Author's response to reviews

Title: Interpersonal psychotherapy (IPT) for late-life depression in general practice: a feasibility study

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Author's response to reviews: see over
Dear editor

Thank you for reviewing our manuscript entitled “Interpersonal Psychotherapy (IPT) for late-life depression in general practice: a feasibility study”. We agree with most of the constructive comments made by the referees and have adapted the manuscript accordingly. In the appendix we have detailed the comments made by the referees and the appropriate adjustments.

We hope you find the manuscript fit for publication in its current form.

Kind regards

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APPENDIX

Reviewer 1, John Markowitz

General comments:
The reviewer states that the research question addressed in this paper: "how to integrate mental health into health settings?" is an unsolved and important public health problem. However, he argues that the current paper cannot be called a feasibility study because it was not designed as a prospective study of mental health possibilities in the primary care milieu. He suggests that this was a post hoc study of feasibility.

The fact is that the Dutch Organization for Health Research and Development which funded the project (ZONmw, Project number 1360.0005 “Feasibility of a transmural psychotherapy intervention for late-life depression) was explicitly interested in the feasibility of introducing IPT for elderly patients in general practice in the Netherlands. We assumed that the feasibility question could not be answered without gathering effectiveness data (an argument the reviewer also mentions at point 7f). Therefore, we chose to carry out a randomized clinical trial, and to describe feasibility aspects that we encountered during this trial. The aim of our study was less broad than the reviewer suggests, we wanted to focus on the introduction of IPT specifically, and not on how to integrate mental health (in a broader sense) in health settings. In the Netherlands, as in many other countries IPT is advised in all depression treatment guidelines, but it is only very sparingly used.

We regarded this study as a first step: we explored whether it was possible to organize IPT in the effectiveness trial, we pragmatically recorded organizational barriers and facilitating factors and studied the effectiveness of the intervention. We assumed that when we would succeed, and the intervention should prove to be effective that we made it likely that IPT could be further disseminated and that organizational changes to support the implementation of this intervention in real-life practice could be supported.

To address the comment of the reviewer that feasibility study is not the correct term to use for the kind of data we present, we changed the title of the manuscript into: "Interpersonal psychotherapy (IPT) for late-life depression in general practice: uptake and satisfaction by physicians, therapists and patients" (instead of feasibility study).

To make our strategy more explicit, we rewrote the last paragraph of the background: "Our study focuses on the feasibility of providing IPT for depressed elderly patients in general practice. We recorded feasibility data in a randomized clinical trial, because feasibility data are only relevant when an intervention is effective. The effectiveness of IPT for elderly depressed patients in general practice had not been demonstrated before. In our effectiveness trial, IPT provided by mental health workers was compared with care as usual provided by the general practitioner (GP). The feasibility and barriers to the introduction of IPT in the general practices as encountered in our trial are described in this paper. The effectiveness results of our study have been detailed in a separate paper [16]. In the discussion session of this paper we summarize the effectiveness results and integrate them with our findings described in this paper. Then we discuss whether there are grounds to support the dissemination of IPT for elderly patients in real-life general practice."
In the abstract, last sentence of methods we added: *and effectiveness data summarized*. And at the end of the results we added: *IPT was superior to usual care in patients with moderate to severe depression.*

**Major Compulsory revisions**

1. The reviewer states that the issue is presented as explicitly related to IPT, while any other mental health intervention might raise the same issues. We partly agree with this comment. Indeed, some generic barriers have to be overcome before any psychotherapy intervention can be delivered within general practice, but several aspects are specific to IPT. As mentioned before, IPT is disseminated relatively poorly, in contrast to cognitive behavioral therapy. In many countries CBT and its derivates have found its way in real-life practice. Societies for CBT are widespread, and they already have training programs and memberships. This is not yet the case for IPT, and therefore it is interesting to describe what happens when one wants to introduce IPT in general practice outside the IPT research centers and their networks in the USA. To address this point we rewrote the first paragraph of the discussion: *In this paper we explored the feasibility and barriers to the introduction of IPT for depressed elderly patients in general practice. Some issues are generic and have to be overcome before any psychotherapy intervention can be delivered within general practice; others are rather specific to IPT. With regard to organizational barriers to providing evidence based psychotherapy within general practice: Mental health organizations joined the project, because the transfer of expertise from specialized care to the primary care setting has high priority in Dutch health policy. In the Netherlands the distances from the secondary care institutions to the general practices can be relatively easily overcome, and in the majority of the general practices office space can be arranged for the mental health workers. General practitioners felt supported by the mental health workers in the treatment of the depressed elderly. With regard to IPT: Although there were no trained IPT therapists available, it was feasible to organize IPT training and supervision. Mental health organizations were willing to give their therapists time to be trained in IPT, because they wanted to support the dissemination of this short term, evidence based form of psychotherapy within their organization. IPT proved to be an attractive therapy for the older patients in real-life practice and for the therapists. General practitioners were positive about the structured and clear approach of IPT.*

2. The reviewer suggests discussing possible alternatives to the shuttling of mental health professionals to medical clinics. To address this point we described the organization of mental health care in general practice in more detail, and made our strategy more explicit. At page 6 we now added: *General practitioners cannot deliver IPT themselves because this therapy is very time-consuming and not part of GPs vocational background. In the Netherlands as in many other countries, general practitioners often collaborate with psychologists and counselors from private practices or with psychiatric nurses and psychologists from the regional organizations for mental health care. For practical reasons we chose to approach the organizations for mental health care as a starting point, because they often have networks of general practitioners with whom they collaborate (which facilitated the recruitment of GPs), and we assumed that they were able to make available enough therapists for the project (which made training and supervision of therapists, who were working in one organization, more efficient). For this same last reason, we also approached group private practices for psychotherapy.*
We do not think that there are other options to deliver IPT in primary care practices.

3. The reviewer comments that it should be made clearer earlier in the manuscript that the GPs did not provide the IPT themselves. We added “given by mental health workers” to IPT in the methods section of the abstract and in the last paragraph of the background section. As already mentioned we also added in the methods section: General practitioners cannot deliver IPT themselves because this therapy is very time-consuming and not part of GPs vocational background.

4. We agree with the reviewer that there is a difference between describing the feasibility of introducing IPT in an effectiveness trial (what we did) and the feasibility of implementing this treatment into normal life practice. The long-term implementation would be the next step, which was not the aim of the study. Our aim was more short term. Throughout the text we used the term introduction of IPT. Yet, in the first paragraph of the abstract in the former version of the manuscript, the term implementation was used. We changed this into the feasibility of introducing IPT. By making our strategy more explicit in the background and discussion (as described earlier) we also addressed this point. Moreover, we added as a limitation in the discussion section: A limitation of our approach is that the feasibility findings apply to the situation in the effectiveness trial. Although our trial was carried out in practices that were not affiliated with our university center, and findings were therefore more generalizable than those from efficacy trials, long-term feasibility without the context of a trial, still needs to be studied.

5. The reviewer suggests adding a broader critical review of other research on how mental health care has been delivered in other primary care and managed care settings. As our aim was to focus on IPT explicitly, we summarize data from other studies that have delivered IPT within primary care. In the discussion we added the following paragraph (page 14):

Comparison with other studies introducing IPT in primary care. In three other studies IPT was delivered in primary care settings. [8,14,25]. The recruitment procedures and the target populations differed (regarding age range), which makes it difficult to compare for instance the motivation for IPT. With regard to dropout rates: In the study of Schulberg 50% dropped out in the acute phase, in the PROSPECT study this percentage was 38% compared with 32% in our study. Browne defined adherence as attending 80% of the sessions offered. According to this definition 20% dropped out, compared to 26% in our study, when we use this same definition. Thus, the dropout rates in our study were relatively low, but the proposed number of sessions was also lower than those in the other studies (10 instead of 12 to 16). In the three studies mentioned no information is given about how the therapists were recruited and how they evaluated IPT. No data about possible organizational barriers and facilitating factors are given.

6. The reviewer states that the actual research in this paper is meager and that it should be acknowledged as such, that it is not an intensive evaluation of the program and its participants. As we stated before, we used a pragmatic approach to collect feasibility data alongside a randomized controlled trial. To address this point we made the limitations of our study more explicit in the discussion section (see also comment 7g).
Minor essential revisions

7. 
   a) The sentence: "training materials were developed and translated into Dutch" raised the question whether they initially were developed in another language. This is a misunderstanding. Of course we used the Comprehensive Guide to IPT as a basis for the training materials. We translated and rewrote some essential elements from it and combined these with findings from additional literature and own case examples. At page 7 we now state: We used the Comprehensive Guide to IPT and some additional papers (Sholomskas et al; Miller et al.) on IPT for the elderly as the basis for developing the training materials in Dutch.

b) The reviewer asks for the anchor points of the CSQ-8, and states that it should be made clear that the CSQ-8 hardly addresses patient satisfaction with the particulars of the intervention. He asks for additional information about patient's attitude toward IPT. Moreover, at point 7d he mentions that patient's attitudes to IPT were not assessed at baseline, and that the evaluation questionnaire is minimally described. To address this point, we added the following limitation in the discussion section: The way we measured patients' attitudes towards the intervention can be criticized. We conclude that patients were motivated because of the relatively high percentage of eligible patients that wanted to participate and complied with the therapy, and because of the scores on the client satisfaction questionnaire (CSQ-8). Yet, this questionnaire gives only a global impression of how the intervention was received, no specific information regarding the IPT protocol. Moreover, the mean score of the intervention group gives limited information, because we cannot compare this mean score with a valuable reference score (as this is unknown for this target population). Furthermore, we were not able to compare the scores of the intervention group with that of the usual care group, because the majority of the patients in the control condition did not receive any depression treatment at all and consequently, did not complete the CSQ.

c) The reviewer asks for demographics and prior experience of the psychotherapists. At page 10 we added: Of these therapists 10 were female. Their mean age was 47 yrs (SD 7.8). All therapists had worked for more than five years in mental health care, and 13 had two or more years of experience in working with elderly patients. Of the psychologists, 1 had a psychodynamic background, 4 were trained in cognitive behavioral therapy, and 1 in family therapy. The psychiatric nurses had not been trained before in a specific psychotherapeutic approach. The reviewer also asks how the "specifically trained" raters were trained. Actually, this sentence about the interviewers can be left out of this paper, because participants themselves gave the feasibility data. Indeed, independent interviewers carried out the interviews at baseline and follow-up. They were trained in a 1 ½-day course. Halfway through the project an additional training day was organized, and during the whole study, feedback was given based upon recorded audiotapes of interviews. This was already described in the effectiveness paper.

d) The comments made about specific information regarding patients' attitude towards IPT have been already addressed at point 7b.

e) The reviewer asks whether therapists were reimbursed for travel to and from the primary care site. To answer this question, we added at page 10: "In addition, in the Dutch system, these centers have a duty for outreaching care..."
and have the possibility for remuneration of travel expenses, while private practices have not”. The interviewer also asks how depressive assessments were administered in the primary care setting and how feasible that was. At page 6 we added: Our research assistant visited the general practices about once a month to collect names and addresses from the computerized databases of the GPs, of patients of 55 years or older, who had visited the practice in that last month. These patients were sent a letter on behalf of their general practitioner, in which they were asked to fill in a screening questionnaire, the 15-item Geriatric Depression Scale, GDS-15 [17], and return it to our research center. We already knew from another study that was carried out at our institute that this strategy was more efficient than one in which the GPs or their assistants had to distribute the screening questionnaires. In this paper, our aim was not to focus on the feasibility of screening for depression. Therefore, we do not go into detail about this strategy.

f) The reviewer mentions that feasibility depends on the effectiveness of the treatment delivered and mentions that a dilute dosage of 10 sessions is used, which may have influenced effectiveness. We summarize our effectiveness data at the end of the results section, at page 13. Effectiveness of the IPT intervention in our trial. The effectiveness data are described in a separate paper [16], but we will summarize them here, because feasibility data are only relevant when an intervention has proved to be effective. All patients who entered the study had a DSM-IV diagnosis of major depressive disorder according to the PRIME-MD. In the IPT group, 51% of the patients had no diagnosis of depression at six months follow-up, compared with 34% in the control group ($X^2_{[df]} = 4.21_{[1]}$; $p = 0.04$). In a post hoc analysis, we stratified the sample in patients who had a mild depression at baseline and in patients who had a moderate to severe depression (MADRS cut off score 21). In the group with moderate to severe depression 54% of the patients in the IPT group had no diagnosis of depression anymore at six months, compared with 26% in the control group ($X^2_{[df]} = 4.75_{[1]}$; $p = 0.03$). In the group of patients with mild depression these percentages were 49% and 40% respectively ($X^2_{[df]} = 0.63_{[1]}$; $p = 0.43$). To discuss the influence of the dilute dosage, we added in the discussion, second paragraph: IPT was superior to usual care in patients with moderate to severe depression, not in patients with mild depression. Our screening procedure, using the PRIME-MD as the primary measure to diagnose major depression, yielded many patients with only mild symptoms (57%). To select patients for the intervention, a measure to assess depression severity should be added. When delivered only to patients with moderate to severe depression, the number of sessions should most probably be increased as Shapiro et al. have found that patients presenting with relatively severe depression improved substantially more after 16 than after 8 sessions of IPT [24]. The overall effectiveness of the depression treatment can of course be improved when patients can choose or switch between interventions, and combination therapies can be given, as is done successfully in several collaborative care depression management programmes [8,9].

g) The reviewer states that the inevitable limitations of the report should be listed. Although we mentioned several limitations implicitly in the discussion section we now have made them more explicit in a paragraph limitations in the discussion section (as mentioned before). The reviewer further argues that the
conclusions are overstated, that the authors have hardly proven that there are no impassable barriers to make IPT available. We agree that indeed this conclusion was somewhat overstated and not sufficiently grounded. We changed the conclusion at page 17 and in the abstract into: As it was feasible to organize IPT in an effectiveness trial, and as IPT was effective, there are grounds to support the further implementation of IPT for depressed elderly patients within general practice.

Reviewer 2 Patrick Raue

This reviewer's general comment is that the paper is well written and is about implementing IPT in general practice settings, and considers organizational, clinician and patient variables.

1. The reviewer makes a comment that is comparable to the general comment of reviewer 1 in that the feasibility data were gathered in a randomized effectiveness study, and that therefore this study cannot be considered a true feasibility study. We made several adaptations (see our comments on reviewer 1) to address this point.

2. The reviewer states that it would be helpful to describe the specific and open-ended questions about the intervention for GPs. We added a translated version of the questionnaire for GPs at the end of this letter. In addition, at page 11 we added: The questionnaire started with two open ended questions (“What did you think were positive/negative aspects of delivering IPT transmurally to depressed elderly patients within your practice?”) The following positive aspects were mentioned more than once: 11 GPs gave positive comments regarding the IPT intervention as such (time-limited, practical, patient-friendly and structured); 9 mentioned the easy access of the intervention; 4 GPs mentioned that they felt supported in the depression care for the elderly by this intervention. Negative comments that were mentioned more than once: 3 GPs mentioned that they had had hardly any contact with the therapist. 2 GPs thought that screening was not the right way to select patients, but that referral should be done by the GPs; 2 GPs found the intervention time-consuming. On a specific question about the usefulness of delivering IPT within the practice, all but one of the GPs thought that this intervention lowered the barrier to providing adequate care for a group of elderly patients, who do not want to be referred to specialist mental health facilities. In the last question GPs were asked whether they would use this intervention if it would be available after the end of the research project (yes/no). Again, all but one were positive. The reviewer also asks how organizational barriers and facilitating factors were assessed. As mentioned before we, used a pragmatic approach. The researcher, research assistants and therapists recorded what they did and encountered while organizing and carrying out the intervention, without an a priori checklist.

3. The reviewer asks how many patients failed to initiate treatment. Of the 69 patients who gave informed consent, one did not start therapy. At page 9 we added “ Of the 69 patients who were offered the therapy, 1 failed to initiate and 47 (68%) completed 10 sessions
4. The reviewer asks to provide the range of MADRS scores and to describe what a mean score of 19.4 corresponds to as far as depression severity. We added at page 9: To assess depression severity we used the Montgomery Åsberg Depression Rating Scale (MADRS, range 0-60, higher scores indicate higher severity of depression. The mean score of 19.4 means that on average patients had mild depressive symptoms. [22]

5. The reviewer asks to list the main dropout reasons. We added at page 9: Other reasons for dropout were: somatic diseases (4), organic brain syndrome (1), died (1), long-time stay in other part of the country (2), not motivated (5), and reason not clear (3).

6. The reviewer mentions that a relatively liberal criterion for treatment adherence is used, namely completing 10 sessions of IPT over a 5-month course or terminating therapy earlier with therapist agreement, because the patient was doing well. It is true that in efficacy trials, IPT was given on a weekly basis and for a full course of treatment regardless of early improvement. But, this was a pragmatic trial in real-life practice. Therefore we used a more liberal approach.

7. The reviewer asks whether there were any other incentives for therapists to participate beyond learning a new therapy, and whether their employees supported their work. There were no other incentives; we refer to our answer on comment 7d of the first reviewer.

8. Reviewer two also asks for anchor points of the CSQ. To address this point we made adaptations in the discussion, as was described in our answer to point 7b of reviewer 1. At this point the reviewer again asks for more details about the GP questionnaire. We already addressed this comment in our answer of point 2 of this reviewer.

9. The reviewer comments on our statement that talking about depressive illness to patients with mild depression was not workable. He states that probably the PRIME-MD diagnosis was not valid in these cases. We agree with this comment. As the intervention was not effective in the group of mildly depressed patients, we suggest applying IPT selectively to patients with at least moderate to severe depression. This implies that in addition to the PRIME-MD an instrument to measure depression severity should be added to the selection procedure. To stress this point we added in the discussion at page 14, first paragraph: IPT was superior to usual care in patients with moderate to severe depression, not in patients with mild depression. Our screening procedure, using the PRIME-MD as the primary measure to diagnose major depression, yielded many patients with only mild symptoms. To select patients for the intervention, a measure to assess depression severity should be added. Of course, some of the patients with mild symptoms may develop a more severe depression, and therefore they should be informed about depressive disorder, and their symptoms should be monitored. But in our project it proved to be inappropriate to label their symptoms as a disease (or in IPT terms “give patients the sick-role”). This finding combined with the fact that treatment effect was smaller and not significant in patients with mild depression made us conclude that IPT should be reserved for patients with moderate to severe depression.

Minor Essential Revisions
1. Introduction. The reviewer states that the second sentence on inadequate treatment in real world settings logically belongs towards the end of the paragraph. We moved the sentence to the last part of the paragraph.

2. Introduction. The reviewer suggests referring also to a paper of Schulberg et al in addition to the Freudenstein reference. We chose the Freudenstein reference because it is specifically about the elderly. However, we now changed the sentence into: Some forms of psychotherapy have also proved to be effective in midlife primary care patients [Schulberg et al.], but research on older primary care populations is limited [Freudenstein et al.]

3. Introduction, 3rd paragraph. The reviewer suggests replacing adult by midlife primary care patient. We have made that change.

4. Methods. Severe cognitive impairment was defined as a score on the MMSE of < 18. We added this at page 6.

5. The reviewer states that practice nurses and community psychiatric nurses are mentioned in the abstract (conclusions), but not in the text. We agree that this is an omission. We added in the conclusion, at the end of the paper: “Consolidation may be achieved by making this intervention available through practice nurses or community psychiatric nurses who deliver IPT as part of a more comprehensive depression management program”.

6. In the reference list number 13 and 21 repeated, as did numbers 15 and 25. We have corrected this.
A. What were positive aspects of delivering IPT transmurally to depressed elderly patients within your practice?
   1. 
   2. 
   3. 

B. What were negative aspects of delivering IPT transmurally to depressed elderly patients within your practice?
   1. 
   2. 
   3. 

C. What do you think of letting mental health workers deliver IPT within your practice?
   - I don’t see the advantage of this approach; patients who want psychotherapy can go to secondary care or psychologists in private practices.
   - I’m neutral about this
   - I think this intervention lowered the barrier to providing adequate care for a group of elderly patients, who do not want to be referred to specialist mental health facilities

D. If this transmural intervention would be available after this research project has finished, would you like to use it?
   - Yes
   - No, because