NIHR | Blood and Transplant Research Unit in Organ Donation and Transplantation at Cambridge and Newcastle Universities

Assessing quality of life in solid organ transplant recipients: protocol for a systematic review of the development, content, and quality of available patient-reported outcome measures

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Background

In 2021, 4324 patients received an organ transplant in the United Kingdom[1]. Solid organ transplant recipients can live for long periods following transplantation, with high, albeit varied, 1-to-10 year survival rates in kidney (99% to 86%), liver (95% to 71%), heart (84% to 61%), lung (84% to 38%), and pancreas (96% to 76%) recipients, and 1-to-3 year survival in intestine (91% to 65%) recipients[1]. Given this, it is important to understand how quality of life (QoL) may be impacted in transplant recipients as they return to daily life following transplantation.

While QoL may improve following transplantation[2], patients may still experience psychological distress (e.g. anxiety, concerns about future health)[3,4], physical changes (e.g. weight gain)[5], and social and role challenges (e.g. inability to perform professional role)[6]. The extent that QoL is impacted may be influenced by the organ type, as significantly fewer concerns are reported by heart and lung patients, than kidney and liver patients[7]. Nonetheless, each transplant population may exhibit specific QoL impact (e.g. pulmonary symptoms for lung patients[8]; nausea or appetite loss for kidney patients[9]). This underlines the importance of measuring QoL to capture the potential supportive care needs of transplant recipients; indeed, improving patient experiences can improve patient outcomes[10].

There are numerous generic and transplant-specific patient-reported outcome measures (PROMs) of QoL[11,12]; transplant specific PROMs are useful for patient management, as they are typically more sensitive to changes in outcomes relevant to transplant populations. However, Mahmoudi et al. argue that QoL PROMs can be improved in heart transplantation to more comprehensively examine patient outcomes[13]. This may also apply to other transplant populations, as it is unclear whether PROMs have been developed with a patient-centred approach to ensure that the items are comprehensible and all relevant QoL outcomes have been considered.

When selecting a QoL PROM, it is important to consider its appropriateness, reliability, validity, responsiveness, feasibility, and interpretability[14]. However, the quality of existing PROMs is unclear; this is influenced by the varied levels of rigor in the PROMs' development and validation. Therefore, there is a pertinent gap in the

literature to create a synthesised understanding of the development, content, and quality of existing QoL PROMs for solid organ transplant recipients.

Such findings will be valuable to researchers and the clinical community, as they will help inform PROM selection in different, specific contexts. For example, a researcher may be interested in comprehensively capturing QoL to examine the effectiveness of an intervention[15]. Alternatively, a clinician may value ease of administration and wish to capture QoL aspects, specific to a particular transplant population (e.g. shortness of breath in lung transplant recipients), to help identify potential supportive care needs.

Aim

This systematic review will aim to identify the PROMs available to measure QoL in solid organ transplant recipients, and critically examine their development, content, and quality to inform recommendations for clinical use and future research.

Objectives

1. Identify what validated PROMs are available to measure QoL in solid organ transplant recipients.
2. Examine the development, content, and quality in terms of clinimetric properties, of available organ/transplant-specific QoL PROMs.
3. Document the generic QoL PROMs that have been used and/or validated in solid organ transplant recipients.

Eligibility criteria

Inclusion criteria

A paper will be eligible if: (1) it is an original article, available in English; (2) it reports the development and/or validation of a PROM that measures QoL; (3) the PROM items are available in English and included, or signposted to, within the paper. We will acknowledge, but not review, additional validations in languages other than English; (4) solid organ (including, but not limited to, heart, lung, kidney, liver, pancreas, intestine) transplant recipients are included in the development or validation of the PROM. We will acknowledge, but not review, generic QoL PROMs (e.g. SF-36[16]; EQ-5D[17]) used and/or validated in solid organ transplant research, as their clinimetric properties are generally well established[18,19].

For the purposes of this systematic review, we will define QoL as "*the state of wellbeing that is a composite of two components: the ability to perform everyday activities that reflect physical, psychological, and social well-*

being; and patient satisfaction with levels of functioning and control of the disease"[20]. A measurement of unidimensional QoL (e.g. psychological wellbeing) will be deemed eligible, providing the authors of the relevant paper are explicit that the PROM is considered a measure of QoL.

Exclusion criteria

A paper will be excluded if: (1) the authors do not report any validation for the PROM; (2) the patient is not the respondent; (3) the PROM is targeted at childhood (<18 years old) solid organ transplant or survivors of a transplant received in childhood.

Search strategy

We will search the following six bibliographic databases from inception: MEDLINE (OVID), Embase (OVID), CINAHL (EBSCO), PsycINFO (OVID), Cochrane CENTRAL (Wiley), and Scopus. The search strategy will concern five key concepts, namely: organ, transplant, QoL, PROMs, development/validation.

Search terms will be informed by previously published search strategies on PROMs in solid organ transplant recipients (e.g.[12,15,21]). We will seek assistance from a Senior Library Assistant to formulate a combination of appropriate medical subject headings and keywords; these will be tailored in accordance with the specific subject headings within each database. To retrieve any additional papers for inclusion (including those reporting more details of the PROM's development), we will hand-search the reference lists and forward citations of eligible papers and relevant systematic reviews.

Paper selection

The paper selection process will follow two stages. Firstly, two blinded reviewers will independently screen the titles and abstracts of papers identified through the bibliographic database searches, using Rayyan software. Any paper referring to the development or validation of a QoL PROM for solid organ transplant recipients will be retained for full-text screening. To obtain the full-text of any paper that is not readily available, we will request it from the corresponding author, or use an inter-library loan.

We will define a screening strategy, encompassing the detailed eligibility criteria; both reviewers will then screen the full-texts in accordance with this. Any discrepancies between reviewers will be resolved through discussion, involving a third reviewer where necessary. At this stage, coded reasons will be provided for excluded papers, to ensure transparency when completing the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram[22].

If an existing PROM has been adapted or shortened and has separate validation, this will be included as a separate PROM. Where an existing PROM has been refined (e.g. modified item wording), only the refined version will be included.

Data abstraction

We will create a structured from for data abstraction; this will subsequently be conducted by one reviewer and checked by a second reviewer for accuracy. Disagreements will be resolved through discussion and consensus, involving a third reviewer, where necessary. Where relevant, published papers reporting additional development and/or validation of an included PROM, will inform data abstraction. If multiple papers are available for a PROM, the initial (first published) validation paper will be used to abstract characteristics of the study population. All relevant papers will inform abstraction of the PROM development and content; findings will be pooled across papers to assess clinimetric properties. We will contact corresponding authors of included papers, should we need to request relevant missing information; a three-week turnaround will be permitted, after which, data abstraction decisions will be informed by the available published material.

Abstracted data will include: PROM name, purpose, study setting, target and study population, validations in languages other than English, recall period, response options, scoring, item generation (e.g. patient interviews) and reduction (e.g. item response frequencies), dimensions of QoL measured, and how the dimensions were developed. We will identify common dimensions of QoL and map the content of each PROM to these dimensions; any additional content will be reported as 'other'. To inform usability, we will also abstract data on feasibility (e.g. PROM length, completion time, cost, type and ease of administration) and interpretability (e.g. distribution of scores, percentage of missing items, missing total scores).

Risk of bias

The consensus-based standards for the selection of health measurement instruments (COSMIN) checklist[23,24] will be used to assess the methodological quality of included PROMs. This is divided into 10 measurement properties and includes the evaluation of a PROM's development, content validity, structural validity, hypotheses testing, internal consistency, reliability, measurement error, cross-cultural validity, criterion validity, and responsiveness. However, we will not consider cross-cultural validity in this review as we will only be evaluating the English language versions of PROMs.

The COSMIN manual comprises checklists of 3-35 items for the evaluation of each clinimetric property; rating each item on a four-point scale: *very good*, *adequate*, *doubtful*, or *inadequate*. We will apply the 'worst score counts' principle of COSMIN, whereby the methodological quality rating for an individual clinimetric is determined by the PROM's lowest score for that property. GRADE will be used to summarise the quality of available evidence. Evidence will be downgraded appropriately in accordance with risk of bias, inconsistency, imprecision, and indirectness. Each PROM will be considered *high*, *moderate*, *low*, or *very low* in quality.

Finally, there are quality criteria for nine of the 10 measurement properties (with exception of content validity) to determine whether the outcomes of each clinimetric are *sufficient*, *insufficient*, or *indeterminate*. Ultimately, the assessment of methodological quality will determine how rigorously each PROM has been developed, while the quality criteria will determine the robustness of each PROM.

Data synthesis

We will conduct a narrative synthesis[25] of the included papers. This will be structured in three key areas: PROM development, content, and clinimetric properties. PROMs will be categorised by their related solid organ, where appropriate (e.g. heart, lung, kidney, liver, pancreas, intestine). We will first summarise the general characteristics of each PROM (e.g. PROM description, purpose, study setting, target population, recall period, response options, additional validations in languages other than English). For development, we will consider how the items were generated (e.g. existing literature, patient interviews, expert panels); this will help determine whether the PROM is likely to have good content validity and capture the QoL dimensions that are relevant to solid organ transplant recipients. For content, we will assess which QoL dimensions are examined by each PROM to indicate which PROMs are most comprehensive in their assessment of QoL. For clinimetric properties, we will evaluate the robustness of each PROM (e.g. construct validity, reliability, internal consistency). We will also consider the feasibility and interpretability of each PROM (e.g. PROM length, time to complete, how administered, distribution of scores).

Dissemination plans

Findings from this review will be published in a relevant peer-reviewed journal, and presented at relevant international conferences.

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