PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Study protocol for a cluster-randomized, prospective, parallel-group, superiority trial to compare the effectiveness of a collaborative and stepped care model versus treatment as usual in patients with mental disorders in primary care: The COMET study.
AUTHORS	Heddaeus, Daniela; Dirmaier, Joerg; Brettschneider, Christian; Daubmann, Anne; Grochtdreis, Thomas; von dem Knesebeck, Olaf; König, Hans-Helmut; Löwe, Bernd; Maehder, Kerstin; Porzelt, Sarah; Rosenkranz, Moritz; Schaefer, Ingo; Scherer, Martin; Schulte, Bernd; Wegscheider, Karl; Weigel, Angelika; Werner, Silke; Zimmermann, Thomas; Härter, Martin

VERSION 1 – REVIEW

REVIEWER	Lene Falgaard Eplov Copenhagen Research Center for Mental Health – CORE. Mental Health Center Copenhagen, Denmark.
REVIEW RETURNED	15-Jul-2019

GENERAL COMMENTS	Lene Falgaard Eplov Copenhagen Research Center for Mental Health – CORE. Mental Health Center Copenhagen, Denmark. 15-Jul-2019 The manuscript addresses a focused research topic in evaluating the effectiveness of a collaborative and stepped care model for patients with depressive, anxiety, somatoform and/or alcohol use disorders. and its clinical relevance is obvious. Furthermore, the effectiveness is investigated using the best method, a randomized controlled trial and this is adequate supplemented with a cost-effectiveness evaluation and a process evaluation. The manuscript is a study protocol on an ongoing study, and therefore as mentioned in the instructions for reviewers, very few changes in the methodology is possible, which I have taken into account, reviewing the manuscript. Title The intervention is not compared with treatment as usual but with augmented treatment as usual, and therefore the title has to be changed according to this. Abstract The abstract gives a structured summary of trial design, methods, results, and conclusions. Introduction

	The introduction gives a thorough scientific background and rationale for the study. However, there are some minor issues. • The paragraphs about stepped care are not coherent. In example they end a paragraph with the following “Stepped care has proven to be effective for the treatment of depressive symptoms, however further investigation is required regarding effectiveness and the best manner of delivering this form of care19-21” but start the next paragraph with wiring ”Some trials examined the effects of stepped care on both symptoms of depression and anxiety11 22 23”, and here they use other references and do not sated what these trials have shown.. After that they write “Finally…” but in the next sentences they continue to address stepped care. • Later the authors write: “Taken together, the development of an overarching integrative collaborative and stepped treatment model, which provides evidence and guideline-based treatment for the most common comorbid mental disorders (depression, anxiety, somatoform and alcohol use disorders) in primary care and taking into account the comorbidity between these disorders is necessary. But personality disorders are also a common comorbid mental disorder and the authors need to address this. Why did they not include this disorder? • The rationale for using a cluster design need to be stated here (if following the CONSORT Criteria) or under study design. • In the objective the authors write “an innovative collaborative and stepped care model). Delete innovative. Methods and analysis This section gives a thorough description. However, there are some minor issues. • In the study design paragraph, the authors write: “We decided to compare the intervention to enhanced usual care as this is a health care services research project which investigates in research to improve routine care for patients with mental health disorders. Usual care is defined as control group because the treatment strategies used in the intervention group are not part of usual-care practices. Moreover, in a pragmatic trial where the research question is to determine the collaborative and stepped care intervention is superior to usual care, it is obvious to have usual care as the control group”. I believe this is the rationale for comparing the intervention with an augmented treatment as usual, but I simply do not understand, what the rationale is. • A definition of cluster and description of how the design features apply to the clusters is missing and I recommend that flow charts over the study to be included. • Under the paragraph “Allocation of treatment” the authors describe blinding, therefore perhaps a better name for the paragraph is “Allocation of treatment and blinding”. Furthermore, the authors need to describe if the researchers are blinded. • Outcomes: I recommend a table describing the primary, secondary and explorative outcome more precise. Furthermore, I do not understand why the authors describe outcomes for the cost effectiveness study as well as the process evaluation together with

	RCT outcomes. As these are not outcomes in the RCT, they need to be separate from the RCT outcomes and described in separate sections. • The authors write that a detailed statistical analysis plan will be prepared and finalized before the code is broken. I recommend that the plan is finalized and published on Clinical Trials.gov before they start analyzing. In conclusion this manuscript addresses a focused research topic and uses a relevant design. Furthermore, its clinical relevance is evident. However, the manuscript has the about mentioned weaknesses.

REVIEWER	Bea Herbeck Belnap University of Pittsburgh School of Medicine, USA and University of Göttingen Medical Center, Germany
REVIEW RETURNED	18-Jul-2019

GENERAL COMMENTS	This is a very interesting study that will further enhance our understanding of stepped collaborative care and - if proven effective - may increase treatment of mental health conditions in primary care. I have one major concern. The roles of the GP and the care provider are not clear to be. Are these separate people? Collaborative care employs care managers as non-professional support who work closely with the patient and coordinate care across providers. However, the authors state on page 8 that they do not use care managers. Please clarify. I have several minor comments that are all indicated in attached file. Overall, the manuscript would greatly benefit from a clearer writing style, the help of a native speaker, and proof reading for typos.

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:
Reviewer: 1

"Title: The intervention is not compared with treatment as usual but with augmented treatment as usual, and therefore the title has to be changed according to this."

➔ Thank you very much for bringing this mistake to our attention. We adjusted the title and also the abstract, where the same mistake occurred.

"Introduction: The introduction gives a thorough scientific background and rationale for the study. However, there are some minor issues. The paragraphs about stepped care are not coherent. In example they end a paragraph with the following "Stepped care has proven to be effective for the treatment of depressive symptoms, however further investigation is required regarding effectiveness and the best manner of delivering this form of care19-21" but start the next paragraph with wiring "Some trials examined the effects of stepped care on both symptoms of depression and anxiety11 22 23", and here they use other references and do not sated what these trials have shown.. After that they write "Finally…" but in the next sentences they continue to address stepped care."

➔ Thank you very much for your recommendation to reformulate the paragraphs about stepped care. We reformulated the paragraph as follows: “Stepped care has proven effective for the treatment of depressive symptoms, however, further investigation is required regarding effectiveness for treating other specific disorders, such as somatoform disorders and alcohol-related disorders as well as for comorbid conditions and in order to determine the best manner of delivering this form of care[20-22].
Regarding comorbidity, some trials have examined the effects of stepped care on both symptoms of depression and anxiety[12 23 24]. A stepped care model for panic and generalized anxiety disorders was found to be effective and cost-effective[13 25]. For alcohol use disorders the evidence of the effectiveness of stepped care approaches is limited[26-29].”

“Later the authors write: “Taken together, the development of an overarching integrative collaborative and stepped treatment model, which provides evidence and guideline-based treatment for the most common comorbid mental disorders (depression, anxiety, somatoform and alcohol use disorders) in primary care and taking into account the comorbidity between these disorders is necessary. But personality disorders are also a common comorbid mental disorder and the authors need to address this. Why did they not include this disorder?”

➔ Thank you very much for your valuable hint. In fact, we did not want to focus on the most common **comorbid** mental disorders, but rather on the most common mental disorders in general, i.e. the disorders with the highest prevalence in the population. Therefore we deleted the word “comorbid” in the sentence. According to Roca et al. (Roca M, Gili M, Garcia-Garcia M, et al. Prevalence and comorbidity of common mental disorders in primary care. J Affect Disord 2009; 119(1-3):52-8. doi: 10.1016/j.jad.2009.03.014), mental disorders with the highest prevalence are depression, anxiety, somatoform and alcohol use disorders. We included this information in the first paragraph of the introduction. As the prevalence for personality disorders is not as high as for the mentioned disorders and because we needed to limit the complexity of the trial, as it is already quite complex, we did not integrate this cluster of disorders.

“The rationale for using a cluster design need to be stated here (if following the CONSORT Criteria) or under study design.”

➔ Thank you for your recommendation. To implement it, we added the following explanation in the paragraph “2.1 Study design”: “A cluster randomization design was chosen, because part of the intervention was an initial training for the GPs to improve their skills and practice visits from the study team to implement study procedures and instruments. We assume that GPs and primary care practices who have once been trained and have access to the intervention could no longer treat their patients under control conditions and thus intervention and control conditions would be mixed.”

“In the objective the authors write “an innovative collaborative and stepped care model). Delete innovative.”

➔ Thank you for this recommendation. We deleted “innovative”.

“In the study design paragraph, the authors write: “We decided to compare the intervention to enhanced usual care as this is a health care services research project which investigates in research to improve routine care for patients with mental health disorders. Usual care is defined as control group because the treatment strategies used in the intervention group are not part of usual-care practices. Moreover, in a pragmatic trial where the research question is to determine the collaborative and stepped care intervention is superior to usual care, it is obvious to have usual care as the control group”. I believe this is the rationale for comparing the intervention with an augmented treatment as usual, but I simply do not understand, what the rationale is.”

➔ Thank you very much for this feedback. In order to increase comprehensibility, we have reworded this passage as follows: “We selected treatment as usual as the control condition

because the research question is to determine if collaborative and stepped care is superior to usual care. In order to ensure the comparability of intervention and control condition, both groups are to be recruited identically. This recruitment procedure includes a computer-based screening and guideline-based diagnostic process including feedback on the screening results and a diagnostic checklist. Since this computer-based screening and diagnostic procedure is not part of German routine care, we consider the comparison condition as an augmented treatment as usual (aTAU)."

"A definition of cluster and description of how the design features apply to the clusters is missing"

➔ Thank you very much for this advice. To clarify this, we added the text passage: "Clusters are defined as primary care practices. A cluster randomization design was chosen, because part of the intervention was an initial training for the GPs to improve their skills and practice visits from the study team to implement study procedures and instruments. We assume that GPs and primary care practices who have once been trained and have access to the intervention could no longer treat their patients under control conditions and thus intervention and control conditions would be mixed." In addition, we emphasize the cluster aspect through clearer headings in the sections "2.3 Eligibility criteria" and "2.4 Recruitment" as well as in the participant timeline.

"and I recommend that flow charts over the study to be included."

➔ Thank you very much for your recommendation. Based on the SPIRIT guideline, we have inserted a participant timeline under 2.5 that integrates all aspect of a flow chart. Since SPIRIT does not include any further flow charts and the information would be doubled, we have decided against another flow chart. We would like to ask, if there is information missing in the participant timeline that would be important to present in another flow chart?

"Under the paragraph "Allocation of treatment" the authors describe blinding, therefore perhaps a better name for the paragraph is "Allocation of treatment and blinding". Furthermore, the authors need to describe if the researchers are blinded. "

➔ Thank you for this suggestion. We added the words "and blinding" in the title as well as the sentences: "Nevertheless, the researchers who perform the statistical outcome analysis will be blinded."

"Outcomes: I recommend a table describing the primary, secondary and explorative outcome more precise."

➔ Thank you very much for your recommendation. We inserted a table (Table 2) with primary and secondary outcomes in section "2.8 Outcomes" and explain the measured variables in section "2.10 Data collection methods"

Variable	Outcome Measure	Outcome	Baseline/ T0	T1	T2	T3
Primary Outcome						
Health-related quality of life mental health scale	SF-36 (36 Items)	change in mental health-related quality of life from baseline to 6-month	X	X	X	X
Secondary Outcome						
Disorder-specific symptoms	PHQ-9 (9 Items) GAD-7 (7 Items)	change in disorder-specific symptoms from baseline to 6-month	X	X	X	X

Response of diagnosed disorder(s)	PHQ-15 (15 Items) PHQ-Panic module (15 Items) SSD-12 (12 Items) AUDIT (10 Items)	at least 50% symptom reduction at 6 months on the disorder-specific screening instrument	X	X	X	X
Remission of diagnosed disorder(s)		obtaining a value below the respective clinical cut-off value of the disorder-specific screening instrument at 6 months	X	X	X	X
Health-related quality of life physical health scale	SF-36 (36 Items)	change in physical health-related quality of life from baseline to 6-month	X	X	X	X
Health care utilization	Questionnaire, CSSRI (26 Items)	Change in health care utilization at 6 and 12 months	X		X	X
Quality of Life	EQ-5D-5L (5 Items)	Change in quality of Life at 6 and 12 months	X		X	X

"Furthermore, I do not understand why the authors describe outcomes for the cost effectiveness study as well as the process evaluation together with RCT outcomes. As these are not outcomes in the RCT, they need to be separate from the RCT outcomes and described in separate sections."

➔ Thank you for your clarifying advice. We have restructured the section and added subheadings.

"The authors write that a detailed statistical analysis plan will be prepared and finalized before the code is broken. I recommend that the plan is finalized and published on Clinical Trials.gov before they start analyzing."

➔ Thank you for your recommendation. We plan to finalize the detailed statistical analysis plan in autumn 2019. We will finalize and publish the plan on Clinical Trials.gov before we start analyzing.

Reviewer: 2

"I have one major concern. The roles of the GP and the care provider are not clear to be. Are these separate people? Collaborative care employs care managers as non-professional support who work closely with the patient and coordinate care across providers. However, the authors state on page 8 that they do not use care managers. Please clarify."

➔ Thank you very much for your recommendation to clarify. By the term care provider we mean all practitioners who are involved in the treatment of patients in the network. Those are GPs, psychotherapists, psychosomatics, psychiatrists and inpatient institutions. We use the term GP in the text if we only mean general practitioners. To make define this to the reader we first mention and explain the term in section 1.1 Background and rationale "One approach to account for comorbidity is collaborative care, an evidence-based form of treatment which focuses on systematically integrating multi-professional health care providers (e.g., general practitioners (GPs), specialized mental health professionals)." In section 2.2 Setting it is also explained referring its use in the study "Patients in CSC will be treated in the CSC network by GPs, psychotherapists, psychosomatics and psychiatrists as well as inpatient clinics in Hamburg. The list of all participating care providers can be requested from the study coordinator." We tried to clarify your request by adding subtitles in section 2.3 Recruitment with more precise descriptions for the different levels of study participants. You further recommend to clarify if we use care managers. In contrast to an often-used approach which brings external care managers into GP practices, we will systematically integrate the

resources and competencies of cooperating care providers (GPs, psychotherapists, psychiatrists, psychosomatics, and inpatient facilities) which can more readily create the structures needed to provide a broad spectrum of interventions. We give this information in section 2.7 The CSC Intervention paragraph Collaborative network.

"Overall, the manuscript would greatly benefit from a clearer writing style, the help of a native speaker, and proof reading for typos."

➔ Thank you very much for your recommendation. We have commissioned a native speaker to check the document for linguistic errors.

"Section 1.1. "Background and rationale": 'Burden of mental and neurological disorders': Why lump these together?"

➔ Thank you very much for your question. We reviewed the reference and decided to refer to another publication that does separate neurological and mental disorders. Therefore we changed the relevant sentence as follows: "The burden of mental disorders (including substance use disorders) has increased to 22.8% of years lived with disability (YLD)[2]."

"Section 1.1. "Background and rationale" paragraph 1 last sentence: I am not sure what you mean. Do you want to say that there is a large prevalence?"

➔ Thank you very much for your recommendation to clarify this sentence. We reformulated the sentence as follows: ". In addition, there is a significant degree of overlap between the symptoms of these disorders as well as mixed forms[7 8], which calls for comprehensive health care approaches for addressing concurrent mental disorders in primary care settings[9]."

"Section 1.1. "Background and rationale" paragraph 3 last sentence: The sentence before stated that it is proven effective. What do you mean? Do you mean for specific disorders – and that stepped care has only been proven effective for SOME conditions?"

➔ Thank you very much for your recommendation to clarify this sentence. We reformulated the sentence as follows: "Stepped care has proven effective for the treatment of depressive symptoms, however, further investigation is required regarding effectiveness for treating other specific disorders, such as somatoform disorders and alcohol-related disorders as well as for comorbid conditions and in order to determine the best manner of delivering this form of care[20-22]"

"Section 2.1 "Study design": This is an unusual way of phrasing the groups. Usually both groups are part of the study, but just one group will receive the study intervention. I suggest to re-phrase according to established use."

➔ Thank you very much for your recommendation. We changed the wording for the intervention group from "COMET" to "CSC" (Collaborative and Stepped Care Model).

"Section 2.1 "Study design": I do not understand this. How do you define enhanced usual care vs. usual care. Do the TAU patients receive anything beyond the screening and outcomes assessments?"

➔ Thank you very much for your question. To clarify this paragraph and raise the comprehensibility, we reformulated it as follows: "We selected treatment as usual as the control condition because the research question is to determine if collaborative and stepped care is superior to usual care. In order to ensure the comparability of intervention and control condition, both groups are to be recruited identically. This recruitment procedure includes a computer-based screening and guideline-based diagnostic process including feedback on the screening results and a diagnostic checklist. Since this computer-based screening and diagnostic procedure is not part of German routine care, we consider the comparison condition as an augmented treatment as usual (aTAU). Participants in the aTAU-group will have unrestricted access to usual care for their mental health problems. General practitioners

(GPs) in aTAU will be instructed to continue treatment with affected patients in the same way as they would do outside the study."

"Section 2.1 "Study design", last sentence: The outcomes will be available before the study ends?"

➔ Thank you for informing us of this mistake. We deleted the first part of the sentence.

"Section 2.2 "Setting": Does this imply that they can also get referred to psychotherapists or go to an inpatient clinic? I believe that would be part of usual care?"

➔ Thank you for your question. Yes, this means that participants in the aTAU-group will have unrestricted access to usual care for their mental health problems including psychotherapists, psychiatrists and inpatient institutions, but which must not be part of the network. As this information is already given in section 2.1 "Study design", we deleted the sentence in section 2.2 "Setting".

"Section 2.3. License instead of approval."

➔ Thank you for this recommendation. We changed the word "approval" into "license".

"Section 2.3. last sentence: Do you mean other mental comorbidities? Also not bipolar etc – and they would not be treated for that?"

➔ Thank you for your question. Yes, here mental comorbidities other than those under investigations are meant. If they will be treated or not is not part of the intervention or study. But it is likely that these comorbidities will be detected and treated within the network.

"Section 2.4 "Recruitment" paragraph "Cluster level: Primary Care Practices": What did you then inform them about? This is unclear."

➔ Thank you for pointing that out. We added the missing information as follows: "they will be informed about the concept of the study, research aims and study procedures but not given details concerning the intervention itself."

"Section 2.4 "Recruitment" paragraph "Individual level: Patients": What does this entail? Are there any criteria for choosing these days?"

➔ Thank you for your question. There are no special criteria for the selection of these days except, that recruitment fits in well with the practices schedule and procedures on these days. To make this clearer for the reader, we reformulated the sentence as follows: "Participating GP practices will determine certain days on which recruitment fits in well with their schedule and practice procedures. On these days each patient entering the practice will be informed about the study."

"Section 2.4 "Recruitment" paragraph "Individual level: Patients": Did you train the GPs or inform them about the questionnaires and how to interpret the results?"

➔ Thank you for your question. Yes, GPs are informed about the questionnaires and how to interpret the results. They receive an initial training and practical visits in which these contents will be discussed in detail. These information are given to the reader in the previous paragraph ("Cluster level: Primary Care Practices") and in section 2.7. "The CSC Intervention", second paragraph.

"Section 2.4 "Recruitment" paragraph "Individual level: Patients": How did you define this? Do you have cut-off scores?"

➔ Thank you very much for your question. With the expression "study relevant diagnoses" we meant the diagnoses under investigation in the intervention. There are Cut-off scores for the screening tests, but the criteria for giving an ICD-10 diagnoses are defined by the ICD-10.

Therefore, an ICD-10 checklist is shown to the GP on the tablet to help him determine a diagnosis. To explain this to the reader, we have reworded the passage: “The patient's screening scores are presented to the doctor along with the relevance of the score and the cut-off of each test. Screening results may or may not be used by the physician for diagnostic purposes. Integrated ICD-10 diagnostic criteria checklists for the diagnoses under investigation (depressive, anxiety, somatoform and/or alcohol use disorders) support the GP in the selection of the diagnosis. In addition to the selection of the ICD-10-Code the GP indicates the severity of the disorder by classifying it as mild, moderate or severe. If a patient receives one or more of the above mentioned ICD-10 diagnoses and gives his or her informed consent, the patient will be included in the study”.

“Section 2.4 “Recruitment” paragraph “Further care providers for the CSC network: Psychotherapists, psychiatrists, psychosomatics and inpatient institutions”: Please describe in more concrete terms. What are their tasks.”

➔ Thank you very much for your recommendation. We think as well, that it is important to inform the reader about the tasks of the Care providers of the CSC network. As the content of this section is the recruitment, we did not insert this information here but in section 2.7. “Intervention” (paragraph “Collaborative network”, “Collaborative and stepped care interventions” and Table 1.

“Section 2.4 “Recruitment” paragraph “Further care providers for the CSC network”: Also, if a therapists does not sign up, will that limit the pool of therapists you can send the patients to? It is ok to have a small pool, but will that guarantee that patients have access to a therapists readily?”

➔ Thank you very much for this question: Yes, it is correct, that not all of the 910 invited therapists did sign up and the pool of is limited. From previous projects we can derive an approximate estimate of how many secondary care provider we will need for the targeted number of GPs and patients. With this estimate we are aiming for a pool of 20-30 secondary care provider.

“Section 2.7 “The COMET Intervention” paragraph “Collaborative network”: So you will not use care managers? Essential part of the collaborative care model is to use non-professional care managers. I am not sure that you are misleading the reader by calling your model “collaborative care.” Or are you implying that there will be personnel at each practice that will take over the tasks of the “care manager?” please clarify.”

➔ Thank you very much for your recommendation. Yes, it is true, that we do not use care managers. The intervention is a model combining the collaborative and the stepped care approach. We do not follow a specific collaborative care model. To the best of our knowledge, the term collaborative care covers many different forms of care models and the key features are: Integration of mental health professionals in primary care medical settings, close collaboration between mental health and medical/nursing providers and focus on treating the whole person and whole family. In our study the collaborative care approach is realized by establishing a network with all care providers involved in the treatment of patient with mental disorders, introducing an online scheduling platform to enhance patient referrals, quarterly network meetings and financial incentives for personal exchange via E-Mail or telephone. Collaborative Care elements are described in section 2.7. “The CSC Intervention” paragraph “Collaborative network”. To avoid misleading the reader we inserted the following sentence in this paragraph: “In contrast to an often-used approach which brings external care managers into GP practices, we will systematically integrate the resources and competencies of cooperating care providers (GPs, psychotherapists, psychiatrists, psychosomatics, and inpatient facilities) which can more readily create the structures needed to provide a broad spectrum of interventions.”

“Section 2.7 paragraph “Computer-assisted and guideline-based diagnosis and treatment decisions”: Are these part of the algorithm you use, or will the GP make those decisions case by case?”

➔ Thank you very much for your question. These factors are not part of the algorithm. The GP makes the diagnoses case by case. As this was formulated in a misleading way, we have amended the text as follows: “The algorithm of the program on the tablet computer will provide the GP with one or more treatment recommendations for the individual patient that will be based on guideline recommendations for the diagnosed disorder and its degree of severity[31 38-41]. While these recommendations will offer an orientation for therapeutic decisions, the actual treatment decision for one of the evidence-based treatment options will be carried out in cooperation with the patient by integrating individual preferences and needs, thus following the principles of patient-centered care and shared decision-making. Additionally, possible comorbidities and specific characteristics of the disorder(s) are to be taken into account”.

“Section 2.7 paragraph “Collaborative and stepped care interventions”: Will the GPs be trained in the alcohol intervention (1d)? Or are all GPs familiar with the program?”

➔ Thank you very much for your question. GPs will be trained to the single brief alcohol intervention. Usually they are not familiar with the program. To make this transparent to the reader, we added the following information: “For step 1d, the single brief interventions for alcohol use disorders, GPs obtain special training in the context of one of the first network meetings”.

“Section 2.7 paragraph “Collaborative and stepped care interventions”: How are these defined? See also comment above about cut-off scores.

➔ Thank you very much for your question. To improve comprehensibility, we have rewritten the text passage as follows: “In order to address this problem, case management will be implemented. Based on the digital diagnostic information assessed by the GP during the diagnostic process, a member of the study team will follow the treatment pathways of those patients who are diagnosed with a disorder of a high degree of severity. In those cases, the existing monitoring forms filled out by the care providers will be reviewed, and the responsible care provider will be informed if possible deficiencies in care are detected.”

“Section 2.7 paragraph “Collaborative and stepped care interventions”: Is this the GP or who? This is not clear?”

➔ Thank you very much for your recommendation to clarify this. The responsible care provider is the one who carries out the current treatment. We defined the responsible care provider in table 1. To make this clearer, we added “responsible” in the table 1 and referred to that table in the text.

“Section 2.7 paragraph “Collaborative and stepped care interventions”: I am a little confused about the term “care provider” Do you mean to say that a member of the study team monitors ALL care providers (as listed in Table 1) – or is there another “care provider” involved? It would help to explain a) who is monitoring the intervention; b) who is delivering the intervention c) other than what is listed in Table 1, how are the steps applied in each case. Maybe an example would help the reader.

➔ Thank you very much for your recommendation to clarify this. A member of the study team does NOT monitor care providers. However, patients, for whom the GP in the diagnostic process indicated a disorder of high severity degree, a member of the study team follows the treatment process. To clarify this, we reformulated the text passage as follows: “In order to address this problem, case management will be implemented. Based on the digital diagnostic information assessed by the GP during the diagnostic process, a member of the study team will follow the treatment pathways of those patients who are diagnosed with a disorder of a high degree of severity. In those cases, the existing monitoring forms filled out by the care providers will be reviewed, and the responsible care provider will be informed if possible deficiencies in care are detected.”

"Section 2.7 paragraph "Collaborative and stepped care interventions": Also, if the GP is free to choose the treatment, how can they deviate from the protocol?"

➔ Thank you very much for your question. Yes, you are right. Since treatment decisions are made according to the assessment of the GP and the needs and preferences of the patient, there are strictly speaking no deviations from the protocol. We have therefore deleted the two sentences in question.

"Section 2.8 "Outcomes": Improvement instead of change?"

➔ Thank you very much for your recommendation. We changed the word "change" into "improvement".

"Section 2.8 "Outcomes" paragraph "Secondary outcome measures": I would combine these 3, since they are pertaining to same measures."

➔ Thank you very much for your recommendation. We reformulated the paragraph as follows: "Secondary outcome parameters will be the change in disorder-specific symptoms as measured with the German versions of the major depressive[55], generalized anxiety[56], panic and somatoform modules of the PHQ[57], the SSD-12[58-60] and the AUDIT[61]. We will analyze disorder-specific response (at least 50% symptom reduction at 6 months on the disorder-specific screening instrument) and remission (obtaining a value below the respective clinical cut-off value of the disorder-specific screening instrument at 6 months) for these outcome measures. Further secondary outcomes will be health-related quality of life assessed with the SF-36 physical health score, change in health-related quality of life according to the EQ-5D-5L and health care utilization."

"Section 2.8 "Outcomes" paragraph "Process evaluation": I understand that this is still somewhat in planning, but could you at least state by what means, e.g. questionnaires, open-end interviews, I see they are in Table 2. Maybe refer reader here to Table 2."

➔ Thank you very much for you recommendation. To implement it, we inserted the following sentences: "For the assessment semi-structured qualitative interviews will be conducted at the beginning and at the end of the study with patients, GPs, psychotherapists, psychosomatic specialists and psychiatrists of the CSC-group and the aTAU-group. We will use semi-structured interview guides on implementation, functionality, acceptance and sustainability of the interventions of the CSC. The interview guides include questions regarding possible beneficial and impeding aspects referring to the implementation process, the care model, adoption/assimilation, communication/impact and context. Questions about the implementation of the study will be integrated in the patient interview at T2. For a separate evaluation of the care process, care providers will be asked at baseline and T3 using standardized short questionnaires. Moreover, process evaluation with care providers will be involved in the quarterly network meetings."

"Section 2.10 "Data collection methods" paragraph "Telephone-based patient interview": Different font"

➔ Thank you very much for pointing this out to us. We have corrected the text passage in question.

"Section 2.11 "Data management": I am not familiar with this term. Is this de-identified?"

➔ Thank you very for you wording suggestion. We changed the term pseudonymously into de-identified.

"Section 3 paragraph "Personal information about participants": Is this not unrealistic? In Germany the phone is usually answered with the last name. If several people live in the same household, the assessor has to ask for a specific person."

➔ Thank you very much for your request. It is true, that the phone in Germany is usually answered with the last name, but the name of the patient is not saved or stored and is not given to the interviewer. In the rare cases the patient gives his landline telephone number, the interviewer asks for the person who takes part in the COMET-study. Usually patients give their mobile number. To make this transparent to the reader, we inserted the following sentence: "If the landline telephone number is given, the interviewer will ask for the person who is taking part in the COMET-study."

VERSION 2 – REVIEW

REVIEWER	Lene Falgaard Eplov Copenhagen Research Center for Mental Health – CORE Mental Health Centre Copenhagen Denmark
REVIEW RETURNED	27-Sep-2019

GENERAL COMMENTS	Reading the revised manuscript, I have only one comment. The authors haven't addressed the rationale for comparing the intervention with an augmented treatment as usual adequately. The author writes: "We selected treatment as usual as the control condition because the research question is to determine whether collaborative and stepped care is superior to usual care. In order to ensure the comparability of intervention and control condition, both groups are to be recruited identically. This recruitment procedure includes a computer-based screening and guideline-based diagnostic process including feedback on the screening results and a diagnostic checklist. Since this computer-based screening and diagnostic procedure is not part of German routine care, we consider the comparison condition as an augmented treatment as usual (aTAU). Participants in the aTAU-group will have unrestricted access to usual care for their mental health problems. General practitioners (GPs) in aTAU will be instructed to continue treatment with affected patients in the same way as they would outside of the study". As I read it the augmentation consists of a computer-based screening and guideline-based diagnostic process including feedback on the screening results and a diagnostic checklist. This is a normal procedure when you want to recruit to a RCT and not "augmented treatment", and therefore the authors indeed selected treatments as usual as the control condition, as they state in the first paragraph. Therefore, the authors need to change augmented treatment as usual and aTAU to treatment as usual and TAU throughout the manuscript.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

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The author writes: “We selected treatment as usual as the control condition because the research question is to determine whether collaborative and stepped care is superior to usual care. In order to ensure the comparability of intervention and control condition, both groups are to be recruited identically. This recruitment procedure includes a computer-based screening and guideline-based diagnostic process including feedback on the screening results and a diagnostic checklist. Since this computer-based screening and diagnostic procedure is not part of German routine care, we consider the comparison condition as an augmented treatment as usual (aTAU). Participants in the aTAU-group will have unrestricted access to usual care for their mental health problems. General practitioners (GPs) in aTAU will be instructed to continue treatment with affected patients in the same way as they would outside of the study”.

As I read it the augmentation consists of a computer-based screening and guideline-based diagnostic process including feedback on the screening results and a diagnostic checklist. This is a normal procedure when you want to recruit to a RCT and not “augmented treatment”, and therefore the authors indeed selected treatments as usual as the control condition, as they state in the first paragraph. Therefore, the authors need to change augmented treatment as usual and aTAU to treatment as usual and TAU throughout the manuscript.”

 Thank you very much for your comment. We changed augmented treatment as usual and aTAU to treatment as usual and TAU throughout the manuscript. We changed the rational in the section "study design" as follows: “We selected treatment as usual as the control condition because the research question is to determine whether collaborative and stepped care is superior to usual care. Participants in the TAU-group will have unrestricted access to usual care for their mental health problems. General practitioners (GPs) in TAU will be instructed to continue treatment with affected patients in the same way as they would outside of the study.”