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35 **Abstract**

36 **Objectives:** The aim of this study was to identify themes that determine health-related
37 quality of life (HRQoL) in patients with carotid artery stenosis and identify the patient-
38 reported outcome measures that best cover the identified themes.

39 **Methods:** A systematic review of the main six databases was undertaken to identify primary
40 qualitative studies reporting on the HRQoL of patients with carotid artery stenosis. Quality of
41 studies was assessed using the CASP criteria. Findings from the included studies were
42 analysed using Framework Analysis methodology. The identified themes were mapped
43 against the items/domains from the patient-reported outcome measures used previously in
44 patients with carotid artery stenosis.

45 **Results:** The systematic review identified four papers that fulfilled the inclusion criteria. The
46 included papers reported the views of sixty-two patients with symptomatic carotid artery
47 stenosis; twenty-four of the patients were awaiting assessment for intervention, twenty-six
48 had carotid endarterectomy and twelve were turned down for intervention and received best
49 medical therapy. The overall quality of the included studies was good based on CASP
50 criteria. Framework Analysis identified sixteen themes that were divided into six main
51 domains: anxiety, impact on physical activity, effect on independence, impact on personal
52 roles, psychological impact and symptoms. The best fit generic and disease specific PROMs
53 were the Short-Form 36 (SF-36 ®) and the Carotid Stenosis Specific Outcome Measure
54 (CSSOM) respectively. None of the PROMs covered all the themes identified in the
55 qualitative systematic review.

56 **Discussion:** The findings from the review identified the important themes that affect patients
57 with carotid stenosis disease. The current generic and disease specific patient-reported
58 outcome measures do not cover all themes that impact the HRQoL of patients suffering with
59 this disease. The proposed themes can be used to develop a new disease specific PROMs
60 to measure HRQoL.

61 Introduction

62

63 Carotid artery stenosis (CAS) is a major cause of stroke, accounting for about 20% of all cases
64 **(1-2)**. It is caused by either carotid artery thrombosis or from embolism from carotid artery
65 lesion.

66 Patients with CAS can be asymptomatic or present with transient ischaemic attack (TIA) or
67 stroke. Evidence shows that patients who present with fatal or disabling stroke with previous
68 evidence of CAS can benefit from preventive procedures including carotid endarterectomy
69 (CEA) and stenting **(3-10)**; however, these procedures are not risk free and can be
70 complicated with perioperative stroke. The symptoms and the uncertainty of outcome can
71 impact the daily living of patients with CAS. Therefore, several clinical studies that investigated
72 the efficacy and safety of different preventative interventions used patient-reported outcome
73 measures (PROMs) to investigate the impact of the disease and treatment on health-related
74 quality of life (HRQoL). However, due to a lack of validated PROMs they either used generic
75 PROMs **(11-14)** or developed and used questionnaires without validation **(14)**.

76 Patients presenting with symptomatic and asymptomatic CAS need support to choose the
77 best treatment strategy to help reduce their risk of stroke and improve their HRQoL. Patients'
78 experience of disease and impact of treatment is a major indicator of quality and it is only
79 through better understanding of the impact of the disease on HRQoL that PROMs can be
80 developed. It is argued that PROMs, when designed carefully (e.g. based on input from
81 patients' experiences), can measure the issues of most importance to patients and any
82 changes to their HRQoL because of the disease or as consequence of the treatment they may
83 have received **(15)**.

84

85 The aim of this study was to systematically review the qualitative evidence to identify the
86 impact of CAS and treatment pathway on patients' HRQoL. The identified themes were then
87 mapped against the items and domains from the generic and disease specific PROMs we had

88 previously identified (16,17). The mapping was done to find the PROMs that captured the most
89 important issues to patients with CAS.

90 **Method**

91
92 The systematic review aimed to identify all primary qualitative research studies that
93 investigated the impact of CAS on HRQoL. The inclusion criteria included any patients with
94 CAS and any studies with undefined population were excluded. For further information
95 regarding the inclusion and exclusion criteria refer to **table 1**.

96 This systematic review was undertaken and reported in accordance with the general principles
97 recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses
98 (PRISMA) statement. In accordance with the study protocol (18), searches were conducted
99 from inception up to April 2017 in the following bibliographic databases; CINAHL via EBSCO,
100 Medline and Medline in Process via Ovid, Embase via Ovid, PsycINFO via Ovid, Social
101 Science Citation Index/ Science Citation Index via Web of Science (Thomson Reuters) and
102 Proquest dissertations and theses. No language or date constraints were applied.

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Table 1: Summary of the inclusion and exclusion criteria

Inclusion	Exclusion
Patients' experience of living with carotid artery stenosis and its impact on their health-related quality of life.	Studies not in English
A defined population of participants with a diagnosis of carotid artery stenosis (CAS) who need, have had or are undergoing surgical treatment. Participants undergoing treatment for stroke or transient ischaemic attack (TIA) secondary to a diagnosis of CAS.	Studies with participants under 16 years of age
Studies that include semi-structured interviews, descriptions, focus groups either as stand-alone studies or embedded in a quantitative study. Must include both data collection and data analysis	Patients with Stroke or TIA not related to CAS
Published or unpublished; Full-text or structured abstract with all relevant information	Quantitative studies with no primary qualitative data reported
	Full-text or structured abstract with incomplete or unclear evidence

The search strategy combined condition terms, terms for patient views and terms for qualitative studies (which augmented a qualitative study filter) (19). Further details of the search strategy are provided in **Appendix 1** (supporting information).

Study selection

The search results were uploaded into Endnote X8™ (Thomson Reuters, Philadelphia, USA), two reviewers (AA, AH) independently screened the titles for inclusion and exclusion in accordance with the set criteria in the protocol. All titles were examined, and any citations that clearly did not meet the inclusion criteria (for example mixed population, quantitative PROMs data) were excluded. For included titles, abstracts were read and for the included abstracts, full-text articles were obtained.

151 **Quality assessment**

152 The Critical Appraisal Skills Program (CASP) qualitative checklist instrument was used to
153 examine the methodological quality of the included studies (20). This was selected for its
154 appropriateness as it is commonly used in qualitative reviews of evidence (21). Two of the
155 authors (AA, AH) independently examined the quality of each study and any inconsistencies
156 were resolved by discussion or involving a third author (GJ).

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158

159 **Data extraction and analysis**

160 The data on authors, year of publication, country of study, number of participants, research
161 aims, methods of recruitment, method of data collection, key results and analysis were
162 extracted and tabulated for all the included studies by the first author. The included papers
163 were uploaded into the qualitative data analysis software NVivo10 (QSR International,
164 Doncaster, Victoria, Australia) and the primary and secondary text (patient quotes reported in
165 the articles and themes), were analysed. The inductive process of framework analysis was
166 used since in a previous review (17); the PROMs used for this condition were examined for
167 their validity and their conceptual domains were used to give a basis for the qualitative data
168 synthesis (22). The first stage of the framework analysis was reading all the included papers
169 and identifying common themes from within and across the articles. The second stage
170 involved establishing a thematic framework by creating an initial coding scheme for the main
171 themes; and then making an index of themes. In the third stage the thematic framework was
172 applied to all the primary and secondary data. In the final stage themes were examined for
173 their conceptual similarities and differences (Mapping and interpretation stage). The second
174 author (AH) checked all the themes that were identified and differences in conceptualization
175 were discussed and adjusted involving a third senior author (GJ).

176

177 **Triangulation of PROMs items with qualitative themes**

178 A triangulation of evidence was performed to examine how the items within generic and
179 disease specific PROMs corresponded to themes from the qualitative review (23,24). The
180 items from generic and disease specific PROMs used in patients with CAS (17) were
181 examined in detail. The items from these instruments were mapped against the themes
182 identified, and two researchers (AA, AH) reviewed both the themes from the qualitative review
183 and the items/ from each PROM to evaluate whether the concepts were the same
184 (agreement), offered similar concepts (partial agreement) or were not present (silence). The
185 aim was to identify whether any of the instruments covered the issues that are important to
186 patients with carotid artery disease.

187 **Results**

188

189 The database searches identified 1095 citations; after removing duplicates, 874 titles were
190 assessed and subsequently fifteen full-text papers were reviewed in detail. Finally, only four
191 papers fulfilled the inclusion criteria and were included in the qualitative evidence synthesis
192 **(Please see PRISMA chart (Figure 1))**. The studies included in the qualitative synthesis are
193 summarized in table 2.

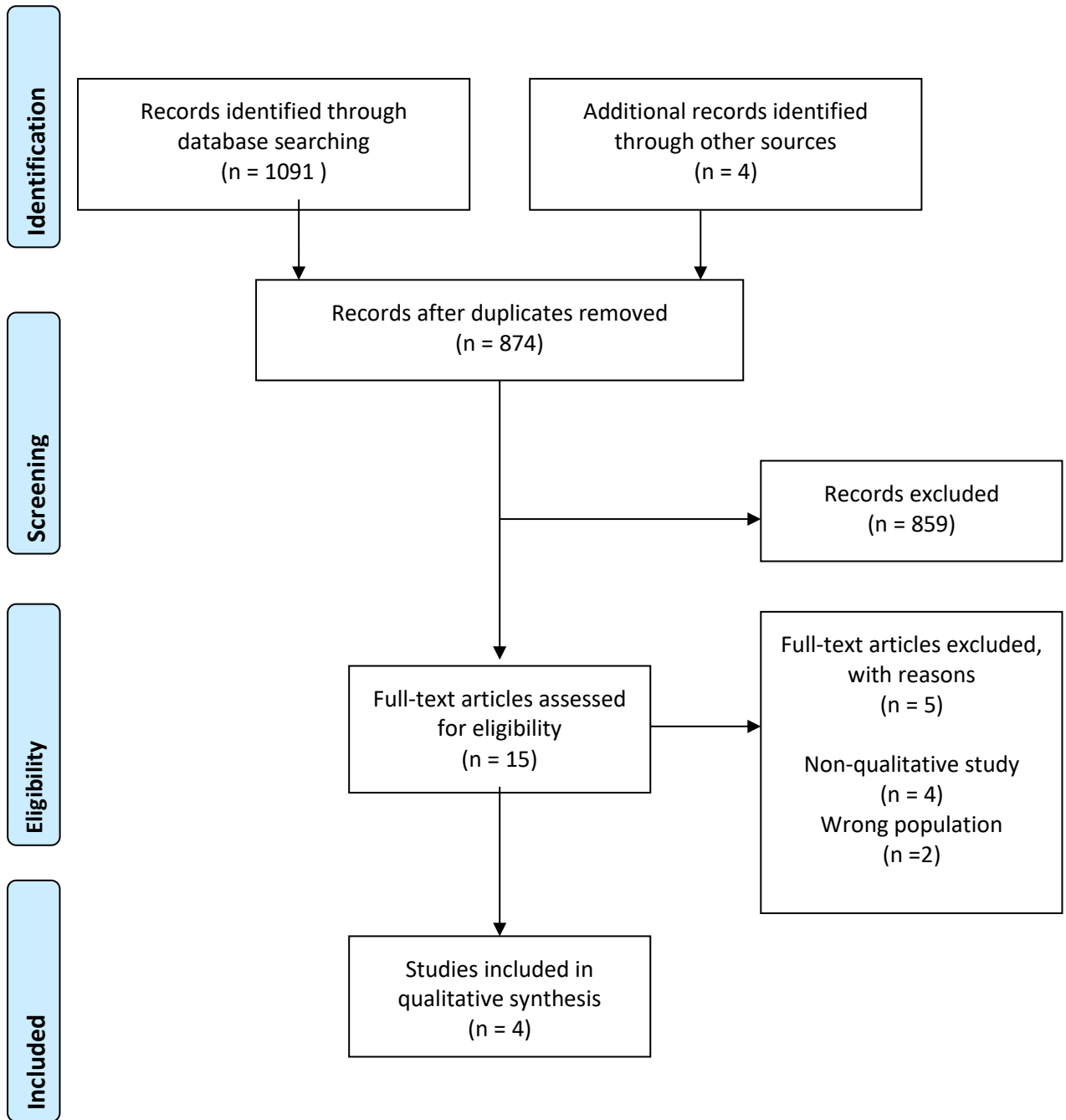
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Table 2. Qualitative studies exploring living with carotid artery stenosis

Author (Year)	Country	Research Design	Method of Analysis	Age (years)	Sample	Diagnosis /Treatment	Study Aims and Objectives
Gibson (2002)	UK	Qualitative semi-structured interviews	Grounded Theory	Age, mean 70.9 (50-79)	6 Participants Male (%): 50	Symptomatic carotid stenosis Medical management: 1 Post CEA: 5	Explore ways in which patients comprehend and live with risk of CEA or medical management only for carotid stenosis.
Halin <i>et al.</i> (2002)	Sweden	Mixed methods including a qualitative component using semi-structured interviews	Thematic analysis	Age, mean 71 (56-80)	20 Participants Male (%): 60	Symptomatic carotid stenosis Medical management, no intervention: 1 Post CEA: 11 Pre-CEA or Stent: 8	Assess quality of life of patients with carotid artery stenosis
Gibson & Watkins (2012)	UK	In-depth interviews	Grounded Theory	Age, Mean 71.6(50-80)	16 Participants Male (%): 65	Symptomatic carotid stenosis	Explore the lived experience of patients with TIA secondary of carotid stenosis
Gibson & Watkins (2013)	UK	In-depth semi-structured interviews	Thematic analysis	Age, mean 70.2 (50-80)	20 Participants Male (%): 65	TIA/Recovered stroke Post CEA: 10 Medical management: 10	To examine the use of formal and informal knowledge by patients in making decisions about (CEA) and medical treatment after TIA/ recovered stroke caused by carotid stenosis

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Figure 1. PRISMA Diagram: CS Qualitative Systematic Review



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277 Three of the included studies were from the UK (25, 27-28) and one from Sweden (26). The
278 studies were published between 2002 and 2013; the age of patients with carotid artery
279 disease in the included studies ranged from 50-80 years, and the percentage of male
280 participants was 50-65%. The included studies reported the views of sixty-two patients with
281 twenty-four of the patients awaiting assessment for surgery, twenty-six had surgery and
282 twelve were turned down for intervention and received best medical therapy.

283

284 **Quality assessment**

285 The overall quality of the included studies was good, and all the studies scored “yes” for
286 almost all the criteria set in the CASP checklist (10); Only one study scored ‘can’t tell’ on the
287 rigour of the data analysis (25). For further detail on the quality of the included studies see
288 appendix 2.

289 **Analysis**

290 The Framework Analysis of the primary and secondary data of the included papers identified
291 sixteen themes. These were divided into six main domains comprising; anxiety, impact on
292 personal roles, impact on physical activity, impact on social activity, psychological impact and
293 symptoms. Please see Table 3 for further details.

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Table 3: Themes identified from qualitative research studies of patients with carotid artery stenosis.

Themes (Domains in bold font)	Gibson (2002)	Halin <i>et al.</i> (2002)	Gibson & Watkins (2012)	Gibson & Watkins (2013)
Anxiety				
Fear of stroke	√	√	√	√
Fear of becoming a burden	√	√	√	√
Fear of operation	√	√		√
Uncertainty about future	√	√	√	√
Impact on personal roles & activities	√	√	√	√
Impact on physical functioning	√		√	√
Effect on independence	√	√	√	√
Psychological impact				
Happiness	√		√	√
Health perception	√			
Symptoms				
Weakness			√	
Numbness or loss of sensation			√	
Loss of ability to speak			√	
Loss of vision			√	
Cognitive function			√	
Duration of symptoms			√	
Neck stiffness	√		√	

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312

313 **Anxiety**

314

315 The anxiety domain had several themes including fear of stroke, fear of becoming a burden,

316 worry and uncertainty and fear from consequences of the operation. These four themes were

317 grouped together because of overlapping. The impact of anxiety on daily living of patients

318 suffering with CAS featured in all four studies. Patients experiencing symptoms of transient

319 ischaemic attack (TIA) secondary to CAS expressed concern about fear of stroke, patients

320 said:

321 "I'm afraid of having a stroke and then becoming paralysed" (Pre-operative patient,
322 age not reported) **(26)**

323 "I'd be worrying a lot, yes, wondering when or where or how it (stroke) was going to
324 happen...it would be in the back of my mind...which takes some of the pleasure out of life."
325 (Patient experienced TIA –before CEA) **(27)**

326 "Well, I wouldn't like to be here and have one (stroke) on my own." (*Patient*
327 *experienced TIA –before CEA*) **(25)**

328

329 Two of the major causes for worry from having symptomatic CAS that can cause stroke were
330 uncertainty and fear of becoming a burden. Participants in the included studies reported
331 feeling that their life was put on hold and many were worried that a disabling stroke may make
332 them a burden on others including their family members.

333 "It's the unknown isn't it, that's what makes you fearful, you don't know what's going
334 to happen." (patient after the CEA reflecting on experiences prior to the surgery) **(25)**

335 "I'm afraid of becoming dependent on care" (Pre-operative patient) **(26)**

336

337 The uncertainty about the future and fear of sudden stroke was affecting patients treated with
338 best medical therapy when compared to patients treated with preventive procedures such as
339 CEA or stenting **(27)**. Another source of anxiety was the worry from complications of surgery
340 including death or stroke. Many patients' perceptions about the risk of stroke or death from
341 the preventive procedures were exaggerated **(25)**. Furthermore, many patients had an
342 inaccurate recall of the risks of treatment options offered to them **(25)**.

343 "if somebody tells you there's a 50% chance of having a stroke (without surgery)
344 that's in your mind all the time" (patient after the CEA reflecting on experiences prior to the
345 surgery) **(25)**

346

347 "You're damned if you do and damned if you don't, I mean I'd have a stroke if I didn't
348 have it, and I might have the stroke under the operation." (Patient experienced TIA –before
349 CEA) **(25)**

350

351 Patients with successful revascularisation reported improved psychological wellbeing and
352 felt that they could move on with their lives compared to the time prior to their procedure
353 when they felt that their daily livings were overshadowed by the worry associated with the
354 CAS diagnosis and possible stroke **(25)**.

355 "I'm a happier person, physically and emotionally." (patient after the CEA reflecting on
356 experiences prior to the surgery) **(25)**

357 **Impact on Personal Roles & Activities**

358

359 Some participants in the included studies described the onset of symptomatic CAS to have
360 put a hold on their life and without the preventative surgery, they would have not been able
361 to carry on with their personal roles and daily activities **(25)**. Some patients took many
362 measures in their daily living to avoid activities that they perceived may increase their risk of
363 further TIA or major stroke. For instance, some patients made changes to their diet **(26)**.

364 One patient said:

365

366 "I'd have been worried about having a stroke, it curtailed my activities" (Post-
367 operative patient) **(26)**

368

369 **Impact on Physical Functioning**

370

371 Participants in three included studies described varying impacts on their ability to care for
372 themselves independently **(25,27-28)**. The anxiety associated with further TIA or strokes as
373 well as residual symptoms of strokes had an impact on the physical functioning of the
374 patients **(25)**. Some changes were advised by doctors, while other changes were made
375 spontaneously by patients **(26-27)**. Patients also suggested that the symptomatic CAS
376 causing TIA dramatically changed their perception about their physical health, Furthermore,
377 attitude of family and friend reinforced this view of diminished physical function **(27)**.

378 "I've always kept my health...this has absolutely shattered me." (Patient experienced
379 TIA) **(27)**

380 “you’re not as fit as you thought you were, everybody’s always telling me to be
381 careful, and have a rest...people around me have sort of convinced me that I’m a bit
382 fragile...” (Patient experienced TIA) **(27)**.

383 **Effect on Independence**

384
385 All the included studies reported that patients suffering with CAS felt that their social life and
386 independence were compromised because of the disease and potential consequences.
387 Patients expressed concerns about the impact of the disease and possible consequences of
388 on their independence.

389 “I’m afraid of becoming paralysed and dependent on care” (patient reporting after
390 surgery) **(25)**
391

392 “I’ m enjoying life and I want it to go on, without having a stroke” (patient reporting
393 after surgery) **(28)**
394
395

396 **Psychological Impact**

397
398 Patients suffered with issues related to their health perception; the diagnosis had adverse
399 consequences for many patients; with some reporting that they felt their daily life is being
400 shattered with the new diagnosis **(27)**.

401 Some patients developed low mood when they understood the risks associated with their
402 disease, however, on the other hand, patients who had the operation and did not experience
403 any complications reported that they felt happier emotionally because of dealing with a
404 potentially significant disease that made them felt unhappy **(25, 27-28)**. One patient
405 reported:

406 “I’m a happier person, physically and emotionally.” (patient reporting after
407 surgery) **(25)**
408

409 **Symptoms**

410

411 The symptomatic outcomes that were reported by the patients could be divided broadly into
412 three main groups: symptoms associated with TIA and post-intervention symptoms. Patients
413 experiencing TIA reported classical symptoms including loss of sensation, weakness,
414 temporary loss of ability to speak and loss of vision **(27)**.

415 "I couldn't pick anything up at all, I had great difficulty in using the knife and
416 fork...and then suddenly it came back."(Patient reporting TIA symptoms) **(27)**

417 "I just thought a film had come over my eye." (Patient reporting TIA symptoms) **(27)**

418

419 Patients described symptoms of neck pain and discomfort at the site of operation to treat
420 CAS following CEA **(25)**.

421 "...did feel better, apart from residual minor discomfort from surgical incision
422 pain and neck stiffness." (patient reporting after surgery) **(25)**
423

424 Lastly, some patients described loss of cognitive function that was noticeable by their family
425 and caused concern for the patient **(25)**.

426 "I have difficulties taking part in advanced discussions"(patient with carotid artery
427 stenosis) **(25)**

428 **Triangulation**

429 The identified themes were compared to items from PROMs that were identified in a recent
430 study **(17)**. These PROMs include the carotid artery disease quality of life questionnaire
431 developed by the Carotid revascularisation Enarterectomy vs. Stenting Trial group (CREST
432 Randomised controlled trial), Carotid Stenosis Specific Outcome Measure developed by
433 Ivanova et al **(28)**, Dizziness Handicap Inventory (DHI), Hospital Anxiety and Depression
434 Scale (HADS), EuroQoL-5D (EQ-5D), and the Short-Form 36 (SF-36®). Two reviewers (AA,
435 AH) examined the overlap between the themes in the qualitative review and items in the
436 PROMs. When there was complete overlap between the theme and an item in an instrument
437 an agreement score (+) was awarded; however, when the theme is covered in a general
438 question a partial agreement score was awarded (+/-).

439 None of the identified PROMs covered important HRQoL themes such as fear of stroke or fear
440 from the operation as well as uncertainty about future caused by the diagnosis of the disease
441 as well as the symptoms. Many of the symptoms described in the qualitative evidence
442 synthesis of this study were not included in the PROMs used previously. The generic PROM
443 that captured most of the important issues for patients with CAS was the SF-36 ® and the
444 disease specific PROM was the PROMs for carotid artery disease developed by Ivanova et al
445 (28). However, both PROMs did not cover all the themes identified in this review. For further
446 details on the results of triangulation see table 4.

447 **Table 4: Themes identified from the qualitative review mapped against items of**
448 **validated PROMs**

Themes	CREST trial PROMs	CSSOM	DHI	HADS	EQ-5D	SF-36
Anxiety	-	+	+/-	+	+	+
Fear of stroke	-	-	-	-	-	-
Fear of becoming a burden	-	+	-	-	-	-
Fear of operation	-	-	-	-	-	-
Uncertainty about future	-	-	-	-	-	-
Impact on personal roles & activities	-	+	+	+/-	-	-
Impact on physical functioning	+/-	+	+/-	-	+/-	+
Effect on Independence	-	-	+/-	-	-	-
Psychological impact	-	+	+	+	+/-	+
Happiness	-	+	+	+	-	+
Health Perception	-	-	-	-	-	-
Symptoms	+/-	+	+	-	-	-
Weakness	-	+	+/-	-	-	-
Numbness or loss of sensation	-	+	-	-	-	-
Loss of ability to speak	-	-	-	-	-	-
Loss of vision	-	+	-	-	-	-
Cognitive function	-	+	-	-	-	-
Duration of symptoms	-	-	-	-	-	-
Neck Stiffness	+	+	-	-	-	-
<p>Abbreviations: Carotid revascularisation Enarterectomy vs. Stenting Trial (CREST Randomised controlled trial), Dizziness Handicap Inventory (DHI), Hospital Anxiety and Depression Scale (HADS), EuroQoL-5D (EQ-5D), and Medical outcomes study 36-item short form (SF-36 ®), Carotid Stenosis Specific Outcome Measure (CSSOM).</p> <p>Scores: -, silence; +/-, partial agreement; +, agreement.</p>						

450 **Discussion**

451

452 We identified six domains that impacted upon the HRQoL of patients with CAS throughout
453 their care pathway. These include anxiety, impact of the disease on personal roles/ activities,
454 impact on physical functioning, impact on social functioning, psychological impact, and
455 symptoms associated with it.

456 The HRQoL of patients with CAS undergoing either revascularisation or best medical
457 therapy have only been measured using generic PROMs, anxiety specific PROMs and
458 questionnaires developed by clinicians with no validation (RCT) **(5-11)**. A single RCT
459 attempted to develop a disease specific PROM for patients with CAS **(11)** however, the
460 instrument was made of the six items suggested by clinicians and, more importantly, patients
461 were not consulted. Furthermore, there was no further validation for this PROM.

462 Outcome measures, such as 30-days mortality, stroke free survival and re-stenosis have
463 been used to compare outcomes between different interventions, as well as best medical
464 therapy for patients with symptomatic and asymptomatic CAS, although these are important
465 outcomes, however, HRQoL, if measured with a comprehensive and valid PROMs can be a
466 valuable measure of outcomes and help both patients and decision makers when deciding
467 on treatment strategies for CAS in the future. The themes from this review can be used to
468 develop a more tailored PROM that can be used in routine clinical practice both to inform
469 discussion between patients and clinicians, as well as, a quality measure of the carotid
470 revascularisation service.

471

472 One of the strengths of this study is that the qualitative review included patients at different
473 stages of their care pathway including sixty-**two** patients with symptomatic carotid artery
474 stenosis; twenty-four of the patients waiting for to meet a clinician to decide whether they are
475 suitable for surgery or stenting, twenty-six patients had carotid endarterectomy with no
476 complications and twelve patients turned down for surgical or interventional radiology
477 procedures. This review used the evidence from the systematic review **(11)** conducted by

478 the same group to evaluate the validity of PROMs used in patients with CAS, this was done
479 to examine the validation evidence for PROMs used in patients with CAS. In the triangulation
480 section of this study the themes from the qualitative review were mapped against the items
481 from the generic and disease specific CAS PROMs that were identified.

482

483 The main limitation of this study is that it relies on the primary and secondary data of existing
484 studies; the samples in one of these studies have been grouped together prior to the
485 operation whereas others included patients along the care pathway, this paper provided the
486 main source for the TIA symptoms themes **(27)**. Furthermore, the studies examined other
487 aspects of treatment including decision making about management and covered aspects of
488 HRQoL during these studies. Additionally, few patients who were treated with best medical
489 therapy or turned down for revascularisation were included in any of the studies. The
490 included papers did not distinguish clearly between patients with resolved stroke symptoms
491 and TIA. Some papers mentioned important themes such as denial of diagnosis and
492 depression but failed to report any primary evidence to support these themes **(27, 28)**.

493

494 Amongst some clinical academic circles HRQoL has confusingly come to be known as
495 anything which is not clinical **(30)**. However, this study demonstrates that, when patients with
496 CAS are asked, the distress related to diagnosis and the risks associated with intervention
497 and lack thereof is integral to this. The review identified anxiety to be an important domain
498 that impacts the HRQoL of patients with CAS and this is related to fear of stroke, uncertainty
499 about future, fear of becoming a burden on others and fear of operation. The disease also
500 had an impact of on the patient independence, physical as well as personal functioning and
501 beyond anxiety had further psychological impact on patients.

502 The findings of this study combine the available qualitative evidence on the impact of CAS
503 and its associated treatments on the patients' HRQOL. One of the strongest finding of this
504 study is that none of the generic and disease specific PROMs covered all the important
505 issues for CAS patients revealed by this qualitative systematic review. The identified themes

506 can be used to develop a disease specific PROM and this instrument can be validated in
507 future clinical studies or service improvement surveys.

508

509 **“Data Availability Statement”**

510 The analysis data cannot be shared since some of the papers included in the systematic
511 review have copy rights and these prohibit publishing them in other journals but allow
512 researchers to use them for secondary analysis. These papers were uploaded into the
513 software in which we performed the analysis. Supplementary materials are included
514 regarding the search strategy and analysis.

515 **Compliance with Ethical Standards**

516 **Acknowledgment**

517

518 Ahmed Aber contributed to the analysis and interpretation of data, drafting of the manuscript,
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520 drafting of the manuscript; Helen Buckley Woods performed the searches for the systematic
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530 **Conflict of interest**

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534

535 **Abbreviations**

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537 CASP: Critical Appraisal Skills Program, CREST: Carotid revascularisation Endarterectomy

538 vs. Stenting Trial, DHI: Dizziness Handicap Inventory, HADS: Hospital Anxiety and

539 Depression Scale, EQ5D: EuroQoL-5D, SF-36®: Medical outcomes study 36-item short

540 form, CAS: Carotid artery stenosis, CEA: carotid endarterectomy, PROMs: patient reported

541 outcome measures, HRQOL: health-related quality of life, PRISMA: Preferred Reporting

542 Items for Systematic Reviews and Meta-Analyses, TIA: transient ischaemic attack, Carotid

543 Stenosis Specific Outcome Measure (CSSOM).

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