

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Association between anxiety, depression and quality of life - Study protocol for a systematic review of evidence from longitudinal studies
AUTHORS	Hohls, Johanna Katharina; König, Hans-Helmut; Quirke, Eleanor; Hajek, André

VERSION 1 – REVIEW

REVIEWER	Dr Amy Blakemore School of Health Sciences, University of Manchester
REVIEW RETURNED	05-Nov-2018

GENERAL COMMENTS	<p>Thank you for the opportunity to review this protocol for a systematic review on the longitudinal association between depression, anxiety and quality of life.</p> <p>This is an important topic for a review and the authors clearly describe their proposed methods. However, I think they understate the topic in the introduction and don't clearly make a case as to why it is important that we better understand the relationship between depression, anxiety and quality of life. What do we already know about how poor quality of life worsens outcomes for people in the general population?</p> <p>Strengths and Limitations of the Study</p> <ul style="list-style-type: none">• Point one should be amended to say this is the first review to do this in the general population. There have been others in specific samples of patients, such as those with long term conditions. <p>Introduction</p> <ul style="list-style-type: none">• I would like to see some introduction to the key issues around depression, anxiety and quality of life. Why is it important that we better understand the relationship between depression and anxiety and quality of life.• What did the studies conducted in the specific samples find was the strength of the association between depression, anxiety and quality of life.• The authors state that previous studies have tended to focus on the association between quality of life and depression. However, the study by Blakemore et al. did include anxiety. <p>Methods and Analysis</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none">• In this first point I am not clear what (including disorders as well as symptom severity) refers to. I assume this refers to those reaching caseness for a diagnosis of depression or anxiety as well
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	<p>as those with subthreshold symptoms. Please could the authors clarify this within the text?</p> <ul style="list-style-type: none"> • In the third point, please could the authors clarify if they will be including those studies who measure symptoms using self-report measures such as the PHQ-9, or will it be only measures administered by a clinician. <p>Exclusion criteria:</p> <ul style="list-style-type: none"> • How will assessment of anxiety and/or depression that are not appropriate be defined? <p>Discussion</p> <ul style="list-style-type: none"> • The authors make suggestions as to the kind of questions this review could answer, e.g. are specific quality of life domains particularly affected by specific depression symptoms? I would ask the authors to expand on this, and in relation to the relevant literature, to explain why this is important. How might it help us to develop, improve or target treatments for people with anxiety or depression, or indeed to improve quality of life?
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REVIEWER	Mythily Subramaniam Institute of Mental Health, Singapore
REVIEW RETURNED	10-Nov-2018

GENERAL COMMENTS	It is a straightforward well-designed review. I have no comments on the protocol.
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VERSION 1 – AUTHOR RESPONSE

Reviewer's comments	Authors' response (page and section of amendment in the revised manuscript; citations from manuscript printed in quotation marks, changes are underlined)
Editorial Requests	
Please include the dates of the search in both the abstract and the main methods section.	Thank you for this comment. We added this information in the abstract (p. 2) as well as methods section (p. 6).
Formatting amendments: Patient and Public Involvement	Thank you for this comment. We have added a section on patient and public involvement in the Methods section (p. 9).
Reviewer 1 - Dr. Amy Blakemore	

<p>Thank you for the opportunity to review this protocol for a systematic review on the longitudinal association between depression, anxiety and quality of life.</p> <p>This is an important topic for a review and the authors clearly describe their proposed methods. However, I think they understate the topic in the introduction and don't clearly make a case as to why it is important that we better understand the relationship between depression, anxiety and quality of life. What do we already know about how poor quality of life worsens outcomes for people in the general population?</p>	<p>First of all, thank you for your insightful and helpful comments on the manuscript. We really appreciate them.</p> <p>Please see our reply to your comments on the Introduction section below.</p>
<p>Strengths and Limitations of the Study</p> <ul style="list-style-type: none"> • Point one should be amended to say this is the first review to do this in the general population. There have been others in specific samples of patients, such as those with long term conditions. 	<p>Thank you for your comment. Following your suggestion, we included this point in the Strengths and Limitations section (p. 3):</p> <p><u>“To our knowledge, this is the first systematic review synthesizing and critically assessing evidence from longitudinal, observational studies on the association between anxiety, depression and quality of life, focusing on samples without specific disorders.”</u></p>

Introduction

Thank you for this comment. In accordance with your suggestion, we have expanded the Introduction as well as the Discussion to reflect this in more detail:

- I would like to see some introduction to the key issues around depression, anxiety and quality of life. Why is it important that we better understand the relationship between depression and anxiety and quality of life.

Introduction (p. 4):

“To the best of our knowledge, there are no recent systematic reviews specifically analyzing evidence from longitudinal studies on the association between anxiety, depression and quality of life across all age categories and focusing on samples without specific diseases or disorders (other than anxiety or depression). Looking at longitudinal studies in particular provides the advantage that individual trajectories can be observed over time and thus, temporal associations between the variables can be assessed. Moreover, focusing on observational studies analyzing samples without specific diseases means the effects of interventions or specific illnesses will be limited in terms of impact on this association.”

Discussion (p. 9f):

“Beyond providing an overview of evidence on the association between anxiety, depression and quality of life, and thus highlighting possible gaps in current research, there are a range of questions that could possibly be answered by this review. For example, our study could ascertain whether specific quality of life domains are particularly affected by specific disorders or symptoms across studies over time. Comer et al.⁹ found in a single, cross-sectional analysis in the general population, that different anxiety disorders were associated with varying decrements in different health-related quality of life domains. If this type of finding were observed over several longitudinal studies in the course of our systematic review, our study could also inform clinical research. Identification of the specific domains impacted by anxiety/depression, for example, could act as the starting point for the analysis of treatment goals or the analysis of the effectiveness of interventions aiming to improve quality of life. However, as intervention studies, such as randomized controlled trials, will not be included in our review, additional research would need to be undertaken to build on this further.”

- What did the studies conducted in the specific samples find was the strength of the association between depression, anxiety and quality of life.

Thank you for this comment. We have described the strength of the association between anxiety, depression and quality of life reported in previous systematic reviews in more detail (Introduction, p. 4):

“Regarding reviews of disease-specific samples, Blakemore, et al.¹⁵ have analyzed the association between anxiety, depression and quality of life in patients with chronic obstructive pulmonary disease (COPD), and Schram, et al.¹⁶ have focused on depression and quality of life in patients with diabetes. Looking at longitudinal studies in particular, most reviews find a negative association with varying strength of the association. For example, the meta-analysis conducted by Blakemore, et al.¹⁵ in patients with COPD found, that depression and anxiety were significantly related to reduced health-related quality of life at follow-up with moderate to large effect sizes. In contrast, Schram, et al.¹⁶ reported no to small, negative effects of depressive symptoms on domain-specific quality of life in samples of patients with diabetes.”

<ul style="list-style-type: none"> • The authors state that previous studies have tended to focus on the association between quality of life and depression. However, the study by Blakemore et al. did include anxiety. 	<p>Thank you for this comment. It is correct that Blakemore et al. (2014) included anxiety in their study, which we also stated in the Introduction. However, for reasons of clarity, we have removed the mentioned sentence.</p>
<p>Methods and Analysis</p> <p>Inclusion criteria:</p> <ul style="list-style-type: none"> • In this first point I am not clear what (including disorders as well as symptom severity) refers to. I assume this refers to those reaching caseness for a diagnosis of depression or anxiety as well as those with subthreshold symptoms. Please could the authors clarify this within the text? 	<p>Thank you for this question. To clarify this, we have extended this section in the protocol (p. 5):</p> <p>“- observational studies analyzing the longitudinal association between <u>anxiety/depressive symptoms or disorder and quality of life across all age categories (to analyze the association with quality of life according to severity of anxiety/depressive symptoms as well as for those who fulfill the criteria for a clinical diagnosis)</u>”</p>
<ul style="list-style-type: none"> • In the third point, please could the authors clarify if they will be including those studies who measure symptoms using self-report measures such as the PHQ-9, or will it be only measures administered by a clinician. 	<p>Thank you for this comment. Following your suggestion, we have described the inclusion of the measures in more detail in the Methods and Analysis section (Inclusion criteria, p. 5f):</p> <p>“- studies applying an appropriate measure for anxiety and depression (e.g. psychiatric diagnosis according to criteria of the International Classification of Diseases (ICD), the Diagnostic and Statistical Manual of Mental Disorders (DSM), or using a valid, <u>self-report screening questionnaire, such as the depression scale from the Patient Health Questionnaire (PHQ-9) or the Hospital Anxiety and Depression Scales (HADS)</u>)”</p>

<p>Exclusion criteria:</p> <ul style="list-style-type: none"> • How will assessment of anxiety and/or depression that are not appropriate be defined? 	<p>Thank you for this question. We have described this in more detail (p. 6):</p> <p>“- assessment of anxiety, depression or quality of life not appropriate (e.g. for anxiety/depression not according to ICD/DSM criteria or no valid, self-report screening questionnaire)”</p>
<p>Discussion</p> <ul style="list-style-type: none"> • The authors make suggestions as to the kind of questions this review could answer, e.g. are specific quality of life domains particularly affected by specific depression symptoms? I would ask the authors to expand on this, and in relation to the relevant literature, to explain why this is important. How might it help us to develop, improve or target treatments for people with anxiety or depression, or indeed to improve quality of life? 	<p>Thank you for your questions. Following your suggestions, we have expanded the Discussion section (p. 9f):</p> <p>“Beyond providing an overview of evidence on the association between anxiety, depression and quality of life, and thus highlighting possible gaps in current research, there are a range of questions that could possibly be answered by this review. For example, our study could ascertain whether specific quality of life domains are particularly affected by specific disorders or symptoms across studies over time. Comer et al.⁹ found in a cross-sectional analysis in the general population, that different anxiety disorders were associated with varying decrements in different health-related quality of life domains. If this type of finding were observed over several longitudinal studies in the course of our systematic review, our study could also inform clinical research. Identification of the specific domains impacted by anxiety/depression, for example, could act as the starting point for the analysis of treatment goals or the analysis of the effectiveness of interventions aiming to improve quality of life. However, as intervention studies, such as randomized controlled trials, will not be included in our review, additional research would need to be undertaken to build on this further.”</p>
	<p>Again, thank you for your helpful comments. They help us to improve the quality of the manuscript.</p>

Reviewer 1 - Mythily Subramaniam	
It is a straightforward well-designed review. I have no comments on the protocol.	Thank you for your comment. We appreciate you taking the time and evaluating our study protocol.

VERSION 2 – REVIEW

REVIEWER	Dr Amy Blakemore University of Manchester, United Kingdom
REVIEW RETURNED	11-Jan-2019
GENERAL COMMENTS	Thank you for your responses to my comments. I am happy with the changes made and look forward to seeing your review.