, results and implications are now much clearer. I had a few small comments, listed below. Thank you for allowing me to review this piece of scholarship. FEEDBACK BY SECTION: Background/Introduction: "The fourth aim of this study is to call the attention of policy makers to the fact that outcomes of eating disorders treatment have been overestimated not only in Sweden but in other countries as well." - I would recommend eliminating this aim as it is best reserved for the discussion - it is a useful commentary on the results, but not a scientific aim in and of itself. Methods: I really appreciate the detail and changes to help delineate the methodology. For the section: "Combined outcomes at all clinics The numbers of patients treated, followed-up, and treated to remission have been summarized for all clinics. The number of patients in remission has been related to the number of patients treated as well as to the number of patients followed-up in an attempt to explain the high remission rates publicized in Sweden." -Do you mean to say that descriptive statistics were completed to summarize the patients treated, followed-up, and treated to remission, or that this was previously done? It might be useful to rephrase to clarify, if correct, that this is a new analysis to compare the remission rates. Discussion: The "Outcomes in Sweden" paragraph is especially powerful. Although there is not a lengthy discussion of the statistical problems in other parts of the discussion, the point of how to deal with missing data - particularly long term outcome data - is incredibly important. Addressing missing data through simple xclusion can lead to highly misleading outcomes data.

	The last section of the "Comparison" section is very important and may need a bit more emphasis: "But differences in patient characteristics at admission may contribute to differences in treatment outcomes and even if the published literature indicates that they do not (42), the possibility that such differences exist should be examined." -Are the three clinics examined known to be referral centers for particularly challenging or complex cases? Would you expect these centers to have a different case mix or otherwise not be nationally representative? It may help to emphasize the answers to these questions in the introduction and also in the results slightly more - doing so will help strengthen the case you are making here, or will help with accurate results interpretation, depending on the answers. Implications for policy makers section: There is a jump between the statement that outcomes have been overestimated, and the striking statement that, "Widely publicized "facts" need to be critically examined. Policy makers should be aware that once ill advised policies have been established, retrospectively controlling their evidence basis can be ineffective, and even strengthen the misguided policy (50,51)." If you want to make a bold policy statement in the discussion, it would be helpful for non-Swedes to understand more specifically how prior outcomes studies from the registry have shaped national policy (ie, policy names and numbers, years enacted, etc). I am not Swedish and so while the Swedish policies may be widely known there, it would be helpful to add a paragraph with more background information (I imagine a paragraph such as, "Given the success of CBT-related registry results in year 20XY, a national policy called "[fill in the name]" was enacted doing XYZ…this resulted in the following…" And then I would be more specific about the policy recommendations you are making - should this specific policy be re-evaluated based on the new evidence? Should a specific policy be changed or revoked?

REVIEWER	Long Khanh-Dao Le Deakin Health Economics, Deakin University, Geelong, Victoria, Australia
REVIEW RETURNED	19-Sep-2018

GENERAL COMMENTS	The authors addressed all my concerns.

REVIEWER	Elise Berliner AHRQ, USA
REVIEW RETURNED	17-Sep-2018

GENERAL COMMENTS	This version of the manuscript is much clearer. However, the authors are still not citing the published literature correctly. On page 18, lines 41-42, the authors state that the registry rate "is about half the estimated published 75% rate of remission after on average one year of treatment" (Ref 8). Reference 8 does report an OVERALL 75% rate of remission with a MEDIAN of 12.5 months, but looking at figure 1a in reference 8, only about 30% of patients were in remission at the one year time point consistent with the results from the Rikstat registry. Half the

	patients that reached remission took significantly longer than 12 months. The main points of the manuscript are important (that the follow up is not long enough in Rikstat given that many patients take significantly longer than 12 months for remission in the published literature, that many patients are lost to follow up, and that estimates that do not include patients lost to follow up or clinics with no patients treated to remission is misleading). But I would suggest that the authors go back and make sure that the time frame is clearly and accurately stated with every citation and report of results of the remission rate.

VERSION 2 – AUTHOR RESPONSE

Reviewer 1, Dr Regan Bergmark

I am also pleased to hear that Dr Bergmark thinks that the manuscript is now “much clearer”.

Introduction. One could argue that the fourth aim “to call attention of policy makers to the fact that outcomes of eating disorders treatment have been overestimated not only in Sweden but in other countries as well” is not a scientific aim. But the aim of the manuscript is not “only” scientific, but also to alert policy makers to the problem of overestimated outcomes. This is why I suggested “Public health” as the Primary Subject Heading and “Health policies” as the Secondary Subject Heading when I submitted the manuscript the BMJ Open. As I have mentioned, the BMJ Editor thought that the overestimation of outcomes in Sweden may be a national problem, but because it is not I added some sentences showing the outcomes of CBT for eating disorders have been similarly overestimated, even in the pages of the American Journal of Psychiatry (reference 44), a major mental health journal. I think that the fourth aim is important and I kindly suggest that it should be included in the Introduction.

Methods. The statistics in **Combined outcomes at all clinics** (p 9-10) summarizes all patients treated, followed-up and treated to remission (first sentence) in an attempt to understand the basis for high remission rates that have been publicized in Sweden (second sentence). I have not changed the words “have been” and “has been”, because they are used on purpose throughout the Method section to describe what has been done, not what had been done previously. I believe that readers will understand.

Discussion. I agree with Dr Bergmark that the problem with missing data is “incredibly important” and I think that readers will understand that “simple exclusion can lead to highly misleading outcomes data”. In this case, the problem is so obvious that I think that the data “speak for themselves”.

Dr Bergmark´s suggestion that the discussion of “differences in patient characteristics at admission” “may need a bit more emphasis” is very useful. I have rephrased the final two sentences on lines 27-37, p 21, to follow her advice.

Finally, Dr Bergmark suggests that I add some specifics on how the results in the National Quality Registry for Eating Disorders Treatment have guided policy makers. I agree that this is very important. This is why the point that the registries have a “key role in the development of all aspects of health care”, including in “guiding health care policies” is made in the first paragraph of the Introduction. Dr Bergmark is right in that this may not be known to international readers and I have therefore added a

sentence and a reference to a recent paper that stresses the importance of the registries for policy makers (p 22, last paragraph before Acknowledgements).

I thank Dr Bergmark for her thoughtful re-review, I have enjoyed interacting with her in the review process.

Reviewer 2, Dr Long Khanh-Dao Le

I am delighted to hear that Dr Long Khanh-Dao Le found that I addressed his concerns and I thank him for the time and effort he put into reviewing the manuscript.

Reviewer 3, Dr Elise Berliner

I am pleased that Dr Berliner found the revised version of the manuscript “much clearer” and that she thinks that “The main points of the manuscript are important”.

I agree that the time to remission should be accurately stated. The average times to remission that we have published are: 11.8 months in an RCT with 16 patients, 14.4 months in a group of 168 patients (ref 13; Bergh et al Proc Natl Acad Sci 2002;99:9486), and 12.5 months in a group of 1428 patients (ref 8; Bergh et al Behav Neurosci 2013;127:878). The present manuscript provides similar results and discusses why remission rates vary amongst clinics, including our clinics. The point is made that this kind of variation is to be expected, which is why I use the admittedly flexible words “which is about half the estimated published 75% rate of remission” rather than more inflexible words. I have added the word “about” to the last part of the sentence on p 19, line 5 to avoid inflexibility, and so the sentence reads: “… the rate of remission at the Mando clinic in the Stockholm County Council was on average 33% in 2012-2016 according to the Riksät calculation, which is about half the estimated published 75% rate of remission after about on average one year of treatment.” 33 is not exactly, but “about” 75/2. I do not think that readers will miss the point that it takes more than one year for the other half of the patients to go into remission. Dr Berliner is right in that the time to remission might be very long for individual patient, a fact that will be familiar to most clinicians.

I thank Dr Berliner for her careful review.

VERSION 3 – REVIEW

REVIEWER	Regan Bergmark, MD Center for Surgery and Public Health, Department of Surgery, Brigham and Women's Hospital, Harvard Medical School
REVIEW RETURNED	05-Nov-2018

GENERAL COMMENTS	Congratulations to the authors on this scholarship!

REVIEWER	Elise Berliner AHRQ, USA
REVIEW RETURNED	29-Oct-2018

GENERAL COMMENTS	I am still concerned about the statement " which is about half the estimated published 75% rate of remission after about on average one year of treatment" on page 20, lines 6-8. The authors response states that "I do not think that readers will miss the point

	that it takes more than one year for the other half of the patients to go into remission." However, I think that this is often misinterpreted, as the authors themselves note on page 21 lines 46-48, that radio channel was erroneously making "the claim that “70% of the patients are `cured` within one year”. It would be worthwhile to explain this clearly and completely.

VERSION 3 – AUTHOR RESPONSE

Reviewer 1, Dr Regan Bergmark

I am pleased that Dr Bergmark has no more concerns. I thank her for carefully reviewing the manuscript and offering many helpful comments. It is nice to be “congratulated on scholarship”!

Reviewer 3, Dr Elise Berliner

I agree with Dr Berliner that statistical results are “often misinterpreted” and it is possible that readers may not realize that the time to remission is long for some patients. I hesitate to expand on this matter because it is outside of the main topic of the manuscript, and outcomes at three month intervals at all Mando clinics have been published already (supplementary file, reference 8). But to clarify this matter I have inserted a sentence on lines 46-50 on page 18. I hope the sentence meets with Dr Berliner´s approval. I think that we should comply with the constraints imposed by the 12 month follow-up period used in Riksät and not expand on what happens after that point in time. Riksät has no data for such a discussion.

I thank Dr Berliner for pointing out the importance of detail and for many excellent suggestions.