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Association between anxiety, depression and quality of life: study protocol for a systematic review of evidence from longitudinal studies

Johanna Katharina Hohls, Hans-Helmut König, Eleanor Quirke, André Hajek

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Department of Health Economics and Health Services Research, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Correspondence to
Johanna Katharina Hohls;
j.hohls@uke.de

ABSTRACT

Introduction Evidence from individual longitudinal studies suggests that anxiety and depression may impact quality of life. However, systematic reviews synthesising current evidence have mainly focused on specific samples. Thus, the aim of this study is to synthesise evidence from longitudinal studies on the association between anxiety, depression and quality of life in a systematic review.

Methods and analysis A systematic review of evidence from longitudinal studies analysing the association between anxiety, depression and quality of life will be conducted, taking into account the current Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. Several electronic databases from relevant fields of research (PubMed, PsycINFO, PSYNDEX, EconLit, NHS EED) will be searched in September 2018 using defined search terms, with an updated search planned. Moreover, reference lists of included studies will be searched manually. Study eligibility will be appraised in a two-step process against pre-defined inclusion/exclusion criteria. Primarily, information on study design and assessment, statistical methods, participant characteristics as well as results regarding our research question will be extracted. The quality of included studies will be assessed using an appropriate tool. Study selection, data extraction and assessment of study quality will be performed by two reviewers. Disagreements will be resolved through discussion or by inclusion of a third party. Results will be synthesised narratively in text and tables. Depending on the number and heterogeneity of the studies included, a meta-analysis will be performed.

Ethics and dissemination As no primary data will be collected, approval from an ethics committee is not required. Results will be disseminated through conference presentations and publication in a peer-reviewed, scientific journal.

PROSPERO registration number CRD42018108008.

Strengths and limitations of the study

- To our knowledge, this is the first systematic review synthesising and critically assessing evidence from longitudinal, observational studies on the association between anxiety, depression and quality of life, focusing on samples without specific disorders.
- The study's focus on longitudinal evidence from observational studies should strengthen the conclusions drawn from our results and may facilitate causal inference across studies.
- Two independent reviewers are involved in the processes of study selection, data extraction and quality assessment.
- Due to the possible heterogeneity between studies, conducting a meta-analysis may not be appropriate.

INTRODUCTION

Anxiety and depression are among the most prevalent mental health problems across all age categories.[1–3] Both disorders have been associated with a considerable economic burden,[4–6] as well as adverse implications for the affected individual, such as increased risk for physical comorbidities, for example, cardiovascular disease.[7 8] Moreover, individual cross-sectional and longitudinal studies have suggested that anxiety and depression are related to a reduced quality of life in samples with and without specific diseases.[9–12]

There are several systematic reviews that have synthesised evidence on the association between anxiety and/or depression and quality of life previously. However, existing reviews are limited with respect to the samples analysed. For example, some reviews have focused on certain age categories,[13 14] or samples with specific diseases.[15 16] Specifically, Creighton *et al*[13] as well as Sivertsen *et al*[14] have analysed the association between anxiety or depression and quality of life in older people. Regarding reviews of disease-specific samples, Blakemore *et al*[15] have analysed 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.

To the best of our knowledge, there are no recent systematic reviews specifically analysing 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 analysing samples without specific diseases means the effects of interventions or specific illnesses will be limited in terms of impact on this association.

Thus, to add to the present literature, we aim to synthesise current longitudinal, observational studies on the association between anxiety, depression and quality of life, as well as assess the quality of existing studies.

Objective

This paper provides the protocol for a systematic review that aims to synthesise and critically appraise longitudinal, observational studies assessing the association between anxiety, depression and quality of life. The studies of interest are those analysing participants from all age categories with anxiety/depression, as well as those that include samples without a specific disease or receiving a specific intervention, applying valid measures for the main variables.

METHODS AND ANALYSIS

This systematic review protocol was developed taking into account the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols guidelines.[17] The study is registered with the International Prospective Register of Systematic Reviews (PROSPERO, registration number: CRD42018108008, under https://www.crd.york.ac.uk/PROSPERO/).

Eligibility criteria

Studies will be assessed for inclusion according to the inclusion/exclusion criteria outlined below. Before the final eligibility criteria are applied, they will be tested against a sample of 100 titles/abstracts and refined should further clarification be required.

Inclusion criteria

- Observational studies analysing the longitudinal association between anxiety/depressive symptoms or disorder and quality of life across all age categories (to analyse the association with quality of life according to severity of anxiety/depressive symptoms as well as for those who fulfil the criteria for a clinical diagnosis).
- Studies analysing samples with anxiety/depression or samples without a specific disease (other than anxiety/depression).
- Studies applying an appropriate measure for anxiety and depression (eg, 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 self-report screening questionnaire, such as the depression scale from the Patient Health Questionnaire [PHQ-9] or the Hospital Anxiety and Depression Scales [HADS]).
- Studies applying an appropriate measure for quality of life (eg, the 36-item Short Form Health Survey).
- Publications in German or English language, published in peer-reviewed journals.

Exclusion criteria

- Studies not focusing on the association between anxiety or depression and quality of life over time.
- Studies only analysing disease-specific samples (meaning conditions other than anxiety/depression) or samples receiving specific interventions.
- Study design other than observational.
- Assessment of anxiety, depression or quality of life not appropriate (eg, for anxiety/depression not according to ICD/DSM criteria or no valid, self-report screening questionnaire).
- Studies not published in peer-reviewed journal or in language other than German or English.
- Information sources and search strategy.

As quality of life is an outcome analysed in several fields of research, such as medicine, psychology and health economics, several databases from multiple scientific fields (PubMed, PsycINFO, PSYNDEX, EconLit, NHS EED) will be searched electronically in September 2018. It is planned to update the search prior to the submission of the final review to ensure that it contains the most recent evidence. The electronic database search will be conducted using predefined search terms, including *anxiety disorder*, *depressive disorder*, *anxi**, *depress** (truncated to also capture studies using terms such as *anxious* or *depressed*), *quality of life*, and *longitudinal study*. The PubMed search strategy is provided in table 1. There will be no restriction on location or time of the publication. Where possible, search terms will be entered as Medical Subject Headings (MeSH), or keywords in the title/abstract. As needed, the search will be modified according to the specific requirements of each database.

Additionally, the reviewers will search the reference lists of included articles for further relevant articles.

Data management

All records retrieved in the database search will be imported into the literature management software EndNote to facilitate the management of the references.

Table 1 PubMed search strategy

Number	Term entered
#1	anxi*[Title/Abstract] OR depress*[Title/Abstract]
#2	Anxiety Disorder[MeSH]
#3	Depressive Disorder[MeSH]
#4	#1 OR #2 OR #3
#5	Quality of Life[MeSH]
#6	Longitudinal studies[MeSH]
#7	#4 AND #5 AND #6

Should it be possible to conduct a meta-analysis, Stata (StataCorp, College Station, Texas) will be used for the quantitative analysis.

Study selection process

All studies obtained in the electronic and manual search will be assessed for inclusion/exclusion in a two-step process ([1] title/abstract screening and [2] screening of full texts). Before the final selection criteria are applied, the criteria will be pre-tested against a sample of 100 titles/abstracts and, if necessary, refined afterwards. The study selection process will be conducted independently by two reviewers (JKH and EQ) using the previously defined and refined selection criteria. Disagreements between the two reviewers will be resolved through discussion or by inclusion of a third party (AH).

Data collection process and data items

The data extraction process will involve two reviewers as well (JKH and EQ). One reviewer will extract relevant data items from the studies in standardised form, and the second reviewer will cross-check the extracted data. Again, in case of disagreements consensus will be reached through discussion or by inclusion of a third party (AH). In cases where relevant data cannot be extracted or require clarification, the authors of the study will be contacted.

Data items to be extracted from the original studies include information on study design, definition and assessment of the main variables of interest, sample characteristics, statistical methods, as well as results regarding the longitudinal association between anxiety, depression and quality of life.

Assessment of study quality/risk of bias

The quality of the individual studies will be assessed using a quality assessment tool appropriate for longitudinal, observational studies, such as the Newcastle-Ottawa Scale[18] or the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.[19] For example, the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies comprises 14 quality criteria to assess the internal validity of a study, through consideration of potential forms of bias.

Each study included in the final synthesis will be appraised for study quality by two reviewers (JKH and EQ) independently. Should there be disagreement, consensus will be reached through discussion or by inclusion of a third party (AH). Results from the quality assessment will be included in the study synthesis.

Data synthesis

Following its completion, the study selection process will be illustrated by means of a PRIMSA flowchart. The results from data extraction and quality assessment processes will be synthesised qualitatively in text and tables. If possible, results will be categorised according to specific disorder/symptoms analysed in the studies (anxiety/depression) or quality of life domain/measure analysed.

Egger *et al*[20] advise caution when conducting meta-analyses to pool results specifically from observational studies, as this may result in precise but incorrect estimates, due to confounding and bias within the included studies. However, recommendations on conducting a meta-analysis on data from observational studies vary, and to date there is no agreed on, comprehensive methodological outline for such analyses. For the most part, current recommendations centre around whether to, and how one should, pool the data.[21] Whether a meta-analysis is performed (in view of the number of studies included as well as their heterogeneity) in our study, and how the analysis is conducted (ie, method used for the standardisation of the outcome measure as well as statistical methods for calculation of the overall effect), will be discussed in the final systematic review, with reference to current recommendations.

Thus, only if appropriate, a meta-analysis will be performed to obtain a pooled, quantitative estimate. Moreover, if a meta-analysis can be performed and a sufficient number of studies can be included in the synthesis, we plan to perform subgroup analyses (eg, by gender, age) or sensitivity analyses (eg, excluding studies with lower quality/higher risk of bias) to explore possible sources of heterogeneity as well as check the robustness of the results.

Patient and public involvement statement

The present review protocol did not involve individual patients or public agencies.

DISCUSSION

This systematic review will provide an overview of evidence from longitudinal, observational studies on the association between anxiety, depression and quality of life across all age categories. Moreover, the quality of included studies will be rated. If possible, data will be pooled quantitatively by means of a meta-analysis, and subgroup or sensitivity analyses will be performed.

As stated in the introduction, this review adds to the present literature by additionally including samples without a specific disease (eg, general population samples) and not focusing on a specific age category.

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 randomised controlled trials, will not be included in our review, additional research would need to be undertaken to build on this further. In addition, if studies show different results, possible sources of heterogeneity could be assessed across studies. Heterogeneity might be due to study design and methodology as well as due to sample-specific characteristics. Moreover, subgroups, such as age group or gender, could be analysed.

Finally, longitudinal evidence has several advantages over cross-sectional data. For example, trajectories over time can be analysed within the same individuals. Moreover, applying appropriate methods in longitudinal analysis can take intraindividual heterogeneity into account, which is a key point in the analysis of quality of life.[22] Thus, as it draws from longitudinal evidence across several studies, our systematic review provides the basis for stronger, more definitive conclusions that one would not be able to draw from a single study.

Strengths and limitations

To our knowledge, this is the first study aiming to synthesise and critically appraise evidence from longitudinal, observational studies analysing the association between anxiety, depression and quality of life across all age categories. Focusing on observational studies and samples without a specific illness (other than anxiety or depression), should limit the influence of a specific intervention, treatment or disease on the association between anxiety, depression and quality of life. In turn, this should strengthen the conclusion we can draw from our results. Moreover, another strength is the inclusion of two independent reviewers in the processes of study selection, data extraction and quality assessment. One limitation is that conducting a meta-analysis may not be appropriate due to heterogeneity of existing studies. Thus, it may not be possible to obtain a pooled estimate.

Ethics and dissemination

No primary data will be collected. Thus,approval by an ethics committee is not required. The results from the systematic review are planned to be published in a peer-reviewed journal and presented at scientific conferences.

Contributors The study concept was developed by JKH, H-HK and AH. The manuscript of the protocol was drafted by JKH and critically revised by H-HK, EQ and AH. The search strategy was developed by JKH and AH. Study selection, data extraction and quality assessment will be performed by JKH and EQ, with AH as a third party in case of disagreements. All authors have approved the final version of the manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval As no primary data will be collected, approval by an ethics committee is not required. The results from the systematic review are planned to be published in a peer-reviewed journal and presented at scientific conferences.

Provenance and peer review Not commissioned; externally peer reviewed.

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