1) Title: Patient-Reported Outcome Measures for Abdominal Aortic Aneurysm: A systematic review and qualitative evidence synthesis

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7) Source of funding for research and publication: This review presents independent research funded by the National Institute for Health Research (NIHR) under the Programme Grants for Applied Research programme (RP-PG-1210-12009). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

8) Category for manuscript submission: Review

9) Preliminary findings from this research were presented at the International Society for Quality of Life Research conference in Vancouver, October 2015 (Abstract number 104).

Abstract

Background: The aim was to identify and evaluate existing patient reported outcome measures (PROMs) for use in patients with an abdominal aortic aneurysm (AAA) to inform the selection for use in surgical practice.

Methods: Two systematic reviews were conducted: a systematic review to identify valid, reliable and acceptable PROMs for patients with AAA and a qualitative evidence synthesis to assess the relevance to patients of the identified PROMs items. PROMs studies were evaluated for their psychometric properties using established assessment criteria and their methodological quality using the COSMIN checklist. Qualitative studies were synthesised using framework analysis and identified concepts were then triangulated using a triangulation protocol with the item concepts of the identified PROMs.

Results: Four PROMs from three studies were identified in the first review; the SF-36, the Australian Vascular Quality of Life Index, the AneurysmDQoL and AneurysmSRQ. None of the identified PROMs had undergone a rigorous psychometric evaluation within the AAA population. Four studies were included in the qualitative synthesis, from which 28 concepts important to patients with an AAA were identified. The AneurysmDQoL and the AneurysmSRQ together provided the most comprehensive assessment of these concepts. Fear of rupture, control, ability to forget about the condition and size of aneurysm were all concepts identified in the qualitative studies but not covered by items on the identified PROMs.

Conclusion: Further research is needed to develop PROMs that are reliable, valid and acceptable to patients for use in surgical practice for AAA.

Introduction

Abdominal Aortic Aneurysm (AAA) is a dilation of the abdominal aorta. Recent statistics from the UK screening program suggest an incidence of 1.3% for men[1]. Most AAAs are reported to be asymptomatic but rupture is usually fatal[2]. In 2010 the UK National Health Service (NHS) introduced a National Abdominal Aortic Aneurysm Screening Programme (NAAASP) for all men aged 65 years as a way of improving mortality rates in this population by monitoring and surgical intervention. However, despite an expected increase in elective repairs due to the introduction of screening recent evidence from the National Vascular Registry[3] suggests that the number of repairs is stable or reducing slightly. It is generally recommended that AAAs over 5.5cm be considered for surgical repair. Early detection combined with advances in surgical techniques such as endovascular repair (EVAR) has improved the morbidity and mortality rates[4], although there remains debate about the effect on long term outcomes.

Patient reported outcome measures (PROMs) are questionnaires designed to provide a means of measuring health or quality of life (QoL) from the patient's perspective. They enable post-surgical outcomes (e.g. social functioning, emotional well-being) wider than the traditional measures of outcome such as mortality or morbidity to be recorded[5]. They can capture changes to health status and QoL throughout the process of care and allow information to be recorded on the impact of different surgical techniques to help inform treatment decisions[6]. The use of PROMs is becoming more widespread. Since 2009 the NHS has made it a requirement to collect PROM data from patients before and after surgery in four surgical conditions: hip replacement, knee replacement, varicose veins and groin hernia.

PROMs can be categorised as being generic or condition specific. Both of these may also have utility (preference) values estimated for the responses and therefore become preference-based measures. Generic PROMs allow for comparisons to be made across patient groups and, if preference based, can be used to estimate preference weights for calculating quality-adjusted life years (QALYs), allowing for the economic value of interventions to be assessed. However generic PROMs do not always appropriately measure the specific symptoms and health impact of individual conditions. Condition specific PROMs allow greater detail to be collected on a patient disease group and therefore can be more useful in a clinical setting. It is generally recommended to use both a generic and a condition specific PROM for measuring patient outcomes[7].

There are many PROMs available and it is important to use those that have followed best practice in terms of their development and evaluation in the population in which they are being used. The Food and Drug Administration (FDA)[8] issued guidance on PROM development recommends that the items and domains covered by a PROM are developed through qualitative studies and are "appropriate and comprehensive relative to its intended measurement concept, population, and use"[8].

The overarching aim of the current study was to synthesise and critically appraise the properties of PROMs available for patients with an AAA to aid recommendations for their use in surgical practice. These reviews form part of a larger study funded by the NIHR concerned with selecting PROMs for use in vascular services. The specific objectives were (i) to conduct a systematic review of the literature to identify and appraise the psychometric properties of validated PROMs for AAA; (ii) to carry out a qualitative evidence synthesis of the qualitative literature to identify health and QoL themes reported by patients; and (iii) to triangulate the identified PROM items with the qualitative review themes.

Methods

Two reviews were conducted; the first was a systematic review of PROMs validated in patients with an AAA and the second a qualitative evidence synthesis to identify health and quality of life outcomes from patients.

Review 1: a systematic review of AAA PROMs

The systematic review was reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) recommendations[9]. The study protocol is available at http://www.shef.ac.uk/polopoly_fs/1.550136!/file/Patient_reported_outcome_measures_in_patients_with_abdominal_aortic_aneurysms.

Searches

Systematic searches were undertaken in eight electronic databases and research registers (including Medline and the Cochrane Library) using a two-stage approach. Stage one combined terms for known generic and condition-specific PROMs and terms for AAA. These results were examined for additional PROM terms used in patients with AAA. These terms were added to the preliminary search strategy and combined with a methodological search filter for finding studies on measurement properties[10]. Databases were searched from inception up to September 2014 (Stage 1) and to November 2014 (Stage 2). No language

or date restrictions were applied. Searches were supplemented by hand-searching reference lists of relevant reviews and included studies and contact with experts in the field. Further details of the search strategies are provided in the supplementary appendix 1.

Study selection

All titles were examined and any citations that clearly did not meet the inclusion criteria (e.g. non-human, unrelated to AAA) were excluded. All abstracts and full text articles were then reviewed by at least two individuals (ME and EP). Any disagreements in the selection process were resolved by discussion, with involvement of a third reviewer when necessary (PP). Eligible studies included published articles in English of any study design that reported the psychometric properties of PROMs capturing QoL, health status or functional limitation in patients with AAA. Psychometric properties included the validity (the degree to which the instrument measures what it is supposed to measure); reliability (the degree to which measures are reproducible and consistent over time in patients with a stable condition); responsiveness (the degree to which the instrument detects meaningful change over time if a change truly exists) and acceptability (the degree to which the instrument is acceptable to the patients). Studies reporting only outcomes of treatment satisfaction were excluded. The population of interest were any patients with a diagnosis of AAA undergoing screening or any treatment, regardless of clinical presentation, diagnostic criterion or underlying cause. Studies published in English that reported non-English translations of relevant PROM instruments or PROMs elicited from non-English speakers were excluded. This was considered as a suitable approach to overcome the uncertainty due to language validation and cross-cultural adaptation of PROMs[11].

Data abstraction

Data relating to study design, patient characteristics, type of PROM, methods and outcomes, were extracted by one reviewer into a standardised data extraction form and independently checked for accuracy by a second. Any discrepancies were resolved by discussion, with involvement of a third reviewer. Where necessary, study authors were contacted for missing information or additional data.

Psychometric evaluation and methodological quality assessment of PROMs

The psychometric properties and methodological quality of each PROM were appraised by two researchers (RD and AK). Disagreements in the ratings were discussed and if needed agreed by a third researcher (GJ). PROMs were classified according to whether they were generic or condition specific, generic preference based or condition specific preference based.

Due to lack of consensus on how to appraise PROMs, study-specific criteria adapted from published recommendations were used to evaluate the psychometric performance of identified validated PROMS[8,12-16]. The developed criteria were also consistent with FDA guidance[8] and are outlined in Table 1.

Table 1: Appraisal criteria for assessing the psychometric properties of patient reported outcome measures

Domain	Criteria
Test re-test	The intra-class correlation/ weighted kappa score should be ≥0.70 for group comparisons and ≥ 0.90 if scores are going to be used for decisions about an individual based on their score[13]. The mean difference (paired t test or Wilcoxon signed-rank test) between time point 1 (T_1) and time point 2 (T_2) and the 95% CI should also be reported.
Internal consistency	A Cronbach's alpha score of ≥0.70 is considered good and it should not exceed ≥0.92 for group comparisons as this is taken to indicate that items in the scale could be redundant. Item total correlations should be ≥0.20[15].
Content validity	This is assessed qualitatively during the development of an instrument. To achieve good content validity, there must be evidence that the instrument has been developed by consulting patients, experts as well as undertaking a literature review. Patients should be involved in the development stage and item generation. The opinion of patient representatives should be sought on the constructed scale[13,14,15].
Construct validity	A correlation co-efficient of ≥0.60 is taken as strong evidence of construct validity. Authors should make specific directional hypotheses and estimate the strength of correlation before testing[13,15,16].
Criterion validity	A good argument should be made as to why an instrument is a gold standard and correlation with the gold standard should be ≥ 0.70[16].
Responsiveness	There are a number of methods to measure this including t-tests, effect size, standardised response means or responsiveness statistics Guyatts' responsiveness index. There should be statistically significant changes in

	score of an expected magnitude[33].
Floor-ceiling effects	A floor or celling effect is considered if 15% of respondents are achieving the lowest or the highest score on the instrument[16].
Acceptability	Acceptability was measured by the completeness of the data supplied. 80% or more of the data should be complete[14].

Review 2: a qualitative evidence synthesis

Qualitative searches

In accordance with the study protocol (see https://www.shef.ac.uk/polopoly_fs/1.552397!/file/DP_16_05.pdf) searches were conducted in bibliographic databases (including Medline and CINAHL) in April 2015. The search was based on the search strategy created for the related review of patient reported outcome measures for AAA. The search strategy combined condition terms, terms for patient reported outcomes/patient views and terms for qualitative studies (which augmented a qualitative study filter)[17]. Further details of the search strategies are provided in the supplementary appendix 1.

Qualitative study selection

Two reviewers (RD, PP) read the titles and abstracts for the inclusion/ exclusion criteria. Full text articles were obtained for abstracts that appeared to meet the inclusion criteria for more detailed information. All titles were examined and any citations that clearly did not meet the inclusion criteria (e.g. non-human, unrelated to AAA) were excluded. Eligible studies included published articles in English of primary qualitative studies (e.g. focus groups and interviews) that explored AAA (any patients with a diagnosis of AAA undergoing screening or any treatment, regardless of clinical presentation, diagnostic criterion or underlying cause) patient's experiences, health or QoL. Studies that did not report qualitative themes in their results were excluded. Due to the paucity of qualitative research studies identified in the initial searches a decision was made to include those studies conducted in a non-English speaking population on the basis that they would provide insight into the impact of AAA.

Qualitative data extraction and analysis

Data were extracted and tabulated on authors, date of publication, country of study, number of participants, research aims, method of recruitment, method of data collection, key results

and analysis. The results and discussion sections of each article including primary and secondary text (patient quotes reported in the articles and themes) were coded. The text of each article was analysed using framework analysis[18] to identify themes from within and across the articles. The researcher (RD) familiarised themselves with the themes presented in the results and discussion section of each article. They then went through each section coding to identify initial themes. Text from each of the included studies was collated by the researcher into themes and charted by study to create a framework matrix. Themes were examined for their conceptual similarities and differences. The themes that arose were then checked by a second reviewer with extensive experience of qualitative reviewing (AB) and differences of conceptualisation were discussed and subsequently adjusted.

The Critical Appraisal Skills Programme (CASP) qualitative research checklist was used to assess the methodological quality of the included studies[19]. CASP consists of 10 questions about the qualitative methodology and are answered either as yes, no or unclear.

Triangulation of PROM items with qualitative themes

Items from the identified PROMs were mapped against the themes from the qualitative synthesis to explore whether the PROMs items captured the themes important to patients. A triangulation approach[20,21] was followed whereby the researcher examined the themes from both the qualitative review and the PROM items/ domains to evaluate whether the concepts were the same (agreement), offered similar concepts (partial agreement), appeared to contradict each other (dissonance) or were not present (silence). The FDA[8] recommends that both a generic and condition specific measure are used when collecting patient outcomes. Therefore it was important to examine the extent to which the items within the generic measures corresponded or overlapped with those from the condition-specific measures.

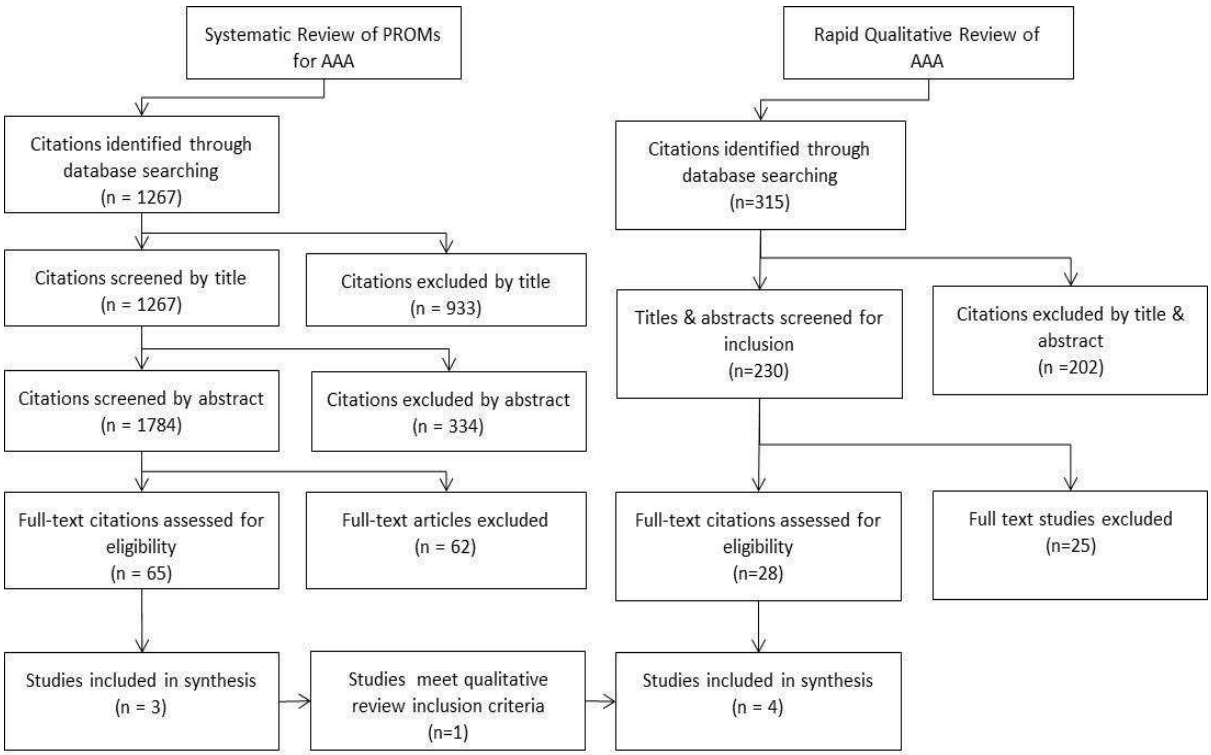
Results

Review 1: systematic review of PROMs

A total of 1,232 records were identified, of which 65 full-text articles were considered potentially eligible for inclusion (including an abstract that reported two measures [the Aneurysm Symptom Rating Questionnaire (AneurysmSRQ) and Aneurysm-Dependent Quality of Life (AneurysmDQoL)][22] which has subsequently been published[23,24]. Following detailed screening, three studies (reporting on four PROMs) were finally included in this review[23-26]. All the included studies reported the validation of PROMs in patients with AAA.

The majority of the excluded articles did not clearly report outcomes or present data evaluating the measurement properties of PROMs. The Aneurysm Treatment Satisfaction Questionnaire (AneurysmTSQ) was excluded as this was a patient satisfaction questionnaire not an outcomes assessment[23,24]. A summary of the process of identifying and selecting the relevant literature is presented in Figure 1.

Figure 1: PRISMA Flow diagram of study selection



Study characteristics

As outlined in Table 2, the three included studies were all prospective studies and undertaken in the UK[23,24], Australia[25] and USA[26]. Two of the studies reported details of designing and piloting the PROMs[23-25], whilst one study only reported details of using a PROM in patients undergoing AAA surgery.[26]

Overall, the studies were of a small to moderate size with the number of patients ranging from 95[26] to 191[23]. The proportion of men in the study samples ranged between 82%[25,26] to 90%[23] and the mean age ranged from between 72 years[26] to 75 years[23,25].

The patients' clinical diagnosis varied across studies. Both Mangione (1997)[26] and Borchard (2006)[25] included patients with comorbidities; however, in Mangione (1997)[26] it was unclear

what these were. Peach (2006)[23] did not report any data related to patient comorbidities. Mangione (1997)[26] included patients undergoing AAA surgery and those who were evaluated pre-operatively and post elective surgery. Peach (2016)[23] included patients who had undergone AAA repair (using open or endovascular techniques), or were under pre-operative surveillance with aneurysm that was below the threshold size for intervention. Bochard (2006)[25] included patients who had undergone AAA repair (both open and endovascular).

Table 2: Studies reporting validation of PROMs in patients with AAA

Author, Country	Study aim(s)	Patient characteristic	PROM(s) measured, Types of validation assessed	Timing of PROM(s) assessment	Authors summary of key findings
Borchard 2006[25] Australia (Tasmania)	To develop a vascular condition specific QoL tool appropriate for patients with AAA and applicable to patients with central and peripheral occlusive vascular disease, and to compare the validity and reliability of this with the SF-36.	N=10 (for design work) N=108 (Questionnaire piloted) Mean age (yrs.): 74.7 Male n (%): 89/108 (82%)	AUSVIQUOL Type: condition specific QoL measure Validation assessed: Reliability, Content validity, Structural validity and Hypothesis testing	NR	The AUSVIQUOL showed better reliability than the SF-36 in all domains and statistically better in the physical function domain ($P < 0.05$). Conclusion: The AUSVIQUOL is an appropriate tool for the QoL assessment of patients with AAA in the clinical setting.
Mangione 1997[26] USA	To examine the responsiveness of SF-36 to clinical changes in three surgical groups (total hip arthroplasty, thoracic surgery for treatment of non -small cell lung cancer, or AAA surgery repair) and to study how QoL changes with time amongst	N=95 Mean age (yrs.): 72 Male n (%): 78/95 (82%)	SF-36 Type: Generic Validation assessed: Internal consistency, Hypothesis testing and Responsiveness	Pre-operatively and at 1, 6 and 12 months after surgery	The findings indicated that SF-36 has evidence of validity internal consistency (Cronbach alpha between 0.86 to 0.92 for different sub-scales) and is responsive to expected changes in HRQoL after elective surgery for these procedures. Conclusion: In AAA the responsiveness

Author, Country	Study aim(s)	Patient characteristic	PROM(s) measured, Types of validation assessed	Timing of PROM(s) assessment	Authors summary of key findings
	these patients				was dependent on the type of surgery and the timing of follow-up, hence, multidimensional measures are needed to fully capture changes in HRQoL after surgery
Peach 2016[23,24] UK	To develop and validate PROMs to assess QoL, symptoms and treatment satisfaction in patients with AAA	N=54 (for design work) N=191 (Questionnaires for quantitative psychometric analysis) Mean age (yrs.): 75 Male n (%): 172/191 (90%)	1.AneurysmDQoL questionnaire 2. AneurysmSRQ Type: Disease-specific Validation assessed: Content validity	Pre-operative, 6 weeks and 12 weeks post operation (but only pre-operative data have been analysed and reported due to low number at follow-up	A set of newly designed and validated PROMS to assess quality of life, symptoms and treatment satisfaction amongst patients with AAA has been designed
Abbreviations: AAA, Abdominal aortic aneurysms; AUSVIQUOL, Australian Vascular Quality of Life Index; AneurysmDQoL, Aneurysm Dependent Quality of Life questionnaire; AneurysmSRQ, Aneurysm Symptoms Rating Questionnaire; PROM(s), Patient reported outcome measure(s); QoL, Quality of life; SF-36, Medical Outcomes Study 36-item Short Form					

PROMs data, psychometric evaluation and methodological assessment

In total, four PROMs were identified where psychometric evaluation had been completed in patients with AAA. One generic PROM was identified; the 36-item Short Form Health Survey (SF-36), one generic vascular PROM; the Australian Vascular Quality of Life index (AUSVIQUOL) and two condition specific PROMs; the AneurysmDQoL questionnaire and linked to this the AneurysmSRQ. The results of the psychometric evaluation and methodological quality (rated using the COSMIN checklist) are presented in the supplementary appendix 2 and 3.

Mangione (1997)[26] examined the responsiveness of SF-36 to clinical changes in three surgical groups (hip arthroplasty, thoracic surgery for treatment of non-small cell lung cancer or AAA repair) and studied how QoL changes with time amongst these patients. The SF-36 was administered to patients with AAA undergoing elective surgery. Patients completed the

SF-36 pre-operatively and at 1, 6, and 12 months after surgery. Patients also completed the Specific Activity Scale (SAS). Responses from the SAS, the five validated health transition questions, and the global health rating questions were used to evaluate the validity of the observed changes in the SF-36. The SF-36 showed evidence of internal consistency and construct validity in the patients with AAA[26]. The correlation coefficient was 0.4 between the 0 to 100 rating rating scale and the mental health scale of the SF-36 while correlations with other domains were lower but statistically significant. Responsiveness assessed using a relative efficiency statistic ranged from 1.1 to 6.7 in the combined construct showing high responsiveness and tests were statistically significant. Although acceptability could not be rated according the agreed criteria one study found that the majority of participants had difficulty completing it suggesting low acceptability[25].

The AUSVIQUOL was developed by Borchard et al (2006)[25] to specifically measure the QoL of patients with vascular disease and of those with AAA in a clinical setting. The items and domains of AUSVIQUOL were determined by examination of a prospective database for frequency of symptoms and an in-depth interview of a random sample of AAA patients. The AUSVIQUOL has three main domains relating to perception of general health; functional, mobility and pain; and psycho-social aspects. The AUSVIQUOL was developed with patients and has excellent content validity[25]; however, the content validity was rated good according to the established psychometric criteria. The construct validity of the tool was tested by comparing it with SF-36 in 60 patients who underwent endovascular AAA repair and 48 patients who underwent open AAA repair using factor analysis and regression analysis. As no correlation coefficients were reported, construct validity could not be rated. To compare the reliability of the two tools, 22 patients were reassessed using SF-36 and AUSVIQUOL. Given the low sample the test re-test reliability was rated poor.

The AneurysmDQol and the AneurysmSRQ, were developed and validated by Peach 2016[23,24]. They used semi-structured interview techniques to explore patients' experience of having AAA in a series of focus groups and in-depth interviews. The information gathered was used to inform design and selection of items for the new tools. The AneurysmDQoL consists of 24-items with 22 domains specific to patients with AAA with a further two additional items to assess overall QoL and the impact of AAA on QoL. The AneurysmSRQ is a 44-item, aneurysm-specific measure, which assesses a wide range of physical and psychological symptoms reported by patients with AAA with two free-text questions. The tools were further completed by 191 patients from the NHS Trusts for psychometric validation assessment. The initial validation of the tools reported the trend scores of the different instruments but did not report psychometric properties of the measures. However,

the tool shows good content validity according to standardised psychometric appraisal criteria[23].

Review 2: qualitative evidence synthesis

Figure 1 presents a summary of the selection process. 315 citations were identified through the database searches, on sifting 85 duplicates were excluded leaving 230 studies. The 230 titles and abstracts were assessed and 202 citations were subsequently excluded from the review. The remaining 28 full text papers were screened against the eligibility criteria and 25 papers were excluded leaving a remaining three studies that met the inclusion/ exclusion criteria. Through the quantitative review an abstract for the development of a new condition specific PROM for AAA was identified[22]. On contacting the authors they agreed to share the methods paper for the PROM development, which was subsequently published[23,24]. This has been included in both reviews; four studies were therefore included in the qualitative synthesis.

The author, research design, study aims, number of participants, diagnosis, mean age, gender and main findings of the studies included in the qualitative synthesis are presented in Table 3. Three of the four included studies were conducted in Sweden in Swedish, although the texts of the articles were published in English[27-29]. Two of the four studies identified carried out semi-structured interviews with patients who had been identified as having an AAA through screening and were being treated conservatively[27,29], one focussed on patients who received surgery for an open repair of the AAA[28] and the final presented a mix of patients including those being conservatively treated, open repair and endovascular repair[23,24].

Table 3: Qualitative studies of patients with an AAA

Author	Research design	Study aims	Patient characteristics	Diagnosis	Main findings
Brännström (2009)[27]	Semi-structured interview	To describe patients' experiences 5 years after being informed about having an AAA in the subgroup of patients with a low SF-36 mental health scores.	N=3 Mean aged=79.5 Male n (%)=100	Participating in QoL study having had an AAA identified at screening.	Patients like professional care despite awareness of having an AAA.
Letterstål (2010)[28]	Semi-structured interviews	To elucidate patients' lived experience of the care pathway of going through open surgery for AAA.	N=10 Mean aged=73 Male n (%)=60	Patients treated with elective open surgical repair for AAA.	It was found that people undergoing surgery were not fully aware of the risks and consequences of having the surgery and were unprepared for the limitations of the recovery period.
Pettersson (2013)[29]	Unstructured interviews	To describe patients' experiences of living with AAA for which they are receiving conservative treatment.	N=10 Mean aged= 72.4 Male n (%)=80	Patients with AAA treated conservatively.	5 themes were identified: sudden knowledge of an undetected condition; putting your life in someone else's hands; waiting in limbo - feeling secure despite concerns; life at stake; feeling obliged not to cause worry.

Author	Research design	Study aims	Patient characteristics	Diagnosis	Main findings
Peach (2016)[23,24]	Focus groups and in-depth interviews	To develop three questionnaires to assess quality of life (QoL), symptoms and treatment satisfaction in patients with AAA.	N=54(41, 13) Mean aged=71.9 Male n (%)=70	AAA repair within 24 months (OR or EVAR) or treated conservatively.	3 PROMs were developed through patient interviews.
Abbreviations: AUSVIQUOL, Australian Vascular Quality of Life Index; SF-36, Medical Outcomes Study 36-item Short Form; AneurysmDQoL, Aneurysm Dependent Quality of Life scale; AneurysmSRQ, Aneurysm Symptoms Rating scale					

Quality Assessment

Against the Critical Appraisal Skills Programme (CASP) checklist[19] it was found that all studies met 'yes' on almost all of the items, showing evidence of being good quality. The item on 'whether the researcher has adequately considered their relationship with participants' was graded as 'can't tell' for two studies[27,28] of the three studies as there was too little information in the published report.

Triangulation of the review data

As presented in Table 4, four overarching themes were identified from the four studies included in the qualitative synthesis: health outcomes, functional outcomes, psychological outcomes, and social outcomes. A summary of the quotes are provided in supplementary appendix 4.

Table 4: PROM items triangulated with the qualitative synthesis themes

Qualitative themes	AUSVIQUOL	SF-36	AneurysmDQoL & AneurysmSRQ
Symptoms			
Feeling no physical symptoms[23,24,27,29]	.	.	+
Pain[23,24,27]	-/+	-/+	+
Gastrointestinal upset[23,24,28,29]	.	.	+
Numbness[23,24,28]	.	.	+
Swelling[23,24,28]	.	.	+
Bruising[23,24]	.	.	+
Weakness[23,24,28]	.	.	+
Heaviness[23,24]	.	.	+
Sleep[28]	-/+	.	+
Lethargy, fatigue[23,24,28]	.	+	+
Weight loss[23,24,28]	.	.	+

Appetite[23,24,28]	.	.	+
Comorbidities[27]	.	.	-/+
Psychological outcomes			
Concern over bodily symptoms[23,24,28,29]	.	.	+
Concern over changes to the size of the aneurysm[29]	.	.	.
Age related health expectations[29]	+	+	+
Ability to forget about the condition[28,29]	.	.	.
Cognitive function[23,24]	-/+	.	+
Anxiety[27-29]	.	.	+
Depression, fatalism, helplessness[29]	.	+	+
Fear of rupture and death[23,24,27-29]	.	.	.
Control[29]	.	.	.
Social outcomes			
Effect on family[23,24,29]	.	+	+
Functional outcomes			
Effect on day to day life[23,24,28]	+	+	+
Sexual Function[27]	.		+
Lifting heavy objects[23,24,28,29]	.	+	-/+
Ability to trave[23,24,28,29]	.	.	+
Financial implications[24]	.	.	+

Key:
. silence
– dissonance
-/+ partial agreement
+ agreement

N.B. AneurysmDQoL & AneurysmSRQ are reported together as they were developed with the same authors.

Symptoms

This theme included 14 health related concepts from the included studies. These were feeling no physical symptoms[23,24,27,29]; pain[23,24,27]; gastrointestinal upset[23,24,28,29]; numbness, swelling, bruising, weakness and heaviness[23,24,28]; sleep[28]; fatigue[23,24,28]; weight loss[23,24,28]; appetite[23,24,28]; changes to the size of the aneurysm and comorbidities[27]. All items but comorbidities and changes to size of the aneurysm were covered by the AneurysmSRQ. The SF-36 was rated as having partial agreement with the pain theme and partial agreement with a question on fatigue/ lethargy. The AUSVIQUOL also asked about pain and sleep but this was combined with another question and therefore was rated as only meeting partial agreement.

Functional outcomes

Functional items were those that related to everyday activities or physical functioning including the effect on day-to-day life[23,24,28], sexual function[27], lifting heavy objects[23,24,28,29],

ability to travel[23,24,28,29] and financial implications[24]. The AneurysmDQoL or the AneurysmSRQ had items that covered all of the identified themes classified under functional outcomes. The AUSVIQUOL and the SF-36 both included an item on every day functioning. The SF-36 included an item on the ability to lift heavy objects.

Psychological outcomes

Concepts included concern over bodily symptoms, age related health perceptions, ability to forget about the condition, cognitive function, anxiety, depression, fear of rupture and control[23,24,27-29]. Fear of rupture, control[23,24,27-29] and ability to forget about the condition[28,29] were all themes that were covered in the qualitative studies but silent in the identified PROMs items. The AneurysmDQoL or the AneurysmSRQ does not have items on concern over aneurysm, ability to forget about the condition, fear of rupture and death or control. The SF-36 includes items on depression and concern over bodily symptoms and the AUSVIQUOL only on concern over bodily symptoms, and partial agreement with cognitive function.

Social outcomes

Two studies detailed the effects of AAA on their families and that this worsened their own concerns. “Patients expressed that their families were worried and concerned about the threat the aneurysm posed to the patient and thereby also to the family circumstances”[23,24,29]. This is in agreement with items on the SF-36 and the AneurysmDQoL.

Discussion

To our knowledge this study provides the first review of the psychometric properties of PROMs for AAA and of the qualitative literature on patients’ experiences of having an AAA. The overall aim of the current review was to synthesise and critically appraise PROMs psychometrically evaluated in an AAA population to make recommendations for their use in surgical practice. The specific objectives were to conduct a systematic review of the literature to identify and appraise the psychometric properties of PROMs validated for AAA; to carry out a qualitative evidence synthesis to identify the health and QoL themes reported by patients; and to triangulate the identified PROM items with the themes from the qualitative synthesis.

The systematic review (review 1) identified four PROMs (from three studies)[23-26] that had undergone psychometric tests for use in patients with an AAA. None of the identified PROMs had undergone full rigorous psychometric testing within the AAA population. The SF-36 showed good evidence of internal consistency, construct validity and responsiveness

but did show some floor or ceiling effects and one of the studies reported that older patients found some of the items irrelevant suggesting low acceptability[25]. The AUSVIQUOL - a generic vascular measure, showed good content validity according to our criteria as it had been developed by interviewing patients with an AAA as well as other conditions, although the qualitative review paper is not included here as it combines the results of all conditions and was thus excluded from the qualitative review [30]. The responsiveness and internal consistency of the AUSVIQUOL had not been assessed. The AneurysmDQoL and AneurysmSRQ are both condition specific measures of health and QoL have compared trend scores but a conventional psychometric evaluation has not been performed yet; but were developed from the most comprehensive qualitative study of AAA patient experiences including those patients who are receiving conservative, OR, or EVAR treatment.

Details for the process of tool development were reported by both Borchard (2006)[25] and Peach (2016)[23,24]. Both studies had potential issues in respect to item identification and retention. The items for the AUSVIQUOL[25] were chosen on the basis of the frequency of reported symptoms from patients undergoing AAA repair but it was unclear as to how these data were captured. Furthermore, validation of item inclusion and reduction was on the basis of semi-structured interviews (n=10) which were centred on the relevance of the items already identified rather than checking the breadth and completeness of the identified domains. The item selection for the AneurysmDQoL[24] was based on focus groups of AAA patients and relied on their recall of their treatment. Questions were constructed for the identified areas from previously existing questionnaires.

The qualitative synthesis (review 2) identified only four studies[23,24,27-29] reporting on patients' experiences of having an AAA. The themes from these studies when mapped onto the items of the identified PROMs found that none of the current PROMs cover all of the concepts from the qualitative studies although the AneurysmSRQ and AneurysmDQoL combined covered 24 of the 28 identified concepts. Fear of rupture was not captured by any of the PROMs despite being recorded as a key theme in all four of the qualitative studies. Similarly, difficulty in forgetting about the AAA was reported in two of the qualitative studies but was not reflected in the items of the PROMs. It could be fear and ability to forget about the condition are associated with distress and so measuring the more general theme of distress was thought to cover this concept. Due to the frequency of patients reporting fear around AAA, further research is needed to explore this theme and whether it is adequately covered by the existing PROMs.

The main strength of the PROMs review (review 1) was the comprehensive two-step search strategy used to identify studies. The review was undertaken by a multi-disciplinary team of

clinical and methodological experts according to the recommended standards. However there were a number of limitations to the review process that should be noted. Firstly, the data extraction for the qualitative synthesis (review 2) and triangulation protocol was applied by a single researcher (RD). It is known that having two reviewers conducting each stage a review reduces the incidence of error [31,32]. In this instance the process and emerging themes were discussed with an experienced qualitative reviewer (AB).

Three of the four studies included in the qualitative synthesis (review 2) had been conducted in Sweden in Swedish[27-29]. The PROMs review (review 1) excluded PROMs not developed in an English speaking population whereas the qualitative synthesis (review 2) did include studies that had been conducted in another language but published in English. Only one of the qualitative studies was conducted in English[24] highlighting the paucity of published research qualitatively exploring patients' experiences of the condition.

Macefield (2014) wrote about the difficulties of comparing concepts PROMs [6]. Items within the AUSVIQUOL lacked clarity over the conceptual domain they were intending to measure making data synthesis with the SF-36 difficult. For example when asking whether pain disturbs sleep in the same question they ask whether pain distorts mobility e.g. "do you have pain or discomfort in your legs or feet that limits your mobility or disturbs you sleep, ulcers on your feet or have you lost a limb?". It is also unclear whether the questionnaire would relate to those who have been identified with an AAA that are not requiring or have not undergone surgery.

Both the qualitative and PROMs studies samples were heterogeneous including patients at different stages of treatment. Of the four identified studies only two included patients post treatment [23,24,28]. There needs to be further exploration of patients post treatment. Peach and colleagues provide the most extensive qualitative study including patients at each stage of treatment [23,24].

Despite recent publications on outcomes for patients with AAA as yet there would seem to be a paucity of qualitative research in this area with only one UK study[23,24] cited. In recommending a PROM for use in clinical practice to measure outcomes from surgery it is important to include measures that both capture the breadth of the patient experience and provide instruments that are reliable, valid and acceptable to patients. Research exploring how to integrate PROMs into the patient pathway is needed. If PROMs are to be integrated into practice it would be useful to administer the PROMs at different stages of each patient's care over at least two time points.

Conclusion

Only four PROMs (two generic and two condition specific) and three qualitative studies met criteria for inclusion in the review. Of the four PROMs identified by the review the condition specific AneurysmSRQ and AneurysmDQoL[23,24] appear to relate best to the themes identified in the qualitative review. No PROM included items on fear of rupture, death or ability to forget about the condition, despite all the qualitative studies identifying these as key issues for patients. Further work needs to be done to explore the psychometric properties of the current measures and whether additional items are needed.

Acknowledgement and Funding

We would like to thank Patrick Phillips, (School of Health and Related Research, University of Sheffield, Sheffield, UK), for providing assistance and advice.

This review presents independent research funded by the National Institute for Health Research (NIHR) under the Programme Grants for Applied Research programme (RP-PG-1210-12009). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

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Supplementary File

Appendix 1:

AAA Search Strategies: Search One

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1. (Aortic aneurysm$ or triple A or true aneurysm$).tw.
2. Aortic Aneurysm/
3. Aortic Aneurysm, Abdominal/
4. 1 or 2 or 3
5. (patient reported outcome$ or patient-reported outcome$).tw.
6. (prom or proms).tw.
7. (disease reported outcome$ or disease-reported outcome$).tw.
8. 5 or 6 or 7
9. "Quality of Life"/
10. "Outcome and Process Assessment (Health Care)"/
11. "Outcome Assessment (Health Care)"/
12. quality of life.tw.
13. qol.tw.
14. outcome measure$.tw.
15. health outcome$.tw.
16. or/9-15
17. (patient adj20 report$).tw.
18. 16 and 17
19. 8 or 18
20. nottingham health profile.tw.
21. health related quality of life.tw.
22. health related qol.tw.
23. health related ql.tw.
24. hrqol.tw.
25. hql.tw.
26. health state utilit$.tw.
27. hsuv$.tw.
28. (euroqol or euro qol or eq5d or eq 5d).tw.
29. (sf6d or sf 6d or sf 6 dimension$ or sf six dimension$ or shortform 6d or shortform six dimension$ or short form 6d or short form 6 dimension$ or short form six dimension$).tw.
30. (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
31. (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
32. (item adj3 short form).tw.
33. (item adj3 shortform).tw.
34. medical outcomes survey.tw.
35. medical outcomes study.tw.
36. mos.tw.
37. psychological general wellbeing index.tw.
38. psychological general well being index.tw.
39. pgwb$.tw.
40. health utilit$.tw.
41. hui$.tw.
42. quality of wellbeing.tw.

43. quality of well being.tw.
44. qwb$.tw.
45. rosser.tw.
46. trade off$.tw.
47. standard gamble$.tw.
48. tto$.tw.
49. qaly$.tw.
50. quality adjusted life year$.tw.
51. quality-adjusted life years/
52. hye$.tw.
53. health$ year$ equivalent$.tw.
54. disutilit$.tw.
55. disbenefit$.tw.
56. "Quality of Life"/
57. "Outcome Assessment (Health Care)"/
58. quality of life.tw.
59. 56 or 57 or 58
60. (preference based or utilit$ or generic preference).tw.
61. 59 and 60
62. (preference$ adj2 (elicit$ or patient$ or population$ or measure$ or based or cost$)).tw.
63. (utilit$ adj2 (elicit$ or patient$ or population$ or measure$ or based or cost$)).tw.
64. or/20-55
65. 61 or 62 or 63 or 64
66. 19 or 65
67. 4 and 66

AAA Search Strategies: Search Two

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
---
1. (Aortic aneurysm$ or triple A or true aneurysm$).tw.
2. Aortic Aneurysm/
3. Aortic Aneurysm, Abdominal/
4. or/1-3
5. time trade off.mp.
6. Watt index.mp.
7. (Rand-36 or Rand36 or Rand 36).mp.
8. self-assessed health.mp.
9. screenQL.mp.
10. general health questionnaire.mp.
11. female sexual function index.mp.
12. Rose questionnaire.mp.
13. Australian Vascular Quality of Life Index.mp.
14. AUSVIQUOL.mp.
15. Nottingham Health Profile.mp.
16. NHP.mp.
17. (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
18. (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).mp. [mp=title, abstract, original title, name of substance word,

subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
19. (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
20. (Hospital Anxiety and Depression Scale).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
21. HADS.mp.
22. Standard gamble$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
23. rosser.tw.
24. (euroqol or euro qol or eq5d or eq 5d or eq-5d or eq-5d VAS).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
25. World Health Organization Quality of Life-BREF.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
26. WHOQOL-BREF.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
27. or/5-26
28. instrumentation.sh.
29. methods.sh.
30. Validation Studies.pt.
31. Comparative Study.pt.
32. Psychometrics/
33. psychometr*.ti,ab.
34. clinimetr*.tw.
35. clinometr*.tw.
36. "Outcome Assessment (Health Care)"/
37. outcome assessment.ti,ab.
38. outcome measure*.tw.
39. Observer Variation/
40. observer variation.ti,ab.
41. Health Status Indicators/
42. "Reproducibility of Results"/
43. reproducib*.ti,ab.
44. Discriminant Analysis/
45. reliab*.ti,ab.
46. unreliab*.ti,ab.
47. valid*.ti,ab.
48. coefficient.ti,ab.
49. homogeneity.ti,ab.
50. homogeneous.ti,ab.
51. "internal consistency".ti,ab.
52. 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51
53. cronbach*.ti,ab.
54. (alpha or alphas).ti,ab.
55. 53 and 54

56. item.ti,ab.
57. (correlation* or selection* or reduction*).ti,ab.
58. 56 and 57
59. (agreement or precision or imprecision or "precise values" or "test–retest").ti,ab.
60. (test and retest).ti,ab.
61. reliab*.ti,ab.
62. (test or retest).ti,ab.
63. 61 and 62
64. 55 or 58 or 59 or 60 or 63
65. (stability or interrater or inter-rater or intrarater or intra-rater or intertester or inter-tester or intratester or intra-tester or interobserver or inter-observer or intraobserver or intra-observer).ti,ab.
66. (intertechnician or inter-technician or intratechnician or intra-technician or interexaminer or inter-examiner or intraexaminer or intra-examiner or interassay or inter-assay or intraassay or intra-assay or interindividual or inter-individual or intraindividual or intra-individual or interparticipant or inter-participant or intraparticipant or intra-participant).ti,ab.
67. (kappa or "kappa's" or kappas or repeatab*).ti,ab.
68. repeatab*.ti,ab.
69. 65 or 66 or 67 or 68
70. (replicab* or repeated).ti,ab.
71. (measure or measures or findings or result or results or test or tests).ti,ab.
72. 70 and 71
73. (generaliza* or generalisa* or concordance).ti,ab.
74. (intraclass and correlation*).ti,ab.
75. (discriminative or "known group" or factor analysis or factor analyses or dimension* or subscale*).ti,ab.
76. (multitrait and scaling and (analysis or analyses)).ti,ab.
77. 72 or 73 or 74 or 75 or 76
78. (item discriminant or interscale correlation* or error or errors or "individual variability").ti,ab.
79. (variability and (analysis or values)).ti,ab.
80. (uncertainty and (measurement or measuring)).ti,ab.
81. ("standard error of measurement" or sensitiv* or responsive*).ti,ab.
82. ((minimal or minimally or clinical or clinically) and (important or significant or detectable) and (change or difference)).ti,ab.
83. (small* and (real or detectable) and (change or difference)).ti,ab.
84. (meaningful change or "ceiling effect" or "floor effect" or "Item response model" or IRT or Rasch or "Differential item functioning" or DIF or "computer adaptive testing" or "item bank" or "cross-cultural equivalence").ti,ab.
85. 78 or 79 or 80 or 81 or 82 or 83 or 84
86. 52 or 64 or 69 or 77 or 85
87. 4 and 27 and 86

Databases and Research Registers which were searched:

- MEDLINE and MEDLINE In Process: Ovid.
- EMBASE: Ovid.
- Cochrane Library
    - Cochrane Database of Systematic Reviews (CDSR)
    - Database of Abstracts of Reviews of Effects (DARE)
    - Cochrane Central Register of Controlled Trials (CCRCT)
    - Health Technology Assessment Database (HTA)
    - NHS Economic Evaluation Database (NHS EED)
- CINAHL

- PROQOLID
- PsychINFO
- Science Citation Index Expanded (SCIE): Web of Science

AAA Qualitative Literature Review

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1 (Aortic aneurysm$ or triple A or true aneurysm$).tw.
2 Aortic Aneurysm/
3 Aortic Aneurysm, Abdominal/
4 or/1-3 (38292)
5 *Attitude to Health/
6 *Self Care/
7 *Health Knowledge, Attitudes, Practice/
8 (patient* adj4 (feeling* or emotion* or view* or symptom* or perception* or attribute*)).ti,ab.
9 ("health related quality of life" or "health related qol" or "health related ql" or hrqol or hql or "patient reported outcome*" or "patient-reported outcome*" or prom or proms or "disease reported outcome*").ti,ab.
10 ("quality of life" or "qol" or "outcome measure*" or "health outcome*").ti,ab.
11 *"Quality of Life"/
12 *"Outcome Assessment (Health Care)"/ or *"Outcome and Process Assessment (Health Care)"/
13 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14 (qualitative* or findings or interview*).mp.
15 focus groups/ or interviews as topic/
16 exp qualitative research/
17 14 or 15 or 16
18 14 or 15 or 16
19 4 and 13
20 17 and 19

****

Databases and Research Registers which were searched:

- MEDLINE and MEDLINE In Process: Ovid.
- EMBASE: Ovid.
- CINAHL: EBSCO
- PROQOLID
- PsychINFO
- Science Citation Index Expanded (SCIE): Web of Science
- Social Science Citation Index
- Proquest dissertation and theses

Appendix 2. Summary of the psychometric properties of generic and condition-specific PROMs in patients with an AAA.

PROM	Internal consistency	Test-retest	Content validity	Construct validity	Responsiveness	Floor/ ceiling	Acceptability
Generic PROMs							
SF-36							
Mangione (1997)[26]	+	0	0	+	+	-/+	0
Borchard (2006)[25]	0	-	0	-/+	0	0	?
AAA specific PROMs							
AUSVIQUOL							
Borchard (2006)[25]	0	-	+	?	0	0	?
Aneurysm-DQoL							
Peach (2014)[23,24]	0	0	+	0	0	0	0
Aneurysm-SRQ							
Peach (2014)[23,24]	0	0	+	0	0	0	0

Abbreviations: AUSVIQUOL, Australian Vascular Quality of Life Index; SF-36, Medical Outcomes Study 36-item Short Form.

N.B. Criterion validity not displayed.

Psychometric and operational criteria:

0	Not reported
-	Evidence not in favour
-/+	Weak evidence
+	Evidence in favour
?	Methodological/ reporting issues

Appendix 3. Summary of the methodological quality rated using the COSMIN of generic and condition specific PROMs in patients with an AAA.

Instrument	Internal consistency	Reliability	Measurement error	Content validity	Structural validity	Hypothesis testing	Responsive-ness
Generic PROMs							
SF-36 Mangione (1997)[26]	Poor	.	.	.	.	Good	Good
Borchard (2006)[25]	.	Poor	.	.	Poor	Poor	.
Specific PROMs							
AUSVIQUOL Borchard (2006)[25]	.	Poor	.	Excellent	Poor	Poor	.
Aneurysm-DQoL Peach (2014)[23,24]	.	.	.	Excellent	.	.	.
Aneurysm-SRQ Peach (2014)[23,24]	.	.	.	Excellent	.	.	.

Abbreviations: AUSVIQUOL, Australian Vascular Quality of Life Index; SF-36, Medical Outcomes Study 36-item Short Form.

N.B. Criterion validity not displayed and cross cultural validity not displayed.

Appendix 4: A summary of quotes from the qualitative review

Theme	Quotes
Symptoms	"All patients denied symptoms and did not experience the AAA at all: ''No, I do not have any problems at all; I do not feel it."[27] "During focus groups, patients reported a wide range of symptoms that they attributed to their aneurysm or its repair. The most common of these was pain, with leg pain, lower back pain, abdominal pain and buttock pain being the most common (reported in 7, 5, 4 and 4 groups respectively)."[24] "40% of interviewees reporting some upset in gastrointestinal function"[24] "I was extremely tired, so the first thing I did when I came home was to go to bed. The fatigue felt almost physical and it has taken so long to disappear. When I forced myself awake I got really unbearable."[28] "I slept very badly, I got sleeping pills. You know, there were more psychological issues afterwards (…) things that made one feel a bit anxious. What will happen later? Is everything going to heal as planned?"[28] Having more difficulties with other diseases or problems in life overshadows the awareness about AAA. The patients report that they compare the knowledge of having an AAA with other chronic conditions that they really worry about and suffer from in their daily lives. These conditions, e.g. pain, were significantly worse to live with."[27]
Functional outcomes	"Understanding the seriousness of the situation created distress while waiting for surgery and restricted daily life. Restrictions comprised travelling, heavy lifting and always making sure to be reachable by telephone"[28] "If your aneurysm bursts in the middle of the Atlantic, you're finished. So I don't travel because of that."[29]

Psychological outcomes	"I wasn't worried before, but last autumn, I was scared because my stomach was really upset and I had so much gas and stuff so I thought, well, the first thing you think of when you've got stomach pain is the aneurysm. I rang up and asked if I could come for an earlier check-up."[29] "I worked the whole time to distract my thoughts on what could happen before the surgery had been performed."[28] "ability to think clearly"[24] "if the aneurysm became larger, it was constantly on their minds, and thoughts arose about whether it might rupture or require surgery."[29] The texts also revealed a desire to influence, control, or do something to prevent the aneurysm from growing or rupturing. However, their questions about how to live their lives remained unanswered, leading to a feeling of resignation and fatalism."[24] "Understanding the seriousness of the situation created distress while waiting for surgery and restricted daily life."[28] "Preoperative anxiety was particularly prevalent, with participants mentioning this spontaneously in 8 of the 9 focus groups and describing feelings of having a 'ticking time-bomb inside'. Anxiety about surgical intervention was also noted."[24]
Social outcomes	. "Patients expressed that their families were worried and concerned about the threat the aneurysm posed to the patient and thereby also to the family circumstances."[29]