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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 from inception to September 2018
40 was undertaken to identify primary qualitative studies reporting on the HRQoL of patients
41 with carotid artery stenosis. Quality of studies was assessed using the CASP criteria.
42 Findings from the included studies were analysed using Framework Analysis methodology.
43 The identified themes were mapped against the items/domains from the patient-reported
44 outcome measures used previously in 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 **Conclusion:** 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 **Key Points**

62 **Carotid artery disease is the main cause of stroke; some patients with this disease**
63 **can benefit from surgical intervention to reduce the risk of future stroke.**

64
65
66 **Understanding and measuring quality of life in these patients can guide intervention**
67 **decisions.**

68
69 **This systematic review provides detailed overview of the impact of this disease on**
70 **quality of life**

71

72 **Introduction**

73

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

76 Patients with CAS can be asymptomatic or present with transient ischaemic attack (TIA) or
77 stroke. Evidence shows that patients who present with disabling stroke with previous
78 evidence of CAS can benefit from preventive procedures including carotid endarterectomy
79 (CEA) and stenting **(3-10)**; however, these procedures are not risk free and can be
80 complicated with perioperative stroke. The symptoms and the uncertainty of outcome can
81 impact the daily living of patients with CAS. Therefore, several clinical studies that
82 investigated the efficacy and safety of different preventative interventions used patient-
83 reported outcome measures (PROMs) to investigate the impact of the disease and treatment
84 on health-related quality of life (HRQoL). However, due to a lack of validated PROMs they
85 either used generic PROMs **(11-14)** or developed and used questionnaires without validation
86 **(14)**.

87 Patients presenting with symptomatic and asymptomatic CAS need support to choose the
88 best treatment strategy to help reduce their risk of stroke and improve their HRQoL. Patients'
89 experience of disease and impact of treatment is a major indicator of quality and it is only
90 through better understanding of the impact of the disease on HRQoL that PROMs can be
91 developed. It is argued that PROMs, when designed carefully (e.g. based on input from
92 patients' experiences), can measure the issues of most importance to patients and any

93 changes to their HRQoL because of the disease or as consequence of the treatment they
94 may have received (15).

95

96 The aim of this study was to systematically review the qualitative evidence to identify the
97 impact of CAS and treatment pathway on patients' HRQoL. The identified themes were then
98 mapped against the items and domains from the generic and disease specific PROMs we
99 had previously identified (16,17). The mapping was done to find the PROMs that captured
100 the most important issues to patients with CAS.

101 **Method**

102

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

107 This systematic review was undertaken and reported in accordance with the general
108 principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-
109 Analyses (PRISMA) statement. In accordance with the study protocol (18), searches were
110 conducted from inception up to April 2017 and further updated to September 2018, in the
111 following bibliographic databases; CINAHL via EBSCO, Medline and Medline in Process via
112 Ovid, Embase via Ovid, PsycINFO via Ovid, Social Science Citation Index/ Science Citation
113 Index via Web of Science (Thomson Reuters) and Proquest dissertations and theses. No
114 language or date constraints were applied.

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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 Patients with Stroke or TIA not related to CAD
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	Quantitative studies with no primary qualitative data reported
Published or unpublished; Full-text or structured abstract with all relevant information	Full-text or structured abstract with incomplete or unclear evidence

Table 1: Summary of the inclusion and exclusion criteria

161

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

165

166 **Study selection**

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

173

174 **Quality assessment**

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

180

181

182 **Data extraction and analysis**

183 The data on authors, year of publication, country of study, number of participants, research
184 aims, methods of recruitment, method of data collection, key results and analysis were
185 extracted and tabulated for all the included studies by the first author. The included papers
186 were uploaded into the qualitative data analysis software NVivo10 (QSR International,
187 Doncaster, Victoria, Australia) and the primary and secondary text (patient quotes reported

188 in the articles and themes), were analysed. The inductive process of framework analysis was
189 used for the qualitative evidence synthesis. In another systematic review (17); the PROMs
190 used for this condition were examined for their validity; their conceptual domains were used
191 to give a basis for the qualitative data synthesis (22). The first stage of the framework
192 analysis was reading all the included papers and identifying common themes from within and
193 across the articles. The second stage involved establishing a thematic framework by
194 creating a list of the main themes based on the domains of validated PROMs and common
195 themes in the identified papers. In the third stage the thematic framework was applied to all
196 the primary and secondary data. In the final stage themes were examined for their
197 conceptual similarities and differences. The second author (AH) checked all the themes that
198 were identified and differences in conceptualization were discussed and adjusted involving a
199 third senior author (GJ).

200

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

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

211 **Results**

212

213 The database searches identified 1,095 citations; after removing duplicates, 859 titles were
214 assessed and subsequently fifteen full-text papers were reviewed in detail. Finally, only four

215 papers fulfilled the inclusion criteria and were included in the qualitative evidence synthesis
 216 **(Please see PRISMA chart (Figure 1))**. The studies included in the qualitative synthesis are
 217 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) (25)	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) (26)	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) (27)	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) (28)	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

Abbreviations: Carotid revascularisation Enarterectomy (CEA), Transient ischaemic attack (TIA)

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231 Figure 1. PRISMA Diagram: CS Qualitative Systematic Review

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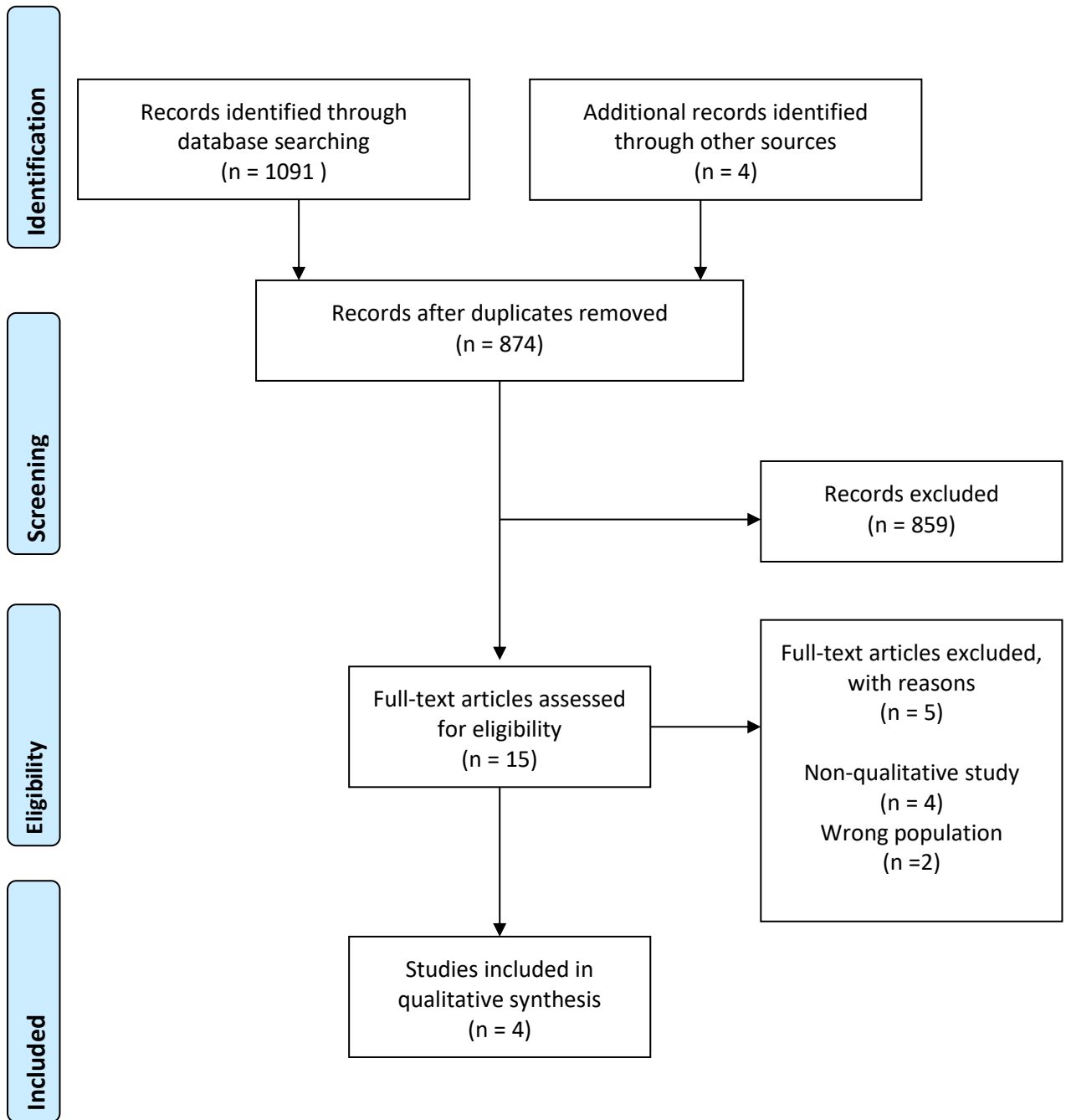
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277 Three of the included studies were from the UK (**25, 27-28**) and one from Sweden (**26**). The
278 studies were published between 2002 and 2013; the age of patients with carotid artery
279 disease in the included studies ranged from 50-80 years, 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 quality of the included studies was assessed independently by two authors (AA, AH)
286 using the CASP checklist (**10**) for qualitative studies, any disagreement on the final score
287 was resolved through discussion and/or involving a third senior author (GJ). The overall
288 quality of the included studies was good, and all the studies scored “yes” for almost all the
289 criteria set in the CASP checklist; Only one study scored ‘can’t tell’ on the rigour of the data
290 analysis (**25**). For detail on the quality of the included studies see table 3.

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301 **Analysis**

302 The Framework Analysis of the primary and secondary data of the included papers identified
 303 sixteen themes. These were divided into five main domains comprising; anxiety, impact on
 304 personal roles, effect on independence, psychological impact and symptoms. Please see
 305 Table 4 for further details.

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Table 4: 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	√	√	√	√
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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321 **Anxiety**

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323 The anxiety domain had several themes including fear of stroke, fear of becoming a burden,
324 worry and uncertainty and fear from consequences of the operation. These four themes
325 were grouped together because of overlapping. The impact of anxiety on daily living of
326 patients suffering with CAS featured in all four studies. Patients experiencing symptoms of
327 transient ischaemic attack (TIA) secondary to CAS expressed concern about fear of stroke,
328 patients said:

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

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

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

336

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

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

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

344

345 The uncertainty about the future and fear of sudden stroke was affecting patients treated
346 with best medical therapy when compared to patients treated with preventive procedures
347 such as CEA or stenting **(27)**. Another source of anxiety was the worry from complications
348 of surgery including death or stroke. Many patients' perceptions about the risk of stroke from

349 the preventive procedures were disproportionate **(25)**, some patients thought that their risk of
350 stroke from the surgery was 50% and this higher than the 2% reported by clinical studies
351 **(3,4)**. Furthermore, many patients had an inaccurate recall of the risks of treatment options
352 offered to them **(25)**.

353 “if somebody tells you there’s a 50% chance of having a stroke (without surgery)
354 that’s in your mind all the time” (patient after the CEA reflecting on experiences prior to the
355 surgery) **(25)**

356

357 “You’re damned if you do and damned if you don’t, I mean I’d have a stroke if I didn’t
358 have it, and I might have the stroke under the operation.” (Patient experienced TIA –before
359 CEA) **(25)**

360

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

365 “I’m a happier person, physically and emotionally.” (patient after the CEA reflecting on
366 experiences prior to the surgery) **(25)**

367 **Impact on Personal Roles & Activities**

368

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

374 One patient said:

375

376 “I’d have been worried about having a stroke, it curtailed my activities” (Post-
377 operative patient) **(26)**

378

379 The anxiety associated with further TIA or strokes as well as residual symptoms of strokes
380 had an impact on the physical functioning of the patients **(25)**.Patients also suggested that

381 the symptomatic CAS causing TIA dramatically changed their perception about their physical
382 health, Furthermore, attitude of family and friend reinforced this view of diminished physical
383 function (27).

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

386 "you're not as fit as you thought you were, everybody's always telling me to be
387 careful, and have a rest...people around me have sort of convinced me that I'm a bit
388 fragile..." (Patient experienced TIA) (27).

389 **Effect on Independence**

390
391 All the included studies reported that patients suffering with CAS felt that their social life and
392 independence were compromised because of the disease and potential consequences.

393 Patients expressed concerns about the impact of the disease and possible consequences of
394 on their independence.

395 "I'm afraid of becoming paralysed and dependent on care" (patient reporting after
396 surgery) (25)
397

398 "I'm enjoying life and I want it to go on, without having a stroke" (patient reporting
399 after surgery) (28)

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401

402 **Psychological Impact**

403

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

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

412 "I'm a happier person, physically and emotionally." (patient reporting after
413 surgery) **(25)**
414

415 **Symptoms**

416

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

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

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

424

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

427 "...did feel better, apart from residual minor discomfort from surgical incision
428 pain and neck stiffness." (patient reporting after surgery) **(25)**
429

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

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

434 **Triangulation**

435 The identified themes were compared to items from PROMs that were identified in a recent
436 study **(17)**. These PROMs include the carotid artery disease quality of life questionnaire
437 developed by the Carotid revascularisation Enarterectomy vs. Stenting Trial group (CREST
438 Randomised controlled trial), Carotid Stenosis Specific Outcome Measure developed by
439 Ivanova et al **(28)**, Dizziness Handicap Inventory (DHI), Hospital Anxiety and Depression
440 Scale (HADS), EuroQoL-5D (EQ-5D), and the Short-Form 36 (SF-36 ®). Two reviewers

441 (AA, AH) examined the overlap between the themes in the qualitative review and items in
 442 the PROMs. When there was complete overlap between the theme and an item in an
 443 instrument an agreement score (+) was awarded; however, when the theme is covered in a
 444 general question a partial agreement score was awarded (+/-).

445

446

447 **Table 5: 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	-	+	+	+/-	-	-
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>						

449

450

451

452 None of the identified PROMs covered important HRQoL themes such as fear of stroke or
453 fear from the operation as well as uncertainty about future caused by the diagnosis of the
454 disease. Many of the symptoms described in the qualitative evidence synthesis of this study
455 were not included in the PROMs used previously. The generic PROM that captured most of
456 the important issues for patients with CAS was the SF-36 ® and the disease specific PROM
457 was the PROMs for carotid artery disease developed by Ivanova *et al* (28). However, both
458 PROMs did not cover all the themes identified in this review. For further details on the results
459 of triangulation see table 5.

460

461 Discussion

462

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

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

473 Clinical outcomes such as 30-days mortality, stroke-free survival, and re-stenosis have been
474 used to compare the efficacy of surgical, radiological and medical therapies for patients with
475 CAS. These are important outcomes, however, HRQoL, when measured using a validated
476 PROM can provide comprehensive data about the impact of different therapies. The themes
477 from this review can be used to develop a more tailored PROM that can be used in routine

478 clinical practice both to inform discussion between patients and clinicians, as well as, a
479 quality measure of the carotid revascularisation service.

480

481 One of the strengths of this study is that the qualitative review included patients at different
482 stages of their care pathway including sixty-**two** patients with symptomatic carotid artery
483 stenosis; twenty-four of the patients waiting for to meet a clinician to decide whether they are
484 suitable for surgery or stenting, twenty-six patients had carotid endarterectomy with no
485 complications and twelve patients turned down for surgical or interventional radiology
486 procedures. This review used the evidence from an earlier systematic review **(11)** by the
487 same group to evaluate the validity of PROMs used in patients with CAS. This earlier
488 systematic review was performed to examine the psychometric validation evidence for
489 PROMs used in patients with CAS. In the triangulation section of this study the themes from
490 the qualitative review were mapped against the items from the generic and disease specific
491 CAS PROMs that were identified.

492

493 The main limitation of this study is that it relies on the primary and secondary data of existing
494 studies. The patients sampled in one of the studies only included patients with CAS waiting
495 for operation (27); whereas, the other three studies included patients on best medical
496 therapy for CAS as well as patients waiting for preventive surgery and patients following their
497 operation. Furthermore, the included studies beside investigating aspects of HRQOL also
498 examined issues such as decision making about management that were not related to
499 HRQoL. Additionally, few patients who were treated with best medical therapy or turned
500 down for revascularisation were included in any of the studies. The included papers did not
501 distinguish clearly between patients with resolved stroke symptoms and TIA. Some papers
502 mentioned important themes such as denial of diagnosis and depression but failed to report
503 any primary evidence to support these themes **(27, 28)**.

504

505 Amongst some clinical academic circles HRQoL has confusingly come to be known as
506 anything which is not clinical (30). However, this study demonstrates that patients with CAS
507 experience distress related to diagnosis and the risks associated with the intervention.
508 These have an adverse impact on their wellbeing and should be taken into consideration by
509 the clinician. The review identified anxiety to be an important domain that impacts the
510 HRQoL of patients with CAS and this is related to fear of stroke, uncertainty about future,
511 fear of becoming a burden on others and fear of operation. Carotid artery disease also had
512 an impact of on the patient independence, the personal functioning and beyond anxiety had
513 a further psychological effect on patients.
514 This systematic review of the qualitative evidence combine all the relevant data concerning
515 the impact of CAS and its treatments on the patients. One of the strongest finding of this
516 study is that none of the generic and disease specific PROMs covered all the important
517 issues for CAS patients revealed by this qualitative systematic review.

518 **Conclusions**

519

520 The identified themes that impact the HRQoL of patients with CAS can be used to develop a
521 disease-specific PROM. Our group designed this instrument and currently validating this
522 PROM in an extensive survey of patients with CAS. The aim is to perform a factor analysis
523 as well as further psychometric studies to ensure the PROM's validity, reliability, and
524 responsiveness.

525

526 **“Data Availability Statement”**

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

532 **Compliance with Ethical Standards**

533 **Acknowledgment**

534

535 Ahmed Aber contributed to the analysis and interpretation of data, drafting of the manuscript,
536 and critical revision; Aoife Howard contributed to the analysis and interpretation of data and
537 drafting of the manuscript; Helen Buckley Woods performed the searches for the systematic
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541

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547 **Conflict of interest**

548

549 Ahmed Aber, Aoife Howard, Helen Buckley Woods, Georgina Jones, Jonathan Michaels
550 have no conflicts of interest directly relevant to the content of this article.

551

552 **Abbreviations**

553

554 CASP: Critical Appraisal Skills Program, CREST: Carotid revascularisation Endarterectomy
555 vs. Stenting Trial, DHI: Dizziness Handicap Inventory, HADS: Hospital Anxiety and
556 Depression Scale, EQ5D: EuroQoL-5D, SF-36®: Medical outcomes study 36-item short
557 form, CAS: Carotid artery stenosis, CEA: carotid endarterectomy, PROMs: patient reported
558 outcome measures, HRQOL: health-related quality of life, PRISMA: Preferred Reporting
559 Items for Systematic Reviews and Meta-Analyses, TIA: transient ischaemic attack, Carotid
560 Stenosis Specific Outcome Measure (CSSOM).

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