STUDY PROTOCOL

REVISED Barriers and enablers to screening and diagnosing depression and diabetes distress in people with type 2 diabetes mellitus; protocol of a qualitative evidence synthesis [version 2; peer review: 1 approved, 1 approved with reservations]

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Abstract

Background: Depression and diabetes distress are common in people with type 2 diabetes (T2DM). These conditions are independently associated with poorer T2DM outcomes and increased healthcare utilisation and costs. Questions remain regarding the most appropriate ways of initially detecting depression and diabetes distress in this group. Diabetes guidelines recommend depression screening in primary care for people with T2DM but their implementation in practice is suboptimal. As health care professionals influence detection practices, their perceptions and experiences of these guidelines can improve understanding of aspects of the guidelines that work, and those which are more difficult to implement in practice. This study describes the protocol for a qualitative evidence synthesis of primary care health professionals' perceived barriers and enablers to screen for and diagnose depression and diabetes distress in people with T2DM.

Methods and analysis: Primary qualitative studies will be identified using a systematic search of electronic databases and supplementary searching. We selected 'best-fit framework synthesis' as the approach to synthesise primary data using the RETREAT (Review question-Epistemology-Time/Timescale-Resources-Expertise-Audience and purpose-Type of Data) framework. Quality appraisal of primary studies and confidence in the overall review findings will be determined using the CASP (Critical Appraisal Skills Programme) and

Open Peer Review

Reviewer Status ✔ ?

	Invited Reviewers	
	1	**2**
version 3 (revision) 30 Sep 2020		
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version 1 25 Oct 2019		

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Any reports and responses or comments on the

the GRADE-CERQual (Grading of Recommendations Assessment, Development, and Evaluation Confidence in the Evidence from Reviews of Qualitative research), respectively.
Discussion: The planned review will provide the first, single point of reference of the available synthesised qualitative evidence on this topic. It will apply recommended approaches to ensure rigor and robustness of study and contribute meaningfully to understanding of how depression and diabetes distress can be initially detected in people with T2DM. This protocol is registered with the International Prospective Register of Systematic Reviews (PROSPERO) [registration number: CRD42019145483].

Keywords
Systematic review, Qualitative evidence synthesis, Qualitative research, Depression, Diabetes distress, Diabetes, Screening, Primary care, Guideline adherence

article can be found at the end of the article.

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REVISED **Amendments from Version 1**

Since submitting version 1, our protocol has been processed by and registered with the International Prospective Register of Systematic Reviews (PROSPERO). Version 2 of our manuscript includes the PROSPERO registration number.

Version 1 of our manuscript specified that we will use the CLUSTER (Citations, Lead authors, Theories, Early examples, Related projects) approach to conduct supplementary searching. In version 2, we have specified that supplementary searching will be informed by the CLUSTER approach, as this is a more accurate description of our intended use of this supplementary search strategy.

Any further responses from the reviewers can be found at the end of the article

Introduction

Depression and diabetes distress are independently associated with adverse outcomes among people with type 2 diabetes (T2DM)[1–5], as well as increased costs to health systems[6–8]. Diabetes distress refers specifically to diabetes-related concerns about self-management, perceptions of support, emotional burden, and access to quality health care[9,10] whereas depression is an affective disorder characterised by depressed mood and anhedonia[11,12]. Both are highly prevalent in the T2DM population; diabetes distress affects approximately 36% of people with T2DM at any one time[13] and depression is estimated as being twice as prevalent in people with T2DM as in the general population[14]. Yet, depression is substantially undiagnosed in people with T2DM[15,16]. For example, national survey data from the United States (US) indicates that of people with type 1 and type 2 diabetes and depression, 45% had never received a depression diagnosis from a general physician[15]. Less is known about the prevalence of undiagnosed diabetes distress in the T2DM population. However, analysis of observational data of 112 outpatients with diabetes identified that symptoms frequently went unrecorded and health professionals often failed to detect depression and diabetes distress[16].

National and international diabetes guidelines recommend routine use of clinical questioning or validated depression and diabetes distress screening tools for initial detection of depression and diabetes distress among people with T2DM in primary care settings[17–20]. Although depression and diabetes distress screening is an effective way to accurately identify symptoms in people with T2DM compared to no screening strategy[21–23], implementation of screening guidelines in routine T2DM care is challenging[24–27]. In the UK, GPs receive financial reimbursement to administer a depression screening protocol to people with at least one chronic condition, including T2DM[28]. However, in primary care patients with at least one chronic condition (coronary heart disease, diabetes and previous stroke) in Scotland, depression screening was administered to less than one third (31%) of patients[24]. In a primary care practice in England, only 72% of diabetes patients received the depression screening protocol, and, less than half of those identified as having possible depression were administered the full symptom measure[26].

Implementation of depression screening guidelines in routine T2DM care may be influenced by a lack of consensus around how and when to screen. For example, there is discrepancy around the specific psychosocial difficulties that should be screened for, when screening should be administered and how screening should be administered[12–15] (*Extended data:* Supplementary File 1). Implementation may also be influenced by patient[29] and health care professional specific factors[27,30–32]. Primary care health professionals report common barriers and enablers to screening and diagnosing depression in T2DM as in general populations; mental health stigma, time constraints[27,30–32], patient-clinician relationship[30–32], and as people with T2DM; normalising depressive symptoms as part of chronic disease[29,31,33], symptom overlap, and mental health stigma[29,31–33]. Previous studies have also identified that primary care health professionals experience unique barriers and enablers to screening and diagnosing depression and diabetes distress in the T2DM population. These include; perceptions of their role and responsibilities[31,32], the perceived value of screening or clinical questioning in the T2DM population[31], and integrating screening protocols into T2DM review visits[27].

Qualitative evidence syntheses of patient and health professional factors consolidate findings from multiple primary studies carried out in different contexts in order to; (1) identify the full spectrum of factors which support and hamper guideline implementation, and (2) highlight gaps in knowledge, and areas of saturation where no further primary research is required[34]. The perspectives of people with T2DM regarding their experiences of depression screening and diagnoses have previously been synthesised[29,33], enabling identification of patient factors influencing detection and diagnosis. While understanding these views is crucial, health professionals are the primary implementers of T2DM depression screening and diagnosis guidelines. Therefore, an in-depth overview of the existing qualitative evidence that captures the perspectives of those responsible for screening and diagnosing depression among people with T2DM is also of paramount importance. Although a previous qualitative evidence synthesis explored general physicians' perceived barriers and enablers to diagnosing depression in primary care in general[30], this has not been previously explored specifically in relation to a T2DM population. Therefore, a qualitative evidence synthesis of the primary care health professional barriers and enablers to screening and diagnosing depression and diabetes distress in people with T2DM can address an important gap in the T2DM literature.

Protocol

This review will synthesise the available qualitative evidence in the literature that explores primary care health professionals' views and experiences of screening and diagnosing depression and diabetes distress in people with T2DM.

Eligibility criteria

Setting. Studies conducted in primary care settings and outpatient diabetes settings, in any country, will be eligible for inclusion.

Perspective. Eligible perspectives are those of any health care professional(s) who screen and diagnose people with T2DM in a primary care setting or in a diabetes outpatient setting. This may include GPs, Practice Nurses, Diabetes Nurse Specialists and Psychologists. Studies including the patient and health professional perspective will be included if the health care professional perspective can be extracted separately from the patient results. Studies that only present the perspectives of people with T2DM or their families will be excluded.

Phenomenon of interest. The phenomenon of interest is the process of screening and/or diagnosing depression and/or diabetes distress in people with T2DM. Studies only focused on the management of people with T2DM and depression and/or diabetes distress will be excluded. Studies about screening, diagnosing and managing people with T2DM and depression and/or diabetes distress will only be included if findings related to screening and/or diagnosis can be extracted separately from results related to management.

Comparison. If results are reported by different types of health professionals, we will compare health professional perspectives.

Evaluation. We will use qualitative evidence to better understand the strategies used by primary care health professionals to screen and diagnose depression and diabetes distress in people with T2DM and to identify primary care health care professional barriers and enablers associated with screening diagnosing depression and diabetes distress in this population.

Studies. Primary research studies that employ qualitative or mixed-methods will be eligible for inclusion. Studies must have used qualitative data collection (e.g. semi-structured interviews, observation) and analyses methods (e.g. thematic analysis, grounded theory). Studies will be peer reviewed journal articles or non-peer reviewed items including unpublished research articles and theses. Non-English language studies, literature reviews and quantitative research studies will not be eligible for inclusion. Multiple-method and mixed-method studies will only be included if qualitative results can be extracted separately from quantitative results. Where the full text is unavailable, we will contact authors in an effort to obtain the full text. If it is not possible to obtain full texts, these studies will be excluded.

Systematic identification of primary research studies

Search strategy. This review will use a combination of systematic searching of the literature using electronic databases and supplementary searching. The following databases will be searched: CINAHL, EMBASE, MEDLINE, PsycINFO, Academic Search Complete, Scopus. These databases and the search terms were selected in consultation with an expert librarian to source peer-reviewed articles across medicine, nursing, gerontology, health services research and psychology disciplines and to identify studies focusing on health professionals' accounts of screening and/or diagnosing depression and/or diabetes distress in people with T2DM. The search will be conducted in all databases in one day by the lead author. The search strategy for MEDLINE is shown in *Extended data:* Supplementary File 2. Certain search terms are truncated, for example depress* or recogni*, to ensure all spellings are captured. Terms will be adapted for individual databases as needed, for example, MeSH terms will be used for MEDLINE. The use of title and abstract will depend on the individual databases. There will be no restrictions on the years searched in order to retrieve relevant studies from the earliest date possible.

Within QES, the approach to searching should be informed by the overarching aim of the synthesis and the approach to analysis[35]. We initially selected an "exhaustive" as opposed to a purposive approach to synthesis fitting with our preliminarily selected best fit framework analysis (see data synthesis for details)[35]. Supplementary searching will be informed by the CLUSTER (Citations, Lead authors, Unpublished materials, Scholar searches, Theories, Early examples, Related projects) approach[36]. The approach employs techniques relevant to different types of systematic reviews in a systematic manner and offers a systematic approach to supplementary searching[36].

Study screening. All references will be imported into Endnote and duplicates removed. The lead author (N.M.G) will screen all titles and abstracts independently using Rayyan QCRI software[37]. Two reviewers will screen 50% of titles and abstracts each, against the eligibility criteria. When there is no abstract, or it is not possible to determine whether to include an article or not, the full text of the article will be retrieved. The lead author will screen all full-text articles, and two other reviewers will each independently screen 50% of the full text articles against the eligibility criteria. Disagreement between reviewers will be discussed among the reviewers to achieve consensus. If necessary, we will consult with the broader review team until consensus is reached. Results of searching, screening and included studies will be reported using the PRISMA flowchart[38].

Data extraction. Data will be extracted using a standardised data extraction form by the lead reviewer. Extracted data for each study will include: the first author, publication year, journal, participant group (type of health professional), setting (country, rural/urban, type of health facility), research methods (method of data collection and analysis, framework used) and outcomes (reported barriers and enablers and related themes). Data will include verbatim quotes from participants and findings reported by the study authors in the results/findings section of included studies[39] because best-fit framework synthesis allows for the integration of primary and secondary data[40]. We will pilot the data extraction form on at least three studies

identified from the list of included studies. The lead author will extract data from included papers and two other reviewers will each independently crosscheck 50% of extracted data for consistency and accuracy to minimize potential bias during extraction. Full text articles and extracted data will be imported and managed within QSR NVivo 10 for data synthesis.

Assessment of quality of included studies

Quality of included studies will be assessed using the Critical Appraisal Skills Programme (CASP) for qualitative research[41,42]. Assessment of study quality will not be a criteria to exclude studies that otherwise met the inclusion criteria, but used to provide insights into the methods used for data collection and analysis[43].

Data synthesis

The RETREAT (Review question–Epistemology–Time/Timescale–Resources–Expertise–Audience and purpose–Type of Data) framework[44] was used to initially select the most appropriate analytical approach. The RETREAT Framework was developed in response to the rapidly growing number of approaches to undertaking qualitative evidence synthesis and to support researchers in selecting appropriate approaches to synthesis. Following initial completion of the RETREAT framework (*Extended data:* Supplementary File 3), we plan to undertake a 'best-fit framework synthesis'[45]. Best-fit framework synthesis was selected because it offers a pragmatic way to develop intervention theory, is a relatively time efficient method and is suited to an aggregative, as opposed to an interpretative approach to analysis[45,46]. However, as the number of studies identified and the heterogeneity of data within identified studies can influence the most appropriate analytic method, we will revisit the RETREAT framework once eligible studies are identified and ensure that best-fit framework synthesis is still appropriate[47].

The data synthesis process will be conducted within QSR NVivo 10 to ensure transparency and clarity in the synthesis process[48]. The lead author will conduct all stages of synthesis from initial coding to interpretation. Two other reviewers will independently analyse a random sample of the data at each stage of the analytic process to enhance consistency of the coding framework and the logic of interpretations. All members of the review team will review and discuss each stage of the synthesis. This will facilitate consensus on the review findings using an iterative approach.

Confidence in the findings

Confidence in the overall review findings will be determined using the GRADE-CERQual approach given its application to support decision making based on qualitative evidence[49] and the availability of resources to support its use[47,50–53]. Application of the CASP forms the methodological limitations component of the GRADE-CERQual assessment. GRADE-CERQual also assesses the relevance of individual review findings (i.e. the extent to which the evidence from the primary studies is applicable to the review question), the coherence of individual review findings (i.e. how well patterns reported are grounded in data from the included primary studies), and the adequacy of the overall review findings (i.e. the richness and quantity of data supporting a review finding). The lead author will carry out each step of the GRADE-CERQual process. Two other reviewers will check for relevance, coherence and adequacy of individual review findings from a selection of data (e.g. from one primary study each). The three reviewers will discuss each phase of the GRADE-CERQual process, and any disagreements will be resolved through discussion and consensus.

Dissemination of findings

Findings will be submitted to a peer-reviewed journal for publication. The findings will also be used to inform the design of an intervention to support screening and diagnosis of depression and diabetes distress symptoms in people with T2DM attending primary care in Ireland. The findings will be shared with identified stakeholders and at academic conferences.

Study status

Database searching for primary studies has been completed.

Discussion

This article describes the protocol of a systematic review to synthesise the available qualitative evidence on primary care health professionals' views and experiences of screening and diagnosing depression and diabetes distress in people with T2DM. The final review results will provide a single point of reference, which can be utilised by key stakeholders in different ways. For instance, the findings may inform; (1) clinicians on ways to adopt or adapt depression and diabetes distress screening practices, and (2) researchers in the design of evidence-informed healthcare interventions to improve processes for detection and diagnosis of depression and diabetes distress in this population[34,54].

The planned review has a number of strengths and limitations. We will apply recommended approaches to ensure rigor and robustness of the study. Specifically, we will apply the GRADE-CERQual approach to appraise the quality of included studies and enhance the usability of the overall findings, and we have applied the RETREAT framework to select the most appropriate approach to synthesis. However, review findings will be limited by what is reported in the included primary studies as we will not seek original data from the primary studies included. The planned review will not capture challenges associated with screening and diagnosing other pertinent psychological difficulties experienced by people with T2DM (e.g. disordered eating, dementia)[55,56].

Diagnosing depression in primary care populations is challenging in general[30]. Supporting primary care health professions to detect depression and diabetes distress in people with T2DM is an important step to help address the high prevalence of depression and diabetes distress in this population[13,14]. This review will identify those aspects of the available best practice guidelines that work, and those which are more difficult to implement in practice. Ultimately, the findings will improve understanding of how depression and diabetes distress can be appropriately identified in people with T2DM in primary care settings[34].

Reporting guidelines

This paper is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses-Protocol (PRISMA-P)[57]. The review will be reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[58] and the Enhancing Transparency in Reporting the Synthesis of Qualitative (ENTREQ) Research guidelines for systematic reviews[59].

We submitted our record to the International Prospective Register of Systematic Reviews (PROSPERO) on August 9th 2019 [PROSPERO ID number 145483]. Due to significant and unexpected demand for the PROSPERO service, our record was processed and registered on November 11th 2019 [PROSPERO registration number: CRD42019145483].

Data availability

Underlying data

No data is associated with this article.

Extended data

Open Science Framework: Barriers and enablers to screening and diagnosing depression and diabetes distress in people with type 2 diabetes mellitus; protocol of a qualitative evidence synthesis, https://doi.org/10.17605/OSF.IO/VF3H2[60].

This project contains the following extended data:

- Supplementary File 1. Summary of depression and diabetes distress screening guidelines for adults with T2DM.
- Supplementary File 2. Search strategy for Medline.
- Supplementary File 3. Use of the RETREAT framework to inform selection of the best-fit framework approach to synthesis.

Reporting guidelines

Open Science Framework: PRISMA-P checklist for Barriers and enablers to screening and diagnosing depression and diabetes distress in people with type 2 diabetes mellitus; protocol of a qualitative evidence synthesis, https://doi.org/10.17605/OSF.IO/VF3H2[60].

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http://www.doi.org/10.17605/OSF.IO/VF3H2

Open Peer Review

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Version 2

Reviewer Report 20 April 2020

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?

Andreas Schmitt

Diabetes Center Mergentheim, Research Institute of the Diabetes Academy, Bad Mergentheim, Germany

Reviewer's report: The article describes the protocol of a qualitative evidence synthesis regarding barriers and facilitators to screening and diagnosing depression and/or diabetes distress (DD) in T2DM according to HCPs' reports. The article is well structured and written, the purpose of the research is reasonable and the planned procedures are valid and follow current guidelines.

Major revision points:

1. The authors underline the need for screening depression/DD in diabetes with evidence suggesting worse health outcomes in affected persons. However, the cited evidence (1–5) does not go beyond cross-sectional associations i.e. does not support depression or DD as predictors of adverse health outcomes. Instead, associations such as depression and HbA1c (likely a bidirectional relationship) or depression and diabetes complications (where depression might be considered to be the consequence rather than antecedence of complications) are referenced. I consider this a poor evidence base for supporting a need for screening, and the existing evidence base is far more conclusive including prospective studies regarding the outcomes HbA1c, incident complications, mortality etc. I would expect a more up-to-date evidence base using studies supporting mechanistic conclusions.

2. The authors claim that "Depression and diabetes distress are independently associated with adverse outcomes among people with type 2 diabetes" (Introduction, first sentence), but the referenced evidence does not support such statement. In fact, four of five cited studies regard cross-sectional associations between either depression alone or DD alone and health outcomes; thus appraisal of independent associations is not possible. Although one of the studies (3) does indeed include both conditions, the findings do not suggest independent associations for depression and DD with the outcome HbA1c (which is a proxy for longer-term health outcomes such as vascular complications as well as acute metabolic complications), instead only DD was associated with HbA1c. On the other hand, the question whether depression or diabetes distress or both are associated with core

outcomes in diabetes is highly relevant, and a number of studies (mostly cross-sectional) have indeed addressed this issue. As there is evidence potentially supporting the authors' claim, I would suggest they either add relevant findings or discount the statement to "both have been associated with adverse outcomes in independent studies" or similar.

3. The authors' precise focus on T2DM is appreciated, and I am aware of the clearly higher prevalence compared to T1DM. However, depression prevalence is similarly increased in T1DM, and DD is also highly prevalent in this group. Accordingly, I do not see why the authors would need to exclude studies regarding T1DM or mixed samples straightaway, while guidelines recommending psychosocial screening and diagnostic refer to T2DM and T1DM, and HCPs may have to deal with both groups so interview reports regarding screening may refer to both diabetes types. I agree that specific inferences and recommendations regarding T2DM or T1DM or both are required, but I cannot see why you should conduct a different study addressing this issue in those with T1DM if one literature search might spot light into both fields. Furthermore, exclusion of T1DM might result in exclusion of all mixed sample studies where results for these groups were not presented separately, despite potential valuable insights to be gained from the HCPs' reports. I suggest considering inclusion of T1DM-related studies. Please also note that the available evidence base from which to include for this systematic review may be limited (Schumann *et al*.'s study of physicians' experiences with depression detection in primary care included only 13 studies, so I assume the evidence base specifically for diabetes may be small), thus inclusion of all studies regarding diabetes rather than T2DM only appears reasonable.

4. The literature is searched without restrictions on the year of publication. However, health care interventions, perspectives, reimbursement and consideration of mental health in primary care have changed significantly across the last decades. Newer evidence will therefore probably be of higher relevance/greater interest. A rationale for not excluding potentially outdated studies might be useful.

5. The authors plan to include non-peer reviewed items such as unpublished research articles and theses. A rationale for including potential 'lower quality' data would be helpful. Did the authors consider weighting such items somehow differently in order to avoid potential bias when comparing their results to more rigorously evaluated peer-review publications?

Minor points:

- Is the number of relevant studies large enough to suggest a systematic review in this field? How many studies of potential interest did the authors identify actually?

- The authors state that "Where the full text is unavailable, we will contact authors in an effort to obtain the full text. If it is not possible to obtain full texts, these studies will be excluded." I assume unavailability implies that buying or renting the article would not be possible, correct? Otherwise, I would expect the authors purchase the relevant literature to avoid exclusion of potentially relevant evidence.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Behavioural diabetes research.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 17 Sep 2020

Niamh McGrath, University College Cork, Cork, Ireland

Response to viewer comment 1 (major): Thank you. We have replaced references 1-5 to include papers demonstrating prospective associations between diabetes distress and adverse type 2 diabetes outcomes and depression and adverse type 2 diabetes outcomes: (p.3, Introduction)
1: Nouwen A, Adriaanse MC, van Dam K, Iversen MM, Viechtbauer W, Peyrot M, Caramlau I, Kokoszka A, Kanc K, de Groot M, Nefs G. Longitudinal associations between depression and diabetes complications: a systematic review and meta-analysis. Diabetic Medicine. 2019 Dec;36(12):1562-72.
2: Naicker K, Johnson JA, Skogen JC, Manuel D, Øverland S, Sivertsen B, Colman I. Type 2 diabetes and comorbid symptoms of depression and anxiety: longitudinal associations with mortality risk. Diabetes care. 2017 Mar 1;40(3):352-8.
3: Hsu HC, Lee YJ, Wang RH. Influencing Pathways to Quality of Life and HbA1c in Patients With Diabetes: A Longitudinal Study That Inform Evidence-Based Practice. Worldviews on Evidence-Based Nursing. 2018 Apr;15(2):104-12.
4: Gonzalez JS, Kane NS, Binko DH, Shapira A, Hoogendoorn CJ. Tangled up in blue: unravelling the links between emotional distress and treatment adherence in type 2 diabetes. Diabetes care. 2016 Dec 1;39(12):2182-9.
5: Aikens JE. Prospective associations between emotional distress and poor outcomes in type 2 diabetes. Diabetes care. 2012 Dec 1;35(12):2472-8.

Response to reviewer comment 2 (major): Author response 2: Thank you. As suggested, we have rephrased the first sentence in the introduction (p.3, Introduction) to read “Depression and diabetes distress have both been associated with adverse outcomes among people with type 2 diabetes”. We have also replaced references 1-5 with references demonstrating causal associations between:
(A) depression and onset of microvascular and macrovascular complications:
Ref 1: Nouwen A, Adriaanse MC, van Dam K, Iversen MM, Viechtbauer W, Peyrot M, Caramlau I, Kokoszka A, Kanc K, de Groot M, Nefs G. Longitudinal associations between

depression and diabetes complications: a systematic review and meta-analysis. Diabetic Medicine. 2019 Dec;36(12):1562-72.
(B) depression among people with type 2 diabetes and all-cause mortality:
Ref 2: Naicker K, Johnson JA, Skogen JC, Manuel D, Øverland S, Sivertsen B, Colman I. Type 2 diabetes and comorbid symptoms of depression and anxiety: longitudinal associations with mortality risk. Diabetes care. 2017 Mar 1;40(3):352-8..
(C) diabetes distress and diabetes self-management behaviours and glycaemic control:
Ref 3: Hsu HC, Lee YJ, Wang RH. Influencing Pathways to Quality of Life and HbA1c in Patients With Diabetes: A Longitudinal Study That Inform Evidence-Based Practice. Worldviews on Evidence-Based Nursing. 2018 Apr;15(2):104-12.
Ref 4: Gonzalez JS, Kane NS, Binko DH, Shapira A, Hoogendoorn CJ. Tangled up in blue: unraveling the links between emotional distress and treatment adherence in type 2 diabetes. Diabetes care. 2016 Dec 1;39(12):2182-9.
5: Aikens JE. Prospective associations between emotional distress and poor outcomes in type 2 diabetes. Diabetes care. 2012 Dec 1;35(12):2472-8.
(D) depression and diabetes self-management behaviours:
Ref 4: Gonzalez JS, Kane NS, Binko DH, Shapira A, Hoogendoorn CJ. Tangled up in blue: unraveling the links between emotional distress and treatment adherence in type 2 diabetes. Diabetes care. 2016 Dec 1;39(12):2182-9.
5: Aikens JE. Prospective associations between emotional distress and poor outcomes in type 2 diabetes. Diabetes care. 2012 Dec 1;35(12):2472-8.

Response to reviewer comment 3 (major): Thank you for highlighting this point. We agree with the reviewer's suggestion of including "T1DM-related studies". For the reasons the reviewer indicated; that primary care health professionals interact with both groups, and the potential limited numbers of T2DM only studies, it was not our intention to exclude mixed T1DM and T2DM studies or diabetes not specified studies. We acknowledge that this is not made explicit in the protocol. To clarify this point, we have added the following sentence (p. 4, Phenomenon of interest): "Studies relating to type 1 and/or type 2 diabetes will be included if studies otherwise meet the inclusion criteria. This includes studies relating to "diabetes" where diabetes type is not specified, mixed sample studies where type 1 and type 2 diabetes are reported or type 1 diabetes only studies. Studies of "chronic conditions" or "multimorbidity" will only be included if findings relating to "diabetes" (not specified or mixed samples), "type 1 diabetes" or "type 2 diabetes" can be distinguished from other conditions included in the study."

While inclusion of T1DM specific studies may indeed have enabled comparison of barriers and enablers across diabetes type, as the review progress has progressed somewhat since submission of the protocol, preliminary findings indicate that eligible studies have focused on highly prevalent chronic conditions, such as heart disease or a combination of chronic conditions. This suggests it is unlikely that searches of T1DM specific studies would have returned additional eligible search results to enable meaningful insight into both fields.

To clarify that the potential relevance to the review question of studies considering diabetes not specified, mixed diabetes samples or Type 1 Diabetes samples, may be downgraded, we added the sentence (p.5, Confidence in the findings'): "Application of the GRADE CERQual enables the reviewers to understand the influence of aspects of our review such as inclusion

of both published and grey literature (methodological component), time of publication, the population of interest (relevance component) on our overall confidence in individual review findings in relation to the review question."

Response to reviewer comment 4 (major): Thank you for raising this point. We have made a number of revisions to the manuscript to clarify the rationale for conducting a search without restrictions on the year of publication:
We added the following sentence to Page 4, 'Search strategy': "This is because despite potential changes in mental health care and perceptions in primary care, individual level factors influencing detection in this population may persist. Persisting factors may include health care professionals' skills relevant to identification of these problems in the T2DM cohort and health care professionals' perceptions of patient factors influencing identification may persist despite organisational and systemic changes."

We added the sentence to Page 5, 'Confidence in the findings': "Application of the GRADE CERQual enables the reviewers to understand the influence of aspects of our review such as inclusion of both published and grey literature (methodological component), time of publication, the population of interest (relevance component) on our overall confidence in individual review findings in relation to the review question."

Response to reviewer comment 5 (major): Thank you. To clarify our rationale for including potentially 'lower quality' data, we added the following to the sentence and supporting reference on Page 5, 'Assessment of quality of included studies' section, sentence 2: "In line with the current default position in the conduct of aggregative type QES, assessment of study quality will not be a criteria to exclude studies that otherwise met the inclusion criteria but used to provide insights into the methods used for data collection and analysis43,44.

And Page 5, 'Confidence in the findings': "Application of the GRADE CERQual enables the reviewers to understand the influence of aspects of our review such as inclusion of both published and grey literature (methodological component), time of publication, the population of interest (relevance component) on our overall confidence in individual review findings in relation to the review question."

Response to reviewer comment 6 (minor): As stated in the introduction "The perspectives of people with T2DM regarding their experiences of depression screening and diagnoses have previously been synthesised29,33, enabling identification of patient factors influencing detection and diagnosis...Although a previous qualitative evidence synthesis explored general physicians' perceived barriers and enablers to diagnosing depression in primary care in general30, this has not been previously explored specifically in relation to a T2DM population." As such, there is a rationale to undertake the study.

Preliminary searches identified 10 potential studies for inclusion and we think this is 'large enough to suggest a systematic review in this field'. This is because qualitative evidence synthesis seeks to provide richer, more complete and transferrable findings relating to the synthesis topic. While the number of studies and depth of evidence contributing to an individual review finding may differ across study findings, our application of the GRADE CERQual will enable us to account for this when determining our confidence in individual

review findings.

Response to reviewer comment 7 (minor): Thank you for highlighting this. Further explanation regarding resources available and efforts made to source the full text has been provided on Page 4, 'Studies' section. This section now reads "Where the full text is unavailable, we will contact authors in an effort to obtain the full text. All reasonable effort will be made to secure potentially relevant studies, including via interlibrary loans or purchase of relevant studies if required. If it is not possible to obtain full texts, these studies will be excluded"

Competing Interests: No competing interests were disclosed.

Reviewer Report 31 March 2020

https://doi.org/10.21956/hrbopenres.14082.r27223

Thordis Thomsen
Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark

Thank you for the opportunity to review this protocol. The protocol describes the background for and methodological approach to reviewing qualitative research on barriers and enablers to systematic screening and diagnosis of diabetes distress and depression in people with T2DM. The review is relevant as it can provide important knowledge for clinicians with regard to developing practice in this important field.

The introduction provides good argument for conducting the review and the objective of the review is clear.

The methods for searching, inclusion of studies, assessing methodological quality, synthesizing data and evaluating and the degree of confidence to place in findings is clearly described.

The discussion presents relevant considerations, including potential limitations of the review.

Is the rationale for, and objectives of, the study clearly described?
Yes

Is the study design appropriate for the research question?
Yes

Are sufficient details of the methods provided to allow replication by others?

Yes

Are the datasets clearly presented in a useable and accessible format?
Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Person-centred interventions for people with T2DM, systematic reviews (quantitative & qualitative), anaesthesiology.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 17 Sep 2020

Niamh McGrath, University College Cork, Cork, Ireland

The authors thank the reviewer for taking the time to review this paper.

Competing Interests: No competing interests were disclosed.